SPECIAL REPORT 17

HEALTH EFFECTS INSTITUTE

January 2010

PRESS VERSION
January 12, 2010

Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects

HEI Panel on the Health Effects of Traffic-Related Air Pollution

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Special Report 17
Health Effects Institute
Boston, Massachusetts

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Publishing history: The Web version of this document was posted at *www.healtheffects.org* in January 2010.

Citation for document:

HEI Panel on the Health Effects of Traffic-Related Air Pollution. 2010. Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects. HEI Special Report 17. Health Effects Institute, Boston, MA.

This report was produced with partial funding by the United States Environmental Protection Agency under Assistance Award CR– 83234701 to the Health Effects Institute; however, it has not been subjected to the Agency's peer and administrative review and therefore may not necessarily reflect the views of the Agency, and no official endorsement by it should be inferred. The contents of this document also have not been reviewed by private party institutions, including those that support the Health Effects Institute; therefore, it may not reflect the views or policies of these parties, and no endorsement by them should be inferred.

 Cameographics, Belfast, Me., Compositor. Printed by Recycled Paper Printing, Boston, Mass. Library of Congress Catalog Number for the HEI Report Series: WA 754 R432.

Cover paper: made with at least 55% recycled content, of which at least 30% is post-consumer waste; free of acid and elemental chlorine. Text paper: made with 100% post-consumer waste recycled content; acid free; no chlorine used in processing. The book is printed with soy-based inks and is of permanent archival quality.

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ABOUT HEI

The Health Effects Institute is a nonprofit corporation chartered in 1980 as an independent research organization to provide high-quality, impartial, and relevant science on the effects of air pollution on health. To accomplish its mission, the institute

- Identifies the highest-priority areas for health effects research;
- Competitively funds and oversees research projects;
- Provides intensive independent review of HEI-supported studies and related research;
- Integrates HEI's research results with those of other institutions into broader evaluations; and
- Communicates the results of HEI research and analyses to public and private decision makers.

HEI receives half of its core funds from the U.S. Environmental Protection Agency and half from the worldwide motor vehicle industry. Frequently, other public and private organizations in the United States and around the world also support major projects or certain research programs. Additional work for this report was funded by the U.S. Federal Highway Administration.

HEI has funded more than 280 research projects in North America, Europe, Asia, and Latin America, the results of which have informed decisions regarding carbon monoxide, air toxics, nitrogen oxides, diesel exhaust, ozone, particulate matter, and other pollutants. These results have appeared in the peer-reviewed literature and in more than 200 comprehensive reports published by HEI.

HEI's independent Board of Directors consists of leaders in science and policy who are committed to fostering the public–private partnership that is central to the organization. The Health Research Committee solicits input from HEI sponsors and other stakeholders and works with scientific staff to develop a Five-Year Strategic Plan, select research projects for funding, and oversee their conduct. The Health Review Committee, which has no role in selecting or overseeing studies, works with staff to evaluate and interpret the results of funded studies and related research.

All project results and accompanying comments by the Health Review Committee are widely disseminated through HEI's Web site (*www.healtheffects.org*), printed reports, newsletters, and other publications, annual conferences, and presentations to legislative bodies and public agencies.

EXECUTIVE SUMMARY

INTRODUCTION

Motor vehicles are a significant source of urban air pollution and are increasingly important contributors of anthropogenic carbon dioxide and other greenhouse gases. As awareness of the potential health effects of air pollutants has grown, many countries have implemented more stringent emissions controls and made steady progress in reducing the emissions from motor vehicles and improving air quality. However, the rapid growth of the world's motor-vehicle fleet due to population growth and economic improvement, the expansion of metropolitan areas, and the increasing dependence on motor vehicles because of changes in land use has resulted in an increase in the fraction of the population living and working in close proximity to busy highways and roads — counteracting to some extent the expected benefits of pollution-control regulations and technologies.

This Special Report, developed by the Health Effects Institute (HEI) Panel on the Health Effects of Traffic-Related Air Pollution, summarizes and synthesizes information linking emissions from, exposures to, and health effects of traffic sources (i.e., motor vehicles). The term *traffic-related exposure* is used in this report to refer to exposure to primary emissions from motor vehicles, not to the more broadly dispersed secondary pollutants such as ozone (O_3) that are derived from these emissions. The report focuses on specific scenarios with a high aggregation of motor vehicles and people — that is, urban settings and residences in proximity to busy roadways.

EMISSIONS FROM MOTOR VEHICLES

Motor vehicles emit large quantities of carbon dioxide (CO_2), carbon monoxide (CO), hydrocarbons (HC), nitrogen oxides (NO_x), particulate matter (PM), and substances known as mobile-source air toxics (MSATs), such as benzene, formaldehyde, acetaldehyde, 1,3-butadiene, and lead (where leaded gasoline is still in use). Each of these, along with secondary by-products, such as ozone and secondary aerosols (e.g., nitrates and inorganic and organic acids), can cause adverse effects on health and the environment. Pollutants from vehicle emissions are related to vehicle type (e.g., light- or heavy-duty vehicles) and age, operating and maintenance conditions, exhaust treatment, type and quality of fuel, wear of parts (e.g., tires and brakes), and engine lubricants used. Concerns about the health effects of motor-vehicle combustion emissions have led to the introduction of regulations and innovative pollution-control approaches throughout the world that have resulted in a considerable reduction of exhaust emissions, particularly in developed countries. These reductions have been achieved through a comprehensive strategy that typically involves emissions standards, cleaner fuels, and vehicle-inspection programs. Recognizing the likely continued growth in the vehicle fleet and the remaining problems in traffic-related air quality, the United States, European countries, Japan, and other countries are continuing to push for even stricter emissions controls in coming years.

Resuspended road dust, tire wear, and brake wear are sources of noncombustion PM emissions from motor vehicles. As emissions controls for exhaust PM become more widespread, emissions from noncombustion sources will make up a larger proportion of vehicle emissions. Noncombustion emissions contain chemical compounds, such as trace metals and organics, that might contribute to human health effects. However, current estimates of these emissions are highly uncertain. Thus, although they are not regulated in the way exhaust emissions are, noncombustion emissions will need to be considered more closely in future assessments of the impact of motor vehicles on human health.

The quantification of motor-vehicle emissions is critical in estimating their impact on local air quality and traffic-related exposures and requires the collection of travel-activity data over space and time and the development of emissions inventories. Emissions inventories are developed based on

complex emissions models (of which the U.S. Environmental Protection Agency's MOBILE6 has been the most widely used) that provide exhaust and evaporative emissions rates for total HC, CO, NO_x, PM, sulfur dioxide (SO_2), ammonia (NH_3), selected air toxics, and green house gases (GHGs) for specific vehicle types and fuels. The quality of the travel-activity data (such as vehicle-miles traveled, number of trips, and types of vehicles) and the complex algorithms used to derive the emissions factors suggest the presence of substantial uncertainties and limitations in the resulting emissions estimates (NARSTO 2005). It should be noted that estimates of PM emissions have had very limited field valuation and verification.

The actual measurement of motor-vehicle emissions is critically important for validating the emissions models. Studies that have sampled the exhaust of moving vehicles in real-world situations (specifically, in tunnels or on roadways) have contributed very useful information about the emissions rates of the current motor-vehicle fleet and also have allowed the evaluation of the impact of new emission-control technologies and fuels on emissions.

Receptor models have been used to estimate the contributions of various types of sources, including motor vehicles, to ambient air pollution. Some of the models (those defined as *chemical mass balance models*) require the knowledge of the chemical profile of both the emissions of all the area sources and the air at the receptor (that is, the impacted location). Other models (referred to as *principal components and factors analyses*) do not require a priori knowledge of the source profiles. The application of these models has yielded a wide range of results on the contribution of motor vehicles to ambient pollution, depending on the model, the location of the monitoring sites, and the other sources present. In U.S. cities, the results show that motor-vehicle contributions range from 5% in Pittsburgh, Pa., under conditions with very high secondary aerosol, to 49% in Phoenix, Ariz., and 55% in Los Angeles, Calif. Outside the United States, estimates of the motor-vehicle contribution to $PM_{2.5}$ ($PM \leq 2.5$ μm in aerodynamic diameter) range from 6% in Beijing, China, to 53% in Barcelona, Spain.

Ultimately, an important goal of emissions-characterization studies is to improve our ability to quantify human exposure to emissions from motor vehicles, especially in locations with high concentrations of vehicles and people. Such characterization requires improving emissions inventories and a more complete understanding of the chemical and physical transformations on and near roadways that can produce toxic gaseous, semivolatile, and particle-phase chemical constituents.

ASSESSMENT OF EXPOSURE TO TRAFFIC-RELATED AIR POLLUTION

Traffic-related emissions contribute to primary and secondary local, urban, and regional (background) pollutant concentrations against a background of similar contaminants emitted from other sources. Traffic emissions are the principal source of intra-urban variation in the concentrations of air pollutants in many cities; thus, population-oriented central monitors cannot by themselves capture this spatial variability. Studies that have examined gradients in pollutants as a function of distance from busy roadways have indicated exposure zones for traffic-related air pollution in the range of 50 to 1500 m from highways and major roads, depending on the pollutant and the meteorologic conditions.

Because it is not practical or feasible to measure all the components of the traffic-pollutant mix, surrogates of traffic-related pollution have been used as a reasonable compromise for assessing the contribution of traffic emissions to ambient air pollution and for estimating traffic exposure. Surrogates can also help in the assessment of spatial and temporal distributions of ambient pollution related to motor vehicles and of traffic-mitigation control strategies.

Two broad categories of surrogates have been used in epidemiology studies to estimate traffic exposure: (1) measured or modeled concentrations of pollutant surrogates and (2) direct measures of traffic itself (such as proximity, or distance, of the residence to the nearest road and traffic volume within buffers). The most commonly used traffic-pollutant surrogates include CO, NO_2, elemental carbon (EC; or black carbon [BC] or black smoke [BS]), PM, benzene, and ultrafine particles (UFP). Exposure models include geostatistical interpolation, land-use regression, dispersion, and hybrid models (the latter combine time–activity data, personal measurements, and models). They incorporate numerous parameters (such as meteorologic variables, data on land use, traffic data, and monitoring data or emissions rates depending on the model) and can improve the spatial representation of the local impact of traffic against a background of regional and urban concentrations. However, the accuracy of the inputs is critical to the usefulness of any given model.

None of the pollutant surrogates considered in the report met all the criteria for an ideal surrogate. Data are not available to assess the ratios of the surrogates to emissions from all sources over time. CO, benzene, and NO_x (in this case NO_2), found in on-road vehicle emissions, are components of emissions from all sources, making it difficult to disentangle the

contributions from motor vehicles from other sources (including some in indoor environments). Primary, on-road vehicle emissions of PM ($PM_{2.5}$ or PM_{10} [PM ≤ 10 μm in aerodynamic diameter]) represent only a small contribution to emissions from all sources, typically around 3%. EC has been used as a surrogate, primarily for diesel exhaust, although it is not a specific marker, unless other sources are ruled out. UFP concentrations are very high in vehicle-exhaust plumes but decrease rapidly with distance from the source, which poses a significant challenge for characterization of the spatial and temporal concentration gradients of UFP from roadway traffic.

With regard to exposure models, the Panel noted that, although proximity models (direct measures of traffic) are the easiest to implement, they are error prone because they ignore the parameters that affect the dispersion and physicochemical activity of the pollutants. Moreover, estimates based on proximity can be confounded by factors such as socioeconomic status and noise. Geostatistical interpolation models are best implemented in conjunction with dense, well-distributed monitoring networks; their chief limitations are the size of the network and the number of measurements needed over time to estimate the spatial distribution of pollution surrogates accurately. Land-use regression is appealing in that it can account for the diversity of sources that contribute to a surrogate; however, the true contribution (in terms of associated variance) of traffic to the regression is not always known or reported. Dispersion models utilize motor-vehicle–emissions and air-quality data and incorporate meteorologic data, but must be calibrated correctly to realize their advantages. These models are very data- and computation-intensive and depend on the validity of the model assumptions. Hybrid models that combine measurements of personal exposure to traffic surrogates or time–activity data with exposure models come closest to a logistically feasible "best" estimate of human exposure.

Factors influencing ambient concentrations of a traffic-pollutant surrogate are related to time–activity patterns, meteorologic conditions, vehicle volume and type, driving patterns, land-use patterns, the rate at which chemical transformations take place, and the degree to which the temporal and spatial distribution of the surrogate reflects the traffic source.

To improve assessment of exposure to traffic-related pollution, a potential solution is the deployment of a large number of monitors in places where concentrations of air pollutants are expected to be highly variable and the population density is high. The use of models that incorporate numerous spatial factors in order to estimate exposures that are more relevant to the individual's exposure situation can also be helpful.

The Panel concluded that the impact of vehicle emissions extends beyond the local scale to the urban and regional scales. What people are exposed to is influenced by their proximity to the sources, the presence of other ambient or microenvironmental sources, and time–activity patterns. If, as the evidence suggests, groups of lower socioeconomic status experience higher exposures than groups of higher socioeconomic status, this merits consideration in the interpretation of epidemiologic findings and in future regulatory actions.

Based on a synthesis of the best available evidence, the Panel identified an exposure zone within a range of up to 300 to 500 m from a highway or a major road as the area most highly affected by traffic emissions (the range reflects the variable influence of background pollution concentrations, meteorologic conditions, and season) and estimated that 30% to 45% of people living in large North American cities live within such zones.

HEALTH EFFECTS OF TRAFFIC-RELATED AIR POLLUTION: EPIDEMIOLOGY AND TOXICOLOGY

In reviewing the epidemiologic literature on the association between exposure to traffic-related air pollution and health outcomes, the Panel developed criteria for the inclusion of studies based on the characterization of traffic exposure. The Panel decided to include only studies that investigated associations between primary emissions from traffic and human health and that provided specific documentation of a traffic source and estimates of exposure on a local scale. Thus, studies that relied exclusively on measurements from a central monitoring site were not included unless the site was in proximity to traffic. The Panel also developed criteria for inferring whether associations between exposure and health outcome were causal by adapting the criteria used by the U.S. Surgeon General in the report *The Health Consequences of Smoking: A Report of the Surgeon General* (U.S. Department of Health and Human Services 2004). In order to deem the evidence sufficient to conclude that association between a metric of traffic exposure and an outcome was causal, it was necessary for the magnitude and direction of the effect estimates to be consistent across different populations and times and to rule out with reasonable confidence chance, bias in subject selection, and confounding (in particular, socioeconomic status). The four inference criteria applied to this review are listed in Table 1. To these criteria the Panel added a traffic-specific coherence criterion (also included in Table 1) to account for the degree of validity of the traffic-specific exposure metrics. As noted earlier, the Panel concluded that

not all traffic-exposure measures have equivalent validity and considered simple measures of proximity to roads or road length and of pollutant surrogates without specific traffic data to be the least specific. The proximity measures are also likely to introduce confounding.

Modeled estimates of exposure to traffic pollution were thought to be, a priori, more valid than traffic density estimates alone because they account for other factors that affect the exposure, such as geography, land use, and meteorology, when making estimates for particular locations. In addition, the validity of estimates can be enhanced by modeling strategies that separately estimate the contribution of traffic and background pollution to personal exposure.

The Panel developed qualitative and quantitative summaries (in tables and figures) for the estimates of the associations between traffic-related exposure and various health outcomes for the studies reviewed, but did not derive meta-analytic summaries by pooling associations estimates because of the lack of equivalence among the exposure measures and populations studied.

The Panel also reviewed the literature on the toxicology of traffic-related pollution. This included studies of direct exposures to traffic emissions (though there were very few in this category), studies that utilized laboratory atmospheres that replicate aspects of the traffic mix (such as concentrated ambient particles, or gasoline or diesel exhaust), and studies of specific components of emissions from motor vehicles. The aim was to identify possible mechanisms by which exposure to traffic pollutants may cause effects and provide an understanding of the role of traffic emissions in the effects being observed in epidemiology studies. While toxicology studies are limited in their ability to capture the full complexity of human exposure — because of the small number of subjects and, in animal studies, the relevance of the results to humans — they offer the opportunity to explore hypotheses on specific pathophysiologic mechanisms of action.

The Panel evaluated whether oxidative stress might be the underlying mechanism of action by which exposure to pollutants from traffic may lead to adverse health effects. Oxidative stress results from events occurring in any tissue in the body when the prooxidant–antioxidant balance is disturbed. This imbalance can happen when the generation of reactive oxygen species, or *free radicals*, exceeds the available antioxidant defenses and is characterized by the presence of increased cellular concentrations of oxidized lipids, proteins, and DNA. Oxidative stress can trigger inflammatory reactions, which lead to an increased production of oxidants by activated phagocytes recruited to the airways, perpetuating the cycle of oxidative injury.

The Panel concluded that, although the evidence supported the hypothesis that oxidative stress is an important determinant of health effects associated with ambient air pollution in general, the extent to which primary traffic-related pollutants contribute to the burden of reactive oxygen species experienced by humans near roadways remains undefined.

The Panel's main conclusions regarding the epidemiologic associations between exposure to traffic-related air pollution and health outcomes and the toxicologic evidence (when available) are presented below for each health outcome. A discussion of the extent to which toxicology studies do or do not provide general mechanistic support for the observations and inferences contributed by epidemiology studies is also provided.

ALL-CAUSE AND CARDIOVASCULAR MORTALITY

Epidemiology

Very few studies of all-cause mortality or cardiovascular mortality and long-term exposure met the criteria for inclusion in the report. Mostly because of the small number of studies, the evidence for an association of all-cause mortality with long-term exposure was classified as "suggestive but not sufficient" to infer a causal association. Additional factors that led to this classification were the substantial differences among populations, time periods, and confounders across studies.

Only four time-series studies of all-cause mortality associated with short-term exposure met the Panel's criteria; these, too, were classified as "suggestive but not sufficient," largely on the strength of one well-done study (Maynard et al. 2007). Two time-series studies based on source-apportionment models were found to have a number of limitations that prevented a stronger statement about inferred causality.

Many of the issues that applied to studies of all-cause mortality applied as well to studies of cardiovascular mortality associated with long-term exposure and led, similarly, to a classification of "suggestive but not sufficient." Only two time-series studies of cardiovascular mortality met the inclusion criteria, and although they both show positive associations, the Panel concluded that, given the overall paucity of studies, the evidence for effects of short-term exposure was "inadequate and insufficient."

CARDIOVASCULAR MORBIDITY

Epidemiology

Studies that documented changes in cardiac physiology (such as heart-rate variability) after short-term exposure to traffic-related pollution (which was assessed using surrogates,

Executive Summary Table 1. Criteria for Assessing the Presence or Absence of Causal Associations in Studies of the Health Effects of Traffic-Related Air Pollution[a,b]

A. *Sufficient Evidence to Infer the Presence of a Causal Association*

The evidence was deemed sufficient to conclude that an association observed between a metric of traffic exposure and a disease (or biomarker of disease) risk was causal in studies where chance, bias, and confounding could be ruled out with reasonable confidence, and the effect estimates were consistent in magnitude and direction.

Traffic-specific criterion. Classification A was applied:

When all studies were of the appropriate quality, at least one study measured traffic density or modeled traffic exposure[c], measures of socioeconomic status were taken into account in distance-only studies, and the studies' results were consistent.

B. *Suggestive but Not Sufficient Evidence to Infer the Presence of a Causal Association*

The evidence was deemed suggestive but not sufficient to conclude that an association between a metric of traffic exposure and a specific disease (or biomarker of disease) risk was causal in studies where chance, bias, and confounding could not be ruled out with reasonable confidence.

Traffic-specific criterion. Classification B was applied:

When all the criteria for Classification A were met except that only studies that used distance-based metrics were available

OR

When all the criteria for Classification A were met except that not all the studies that used distance-only metrics took into account measures of socioeconomic status or the studies took into account measures of socioeconomic status but the results were not consistent.

C. *Inadequate and Insufficient Evidence to Infer the Presence or Absence of a Causal Association*

The evidence was deemed inadequate and insufficient when the available studies were of insufficient quality, consistency, or statistical power to conclude whether a causal association was present or absent.

Traffic-specific criterion. Classification C was applied:

When the results from studies that used distance-only metrics were not consistent

OR

When the results of all studies using distance-only metrics were consistent but all those studies failed to include measures of socioeconomic status

OR

When the results from at least one study based on traffic density or modeled traffic exposure were inconsistent with those from distance-only studies

OR

When the number of distance-only studies was too small.

D. *Evidence Suggestive of No Causal Association*

The evidence was deemed suggestive of no causal association when there were several adequate studies, covering the full range of human exposure levels, that were consistent in not showing a positive association, at any level of exposure, between exposure to a metric of traffic exposure and a disease outcome. (Of course, a conclusion of "no association" is inevitably limited to the conditions, level of exposure, and length of observation covered by the available studies. In addition, the possibility of a very small elevation in risk at the levels of exposure studied cannot be excluded.)

Traffic-specific criterion. Classification D was applied:

When studies were of adequate quality (using distance-only metrics or at least some measures of traffic density or modeled traffic exposure) and were consistent in failing to find an association.

[a] The Panel did not use exposure–response gradations as a criterion because, in virtually all epidemiologic studies, it is difficult to infer meaningful exposure–response gradations from the types of exposure metrics used or the forms of data presented.

[b] This table was adapted from Tables 4.2a and 4.2.b in Chapter 4.

[c] In some cases, this criterion was met when modeling or source-apportionment data were cited to show that a pollution surrogate in the study was reasonably accurate in representing the traffic sources in the study area.

source apportionment, or pseudo-personal monitoring) provided strong evidence for a causal association with the exposure. However, the failure of some studies to consider stress and noise as potential confounders led the Panel to classify them as "suggestive but not sufficient" to infer a casual association. Among the studies that evaluated cardiovascular morbidity, two well-executed studies on hospitalization for acute myocardial infarction were identified (Rosenlund et al. 2006; Tonne et al. 2007). In addition, a prospective study in a German cohort reported an association between living near a major road and coronary-artery calcification as well as higher prevalence of coronary heart disease (Hoffmann et al. 2006, 2007). Collectively, these studies made a very strong case for an association between exposure to traffic-related pollutants and atherosclerosis. However, because of the small number of studies, the Panel classified them as "suggestive but not sufficient" to infer a causal association.

Toxicology

There have been a few toxicology studies that examined the cardiovascular effects of traffic emissions specifically. However, the Panel concluded that the recent toxicology literature provides suggestive evidence that exposure to pollutants that are components of traffic emissions, including ambient and laboratory-generated PM and exhaust from diesel and gasoline-fueled engines, alters cardiovascular function. There is also evidence, albeit inconsistent, for acute effects on vascular homeostasis and suggestive evidence in animal models that repeated exposures to ambient PM in general enhance the development of atherosclerosis. Some studies support the involvement of oxidative stress. Although the evidence from toxicology studies in isolation is not sufficient in terms of a causal association between traffic emissions and the incidence or progression of cardiovascular disease, when viewed together with the epidemiologic evidence, a stronger case could be made for a potential causal role for traffic-related pollutants in cardiovascular-disease morbidity and mortality. The extent to which these associations apply to individuals without underlying cardiovascular disease cannot be determined from the evidence available at this time.

ASTHMA AND RESPIRATORY SYMPTOMS

Asthma is an inflammatory disease of the lung airways characterized by episodic obstruction of the airways, which can lead to chronic obstructive lung disease. The most prevalent form of asthma in children and young adults is allergic asthma, which develops as an immune response to inhaled allergens. Individuals with asthma and other allergic conditions who have an increased tendency to develop immediate and localized reactions to allergens (such as pollens) that are mediated by immunoglobulin E (IgE) are referred to as "atopic."

Epidemiology

In epidemiology studies, asthma is most frequently identified by means of responses to questionnaires that do not make use of a single, universally accepted set of questions, alone or in combination with other criteria. This is further complicated by the challenges of distinguishing factors that affect its onset from those (often the same factors) that lead to its episodic worsening. A history of asthma symptoms (such a wheezing) often is used in epidemiology studies as part of the definition both of asthma's onset (incidence) and of its prevalence and exacerbation.

Respiratory Health Problems in Children: Asthma Incidence and Prevalence Seven studies conducted in four separate cohorts and one case-control study qualified as studies of asthma incidence in children. Eleven studies qualified as studies of asthma prevalence in children. From these studies, the Panel concluded that living close to busy roads appears to be an independent risk factor for the onset of childhood asthma. The Panel considered the evidence for a causal relation to be in a gray zone between "sufficient" and "suggestive but not sufficient." The results found across the studies followed a pattern that would be expected under the plausible assumption that the pollutants really are causally associated with asthma development, if only among a subset of children with some accompanying pattern of endogenous or exogenous susceptibility factors. The conditions that underlie an increased risk for asthma development among children exposed to traffic-related pollutants are not known.

Exacerbation of Symptoms in Children with and without Asthma and Health-Care Utilization for Respiratory Problems Among the more than 20 cohort and cross-sectional studies reviewed that examined the association between exposure to traffic-related pollution and wheezing (an important symptom in the expression and diagnosis of asthma) in children, there was a high degree of consistency in finding positive associations, many of which reached statistical significance (i.e., had reasonably precise point estimates of associations). This was true particularly for the large majority of studies that used models to assign estimates of local concentrations of pollutants, such as NO_2 or soot (the carbonaceous component of PM), to the place of residence of the study participants. Studies based on proximity or traffic density also indicated an association between exposure and wheezing. In addition, exacerbation

of other asthma-related symptoms, such as cough or dry cough, was consistently associated with exposure across a variety of exposure measures. Although most studies were not restricted to children with asthma, all these symptoms were more prevalent among those with asthma, and it is very likely that the observed associations were driven by exacerbations of asthma in mixed groups of participants. The Panel concluded that the evidence is "sufficient" to infer a causal association between traffic exposure and exacerbations of asthma but that it is "inadequate and insufficient" to infer a causal association between exposure and respiratory symptoms in children without asthma.

Nine studies assessed the association between exposure to traffic-related pollution and the use of health-care services to treat respiratory problems in children. Most of the studies reported positive associations between exposure and hospital-admission rates, but the majority had methodologic problems that hampered their interpretation. The panel concluded that there is "inadequate and insufficient" evidence to infer a causal association.

Respiratory Health Problems in Adults: Asthma Onset and Respiratory Symptoms The Panel noted that the evidence between exposure to traffic-related pollution and new adult asthma was "inadequate and insufficient" as this was investigated in only one study (Modig et al. 2006). The Panel reviewed 17 studies on respiratory symptoms, of which all but one relied on proximity to roads or traffic-density measures, and concluded that the evidence for a causal association is "suggestive but not sufficient."

Toxicology

The few human studies in which subjects were exposed to realistic traffic conditions (a road tunnel or busy street) are supportive of the possibility that persons with asthma may be more susceptible to adverse health effects (such as decrements in lung function and enhanced responses to allergens) related to such exposure. The Panel's evaluation of the toxicologic data on the respiratory system regarding the effects of components of traffic-related air pollution was that such exposures result in mild acute inflammatory responses in healthy individuals and enhanced allergic responses in allergic asthmatics and animal models.

When the epidemiologic and toxicologic data were viewed together, the Panel noted that a case could be made that there are likely to be causal associations related to exposure to traffic-related air pollution and asthma exacerbation and some other respiratory symptoms. However, given the lack of a large body of toxicologic data based on human and animal exposures to real-world traffic scenarios, the Panel noted that it was hazardous to conclude that causality has been established at this time for all respiratory symptoms at all ages.

LUNG FUNCTION AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Changes in lung function are considered reliable markers of health that reflect the effects of endogenous and cumulative exposure to exogenous factors that might have adverse health consequences. Reduced lung function is strongly associated with future morbidity from a variety of causes and is a predictor of life expectancy (Hole et al. 1996); however, the relevance to health of small, short-term changes has not been assessed. The Panel considered lung function and chronic obstructive pulmonary disease (COPD) together in this review, because the principal criterion for the diagnosis of COPD is based on lung-function measures.

Epidemiology

Lung Function in Children and Adults The studies reviewed were heterogeneous in their design, approach to exposure assessment, and lung-function measures. Given their limited comparability, the Panel concluded that the evidence is "suggestive but not sufficient" to infer a causal association between short- and long-term exposure to traffic-related pollution and decrements in lung function. However, in the case of long-term exposure, there was some coherence in the data, suggesting that (1) long-term exposure is associated with changes in lung function in adolescents and young adults; (2) lung-function measures are lower in people who live in more polluted areas; and (3) changing residence to a less-polluted area in one study is associated with improvements in lung function (Burr et al. 2004). The first and second points are consistent with longer-lasting effects on lung structure and/or function. The third point can be interpreted to indicate that some component of the apparent effects on lung function is reversible or is more the result of short-term exposure.

Chronic Obstructive Pulmonary Disease Because only two of the COPD studies fulfilled the criteria for inclusion in the review and their results were not consistent, the Panel concluded that there is "inadequate and insufficient" evidence for causal associations between exposure to traffic pollution and COPD.

Toxicology

A very limited database of controlled human exposure has shown short-term reductions in forced expiratory volume in 1 second (FEV_1) and increases in inflammation

with exposure to traffic-related air pollution. However, the two end points have not been associated with each other. Virtually no data are available from animal models. There are no studies of traffic-related air pollution and COPD.

While the epidemiology studies do provide suggestive evidence for chronic exposure effects on lung function in adolescents and young adults, there are too few toxicologic data to indicate what mechanisms underlie these observations. The aggregate epidemiologic and toxicologic evidence on chronic exposure to traffic-related air pollution and altered lung function in older adults and the occurrence of COPD is too sparse to permit any inference with respect to causal association.

ALLERGY

Epidemiology

The 16 epidemiology studies on this outcome included in the review not only had to meet criteria for the quality of their exposure data but also had to report at least one of the following: (1) positive skin-prick testing for common aeroallergens; (2) serum-specific IgE to common aeroallergens; (3) a physician's diagnosis of eczema or allergic rhinitis; or (4) use of questionnaires on the history of symptoms of hay fever, seasonal runny nose, rhinitis or conjunctivitis, or itchy eyes. With a few inconsistent exceptions, results based on the skin-prick test reactivity or allergen-specific IgE failed to show associations with any of the traffic-exposure surrogates. Inconsistent results with self-reported symptoms were also noted. The Panel concluded that there is "inadequate and insufficient" evidence to infer a causal association, or even a noncausal association, between exposure to traffic-related pollution and IgE-mediated allergies. Overall, the lack of consistency across epidemiology studies might have reflected a failure to identify susceptible subgroups.

Toxicology

The Panel noted that the toxicology data provide strong mechanistic evidence with respect to the diesel particle component of traffic-generated pollution and IgE-mediated allergic reactions and some evidence for NO_2 and late-phase response to allergen. However, the epidemiology studies were inconsistent. The relevance of the toxicology studies (often by nasal instillation with diesel exhaust particles) to the actual manifestations of non-asthmatic allergic phenotypes (e.g., allergic rhinitis or conjunctivitis, eczema, serum-specific IgE, and evidence of sensitization to aeroallergens) could not be determined.

BIRTH OUTCOMES

Epidemiology

Although a considerable body of data from around the world has identified consistent associations between exposure to ambient air pollution in general and various birth-outcome measures (low birth weight, small for gestational age, and perinatal mortality), only four studies of exposure to traffic-related pollution met the criteria for inclusion in this review. The small number of studies and their limited geographic coverage led the Panel to conclude that there is "inadequate and insufficient" evidence to infer causality.

Toxicology

The toxicology studies reported effects on reproductive organs and sperm functionality in animals, but these outcomes were not evaluated in the epidemiology studies. Among the challenges in interpreting these results are the data limitations and the almost-universal use of very high exposure concentrations that have questionable relevance to actual ambient concentrations. Due to their lack of overlap, the epidemiology and toxicology studies on reproductive health and birth outcomes do not lend themselves to any overall synthesis.

CANCER

Epidemiology

The Panel focused on general-population exposure studies and did not review the extensive epidemiologic literature on cancer from occupational exposure to traffic emission constituents (e.g., benzene and diesel exhaust). Among the studies reviewed, five were of childhood cancers (mainly leukemias, lymphomas, and cancers of the central nervous system), and four of adult cancers (two of lung cancer, one of female breast cancer, and one of several cancers combined). Data on childhood cancers were inconclusive in terms of overall consistency and of specific cancers. Too few data were available in adults. Overall the Panel concluded that the evidence was "inadequate and insufficient" to make inferences for causality between exposure to traffic pollution and cancer.

Toxicology

The toxicologic research summarized included in vitro mutagenicity studies of exposure of cells to PM from traffic pollution, diesel or biodiesel exhaust, and organic components of some of these mixtures, as well as animal carcinogenicity studies after exposure to exhaust from diesel and

gasoline-fueled engines. Although studies in cells demonstrating the capacity of DEP to induce DNA-strand breaks, base oxidation, and mutagenicity provide a possible mechanism for the induction of carcinogenicity by traffic-related pollution, the applicability of in vitro mutagenicity studies to human risk assessment has been questioned. Animal studies have demonstrated the ability of high concentrations of exhaust components in both diesel and gasoline-fueled engines to cause tumors in animals. However, caution must be exercised in extrapolating these data to people exposed to much lower concentrations of pollutants, as seen in the epidemiology studies. Therefore, the Panel concluded that any statement that tries to relate the toxicologic to the epidemiologic data is premature at this time.

OVERALL CONCLUSIONS

Studies have shown that traffic-related emissions affect ambient air quality on a wide range of spatial scales, from local roadsides and urban scales to broadly regional background scales. Based on a synthesis of the best available evidence, the Panel identified an exposure zone within a range of up to 300 to 500 m from a major road as the area most highly affected by traffic emissions (the range reflects the variable influence of background pollution concentrations, meteorologic conditions, and season).

Surrogates for traffic-related exposure have played, and are likely to continue to play, a preeminent role in exposure assessments in epidemiology studies. The optimal selection of relevant surrogates (especially surrogates that are single chemicals) depends on accurate knowledge of the degree to which they represent the chemical and physical properties of the actual primary traffic-pollution mixtures to which humans are exposed, which, in turn, depends on accurate knowledge of motor-vehicle–emissions composition and near-source transformation and dispersion. The Panel concluded that none of the pollutant surrogates (CO, NO_2, UFP, EC, and benzene) is unique to emissions from motor vehicles. Among the surrogates based on traffic-exposure models, the question remains as to the extent to which the proximity model (i.e., the simple distance-to-road measures) should be employed in future epidemiology studies because it is particularly prone to yielding measures potentially containing extraneous information that can lead to the confounding of associations between health effects and exposure. In the Panel's view, the hybrid model is the current optimal method of assigning exposures to primary traffic-related pollution.

Many aspects of the epidemiologic and toxicologic evidence relating adverse human health effects to exposure to primary traffic-generated air pollution remain incomplete. However, the Panel concluded that the evidence is sufficient to support a causal relationship between exposure to traffic-related air pollution and exacerbation of asthma. It also found suggestive evidence of a causal relationship with onset of childhood asthma, nonasthma respiratory symptoms, impaired lung function, total and cardiovascular mortality, and cardiovascular morbidity, although the data are not sufficient to fully support causality. For a number of other health outcomes, there was limited evidence of associations, but the data were either inadequate or insufficient to draw firmer conclusions. The Panel's conclusions have to be considered in the context of the progress made to reduce emissions from motor vehicles. Since the epidemiology studies are based on past estimates of exposure from older vehicles, they may not provide an accurate guide to estimating health associations in the future.

In light of the large number of people residing within 300 to 500 m of major roads, the Panel concludes that the sufficient and suggestive evidence for these health outcomes indicates that exposures to traffic-related pollution are likely to be of public health concern and deserve public attention. Although policy recommendations based on these conclusions are beyond the scope of this report, the Panel has tried to organize, summarize, and discuss the primary evidence in ways that will facilitate its usefulness to policy makers in the years ahead.

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In January 2007, the Board of Directors of the Health Effects Institute (HEI) appointed an expert panel to review and critique the scientific literature on the human-health effects of exposure to emission from motor vehicles. The panel consisted of scientists from a variety of disciplines and was chaired by Ira Tager, a professor of epidemiology at the University of California–Berkeley. HEI is indebted to the panel for its expertise, cooperation, and enthusiasm. A draft of the resulting report was submitted for outside peer review.

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Traffic-Related Air Pollution

A Critical Review of the Literature on Emissions, Exposure, and Health Effects

HEI Panel on the Health Effects
of Traffic-Related Air Pollution

Chapter 1

Introduction

CONTENTS

Chapter 1

Introduction

1.I. RATIONALE

Just over 20 years ago, the Health Effects Institute (HEI) sponsored the publication of the book *Air Pollution, the Automobile, and Public Health,* edited by Watson and colleagues (1988). The book evaluated studies of exposure to air pollution from motor vehicles and of the biologic effects of this exposure. In his foreword to the book, William D. Ruckelshaus, then Administrator of the U.S. Environmental Protection Agency (U.S. EPA*), wrote that the book "should be a model for future endeavors to help quantify environmental risk as a basis for good decision making."

Since then, a substantial literature has emerged on health effects from exposure to emissions from motor vehicles especially near roadways with a high volume of traffic and large populations, on exposure estimation through monitoring and modeling, and on pollutant toxicology. In addition, major advances have been made in the biostatistical analysis of data on exposure and health. Traffic-related emissions contribute to ambient pollutant concentrations against a background of similar pollutants from other sources.

Recent estimates from the World Health Organization's (WHO) Global Burden of Disease (GBD) project on the burden of disease attributable to various risk factors have suggested that, based on the health effects associated with ambient particulate matter (PM), ambient air pollution is associated with as much as 2% of cardiorespiratory mortality, 1% of respiratory infections in children under 5 years of age, and 5% of respiratory cancers (WHO 2002). Although subject to considerable uncertainties, these analyses have led to estimates that ambient air pollution might be associated with as much as 1.4% of the global burden of premature mortality. Given that emissions from motor vehicles might contribute as much as 16% of the PM_{10} and $PM_{2.5}$ (PM with an aerodynamic diameter $\leq$ 10 μm and $\leq$ 2.5 μm, respectively) in ambient air (see Chapter 2), the global burden of mortality associated with motor-vehicle emissions is likely to be substantial. Studies based on various surrogates for exposure to air pollution from traffic have shown associations with atherosclerosis (Hoffmann et al. 2007; Künzli et al. 2005), asthma (McConnell et al. 2006), and decreased lung function (Gauderman et al. 2007). These studies highlight the potential GBD of major chronic diseases that could also be a consequence of exposure to air pollution from traffic.

As awareness of the potential health effects of air pollution from traffic has grown, many countries have mandated increasingly stringent regulations to reduce emissions from motor vehicles. As shown in Figure 1.1, U.S. regulations have resulted in reductions in the six common pollutants (carbon monoxide, nonmethane hydrocarbons, nitrogen oxides, sulfur dioxide, PM_{10}, and $PM_{2.5}$) from all U.S. combustion sources despite growth in gross domestic product, vehicle miles traveled, population, and energy consumption. Reductions in emissions specifically from transportation show similar trends (see Chapter 2).

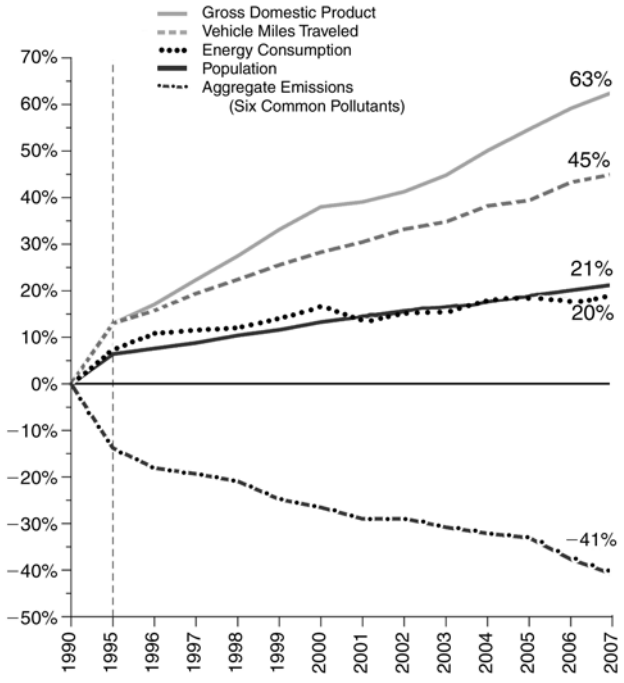

Figure 1.1. Comparison of U.S. growth measures and aggregate emissions from all sources, 1990–2007. (Adapted from U.S. Environmental Protection Agency 2008.)

* A list of abbreviations and other terms appears at the end of this chapter.

This document was produced with partial funding by the United States Environmental Protection Agency under Assistance Award CR– 83234701 to the Health Effects Institute; however, it has not been subjected to the Agency's peer and administrative review and therefore may not necessarily reflect the views of the Agency, and no official endorsement by it should be inferred. The contents of this document also have not been reviewed by private party institutions, including those that support the Health Effects Institute; therefore, it may not reflect the views or policies of these parties, and no endorsement by them should be inferred.

As modern pollution-control technologies spread to developing countries in the years ahead, they can be expected to help improve air quality in these countries as well. However, the growth of the world's motor-vehicle fleet, the rapid expansion of metropolitan areas in developing countries, and the increasing dependence on motor vehicles because of changes in land use (such as the intense development of suburban areas) have resulted in an increase in traffic congestion and in the fraction of the population living and working in close proximity to highways and roads — counteracting to some extent the expected benefits of the pollution-control regulations and technologies.

These mixed trends are likely to continue, and human exposure to air pollution from traffic will continue to be a key concern for researchers, public-health and environmental policymakers, and governments. In this context, a new critical review of the literature on air pollution from traffic and its effects on health seemed timely and warranted.

1.II. GOALS

The goals of this special report are to summarize and synthesize relevant information on air pollution from traffic and its health effects in a coherent framework that links (1) traffic emissions with ambient air pollution in general, (2) concentrations of ambient pollutants with human exposure to pollutants from traffic, (3) exposure to pollutants from traffic with human-health effects and toxicologic data, and (4) toxicologic data with epidemiologic associations. The health effects the Panel considered were disease endpoints (e.g., cardiovascular and pulmonary mortality and morbidity, and cancer) and pathophysiologic alterations that are thought to be on the pathway to future diseases (e.g., pulmonary and vascular inflammation, alteration of the immune system, alteration of the autonomic control and electrophysiology of the heart, and birth outcomes). Although its review of the literature in these areas was comprehensive, the Panel emphasized synthesis and overall coherence rather than exhaustive presentation of all the data from all the studies. Appendix A at the end of this chapter describes the search methods used to compile the bibliography that forms the basis of this report.

The report covers many, but not all, of the topics included in *Air Pollution, the Automobile, and Public Health*. Specifically, it omits many topics in pathology, pathophysiology, and dosimetry. These omissions were necessary because the body of health data available today is much larger than before and the Panel wished to include a more extensive discussion of exposure assessment in relation to the health data. The report also includes a brief review (in Chapter 2) of the atmospheric chemistry, transport, and transformation of traffic-related pollutants, because there was no other recent, comprehensive review of this topic in the literature.

The target audiences for this report are scientists interested in a detailed summary, synthesis, and critique of the relevant literature; those responsible for setting policy and writing regulations; and other affected stakeholders in industry and the general public.

1.III. ORGANIZATION

Figure 1.2 shows how the report is organized. The report's main chapters cover one or more of the topics shown in small boxes.

The report includes the following chapters:

Chapter 2: Emissions from Motor Vehicles covers the growth of the motor-vehicle fleet around the world and considers the implications for current and future emissions. Emissions by vehicle type, the quality of the available emissions databases, and the strengths and limitations of the models used to quantify emissions and derive ambient pollutant concentrations are discussed. Information on the methods used to apportion emissions to sources and to improve emissions estimates is also presented. Finally, physicochemical-transformation processes are described; and a discussion is provided on the monitoring systems needed to quantify expected rapid changes in future fleet emissions and to assess exposure for studies of human-health effects.

Chapter 3: Assessment of Exposure to Traffic-Related Air Pollution discusses issues central to the accurate assessment of the exposure of individuals and populations to air pollution from traffic. Emphasis is placed on primary emissions from traffic (rather than the secondary pollutants derived from them) and the spatial gradients over which these emissions are clearly distinguishable from background pollutant concentrations, i.e., the "zone of influence" of the health effects resulting from these emissions. Measurement of the chief surrogates for exposure to primary emissions, the effects of changes in land use on exposure, differences in exposure from population to population, and various modeling approaches are also discussed in detail.

Chapter 4: Heath Effects: Epidemiology of Traffic-Related Air Pollution reviews epidemiologic studies published from 1980 through October 2008 that have investigated associations between primary emissions from traffic

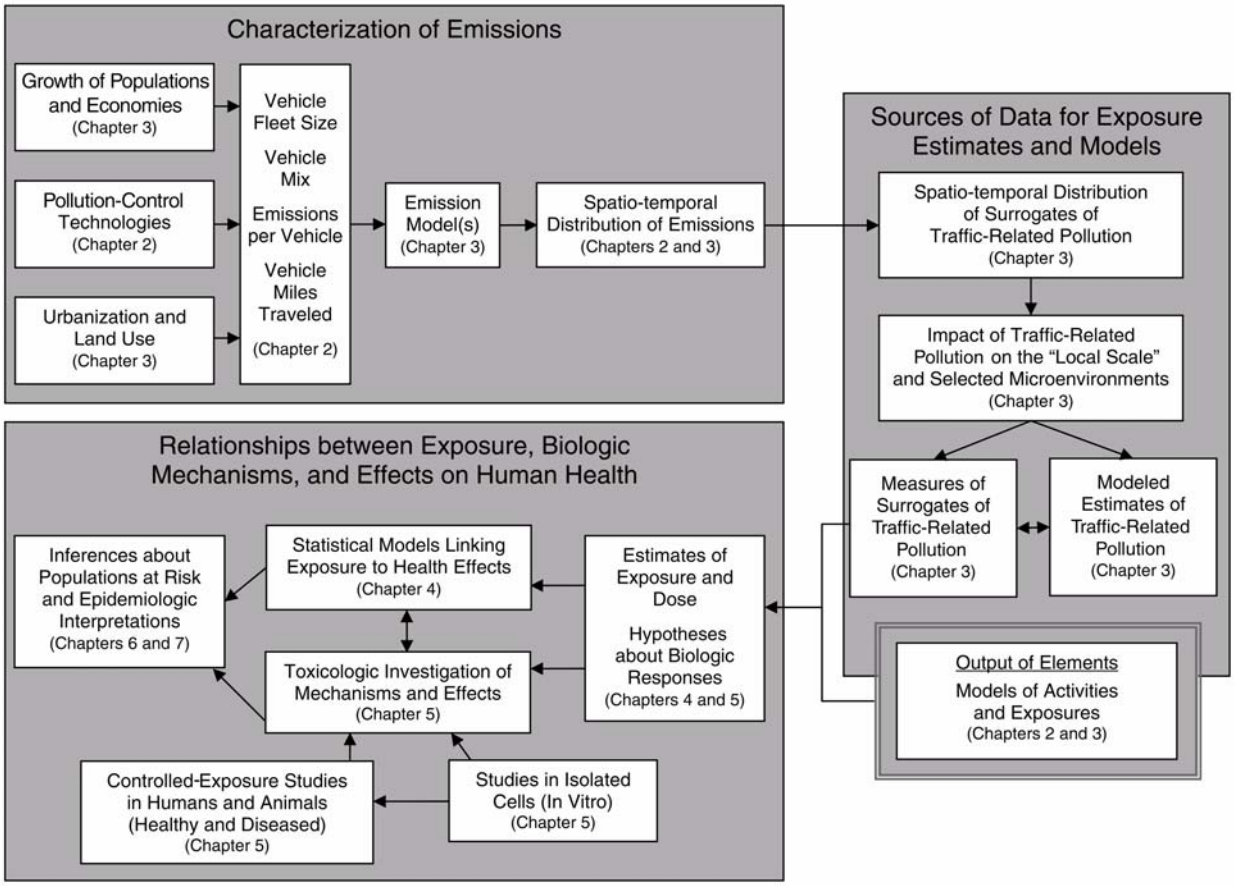

Figure 1.2 Schematic representation of the report's organization. The characterization of emissions and the factors that affect emissions are the starting points in understanding the health effects of traffic-related air pollution. Data on these are the primary inputs for the emissions models and exposure estimates used to characterize exposure. Exposure characterization is the basis of the steps that lead to scientific inferences about the relations between exposure, biologic mechanisms, and health effects. The double-headed arrows emphasize the iterative relationship between epidemiology and toxicology in formulating estimates of health effects on populations.

and human health. The studies are grouped by mortality and morbidity in relation to the principal diseases and health outcomes investigated in the literature. Causal inference and pooling of data are discussed in the context of the types of inferences that can be drawn from the data. The results from several large time-series studies, such as the National Morbidity, Mortality, and Air Pollution Study (NMMAPS) (Samet et al. 2000) and the Air Pollution and Health: A European Approach (APHEA) study (Katsouyanni et al. 1997), are not included in the chapter, because these studies did not use the type of local pollutant data needed to assess the health effects associated with primary air pollutants from traffic.

Chapter 5: Heath Effects: Toxicology of Traffic-Related Air Pollution focuses on what is known about the toxicology of primary air pollutants from traffic as they relate to the major categories of health outcomes studied in the epidemiologic literature. The chapter is exhaustive with respect to this topic but not with respect to the much larger topic of the toxicology of ambient pollutants as a whole. Controlled-human-exposure, animal, and in vitro studies are all addressed.

Chapter 6: A Synthesis of Evidence from Epidemiology and Toxicology compares information from chapters 4 and 5 to identify areas of agreement between epidemiologic and toxicologic data and to identify important gaps and discrepancies between the two in order to help improve understanding of the effects of traffic-related air pollution on human health.

Chapter 7: Conclusions brings together the conclusions from each of the preceding chapters to provide an integrated summary and synthesis of the strengths and limitations of the present state of our knowledge. Instead of making specific research recommendations, the chapter provides sufficient information to allow informed readers to identify promising areas for future research.

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APPENDIX A. SEARCH METHODS

INTRODUCTION

Online searches of the peer-reviewed literature for publications on the topics covered in this review were conducted from October 2006 through July 2007 (and subsequently updated through October 2008) using PubMed (*www.ncbi.nlm.nih.gov/pubmed/*) and Web of Science (*http://isiwebofknowledge.com/*), as described below. Relevant citations were compiled using EndNote software (version X2 for Windows).

Publications were also identified by searching bibliographies, including one developed by Marion Hoyer and Patricia Rowley of the U.S. EPA in June 2007 (personal communication) and the individual bibliographic databases of HEI panel members.

Publications were considered eligible for inclusion if they (1) were published between January 1980 and October 2008 (or were accepted for publication within this time), (2) reported on primary (original) research, and (3) were published in English.

EMISSIONS AND EXPOSURE

Searches for publications on emissions and exposures were conducted using various combinations of the following keywords: air pollution, emissions, mobile source, traffic, elemental carbon, black carbon (BC), nitrogen dioxide, particulate matter, reflectance, roadway, tunnel studies, dispersion modeling, and GIS (geographic information system).

Potentially relevant publications were identified by scanning the titles or abstracts and were combined in a single database of approximately 700 publications, for which the full text was then obtained. Publications were selected for final inclusion on the basis of the importance or representative nature of their findings and the overall quality of the publication.

EPIDEMIOLOGY

Searches for publications on epidemiology were conducted using various combinations of the following keywords: traffic, traffic related, health, pollution, nitrogen dioxide, diesel exhaust, cardiovascular, asthma, environmental epidemiology, exposure assessment, and vehicle emissions.

Potentially relevant publications were identified by scanning the titles or abstracts (and occasionally by a quick reading of the article) to eliminate publications not

focused on traffic-related air pollution, publications on health effects associated with non-ambient air pollution (such as indoor air pollution or water or soil pollution), and publications that were deemed to be primarily toxicologic (although biomarker studies were retained) or policy briefs, editorials, risk assessments, commentaries, or letters. This resulted in a list of 275 potentially eligible publications. The list was then reduced to 168 publications that specifically investigated the human-health effects of traffic-related air pollution. Additional exclusions were made on methodologic grounds, and approximately 30 studies were added after an additional literature search was conducted in October 2008, resulting in the final list of approximately 170 publications on which this portion of the review was based. Publications that investigated the adverse health effects of particulate matter (or its components) but lacked specificity about actual traffic exposure were not included.

TOXICOLOGY

Searches for publications on toxicology were conducted using various combinations of the following keywords: cancer, toxicology, carcinogenicity, mutagenicity, DNA damage, DNA adducts, oxidative stress, cytotoxicity, pregnancy, sperm, and neurotoxicity. The keywords were linked to the following traffic-related keywords: transport related air pollution, transport emissions, traffic pollutants, diesel exhaust, mobile source air toxics, polycyclic aromatic hydrocarbons, volatile organic compounds, CO, NO_2, BC, organic carbon, elemental carbon, and coarse PM. Panel members undertook individual literature searches for authors identified by means of the searches above or known by the members to be conducting relevant research. Given the large number of pollutants and outcomes, the searches were not intended to encompass every publication on the topic. Publications were selected for inclusion on the basis of the importance or representative nature of their findings and the overall quality of the publication. The final number of publications on this topic was approximately 340.

ABBREVIATIONS AND OTHER TERMS

APHEA	Air Pollution and Health: A European Approach
BC	black carbon
GBD	global burden of disease
NMMAPS	National Morbidity, Mortality, and Air Pollution Study
PM	particulate matter
$PM_{2.5}$	PM ≤ 2.5 μm in aerodynamic diameter
PM_{10}	PM ≤ 10 μm in aerodynamic diameter
U.S. EPA	U.S. Environmental Protection Agency
WHO	World Health Organization

Chapter 2

Emissions from Motor Vehicles

CONTENTS

CONTENTS (*CONTINUED*)

Chapter 2

Emissions from Motor Vehicles

2.I. INTRODUCTION

The U.S. Environmental Protection Agency (U.S. EPA) defines sources of emissions from the transportation sector as mobile sources. This term is used to describe a wide variety of vehicles, engines, and equipment that generate air pollution and that move, or can be moved, from place to place. Mobile sources are grouped into two major categories, on-road and nonroad sources, with different regulatory pathways.

On-road, or highway, sources include vehicles used on roads for transportation of passengers or freight. This category includes light-duty vehicles and trucks, heavy-duty vehicles, and motorcycles used for transportation on the road. On-road vehicles may be fueled with gasoline, diesel fuel, or alternative fuels (such as alcohol or natural gas).

Nonroad sources include vehicles, engines, and equipment used for construction, agriculture, transportation (including aircraft, rail, and marine vessels), recreation, and many other purposes. Within these two broad categories, on-road and nonroad sources are further distinguished by size, weight, use, or horsepower.

This report covers emissions, exposures, and health effects from on-road sources, which are generally referred to as motor vehicles. The term "traffic-related emissions" is used to refer to emissions derived from specific scenarios with a high aggregation of motor vehicles and people.

Motor vehicles are a major source of urban air pollution and are increasingly important contributors to global anthropogenic carbon dioxide (CO_2*) and other greenhouse gases (GHGs). As shown earlier, in Figure 1.1, significant progress has been made in the United States in reducing the amount of pollutant emissions from all sources despite substantial growth in energy consumption, the numbers of vehicles, and the miles traveled in vehicles. Total emissions and emissions from motor vehicles in the United States in 1990 and 2007 are compared in Figure 2.1. From 1990 to 2007, estimated motor-vehicle emissions of carbon monoxide (CO), nonmethane hydrocarbons (NMHC), and nitrogen oxides (NO_x) declined by 54%, 48%, and 27%, respectively. For particulate matter (PM) less than or equal to 10 μm in aerodynamic diameter (PM_{10}) and PM less than or equal to 2.5 μm in aerodynamic diameter ($PM_{2.5}$), estimates of emission reductions (which are more uncertain than those for gaseous pollutants) were 34% and 37%, respectively. A detailed description of PM classification by size can be found in Section 3.II of Chapter 3.

As discussed in detail later in Chapter 3, a considerable fraction of the world's people spend significant amounts of time on or near roadways as part of their daily activities. Increases in urban populations, the numbers of cars, vehicle miles traveled, and traffic congestion are just a few of the trends that suggest that exposure to traffic-related air pollution is on the rise, particularly in countries with rapidly growing economies. In addition, land-use practices in these countries have resulted in population increases near traffic, suggesting that motor-vehicle emissions must be considered in the context of their proximity to populated areas.

The allocation of motor-vehicle emissions in space (ranging from tens of meters to tens of kilometers) and time (ranging from minutes to hours) is essential for managing air quality and estimating the population's exposure to air pollutants. This chapter reviews trends in the critical components affecting motor-vehicle emissions and emissions estimates; it also reviews the progress made to date in reducing emissions and their impacts on air quality. The organization of this chapter reflects the building blocks from which emissions inventories are compiled and refined; it is schematically shown in Figure 2.2.

The chapter presents national and international annual trends in motor-vehicle populations. Regulatory actions aimed at reducing motor-vehicle emissions, including emissions-control technologies and fuel-composition modifications mandated to meet various air-quality objectives and standards, are reviewed. Consideration is given to trends affecting traffic-related emissions and the progress that has been made in reducing them. The chapter also presents an overview of the methods used to gather data on motor-vehicle emissions and identifies some of the challenges in improving our ability to predict traffic-related exposures. In order to understand the impact of motor vehicles on air quality and human exposure, it will be necessary to further refine estimates of motor-vehicle emissions in terms of time and space. This calls for transportation models that also better estimate traffic in time and space; emissions-factor models that better transform estimates of travel activities into absolute emissions values; and finally various air-quality models that better transform emissions values into concentration estimates in time and space in relation to the source.

* A list of abbreviations and other terms appears at the end of this chapter.

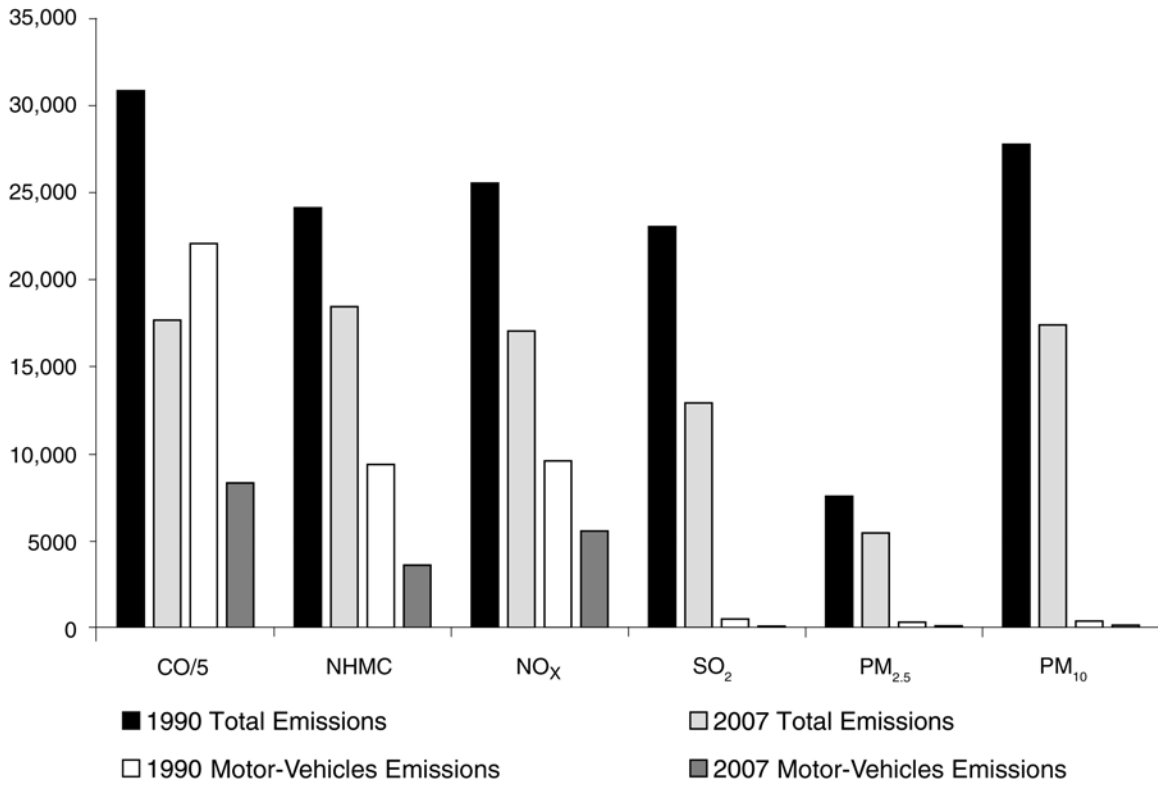


Figure 2.1. Estimates of total emissions and motor-vehicle emissions for 1990 and 2007 by pollutant, in units of 1000 short tons per year. (CO emissions are divided by five [CO/5].) Data from 2005 NEI database projected to 2007 (U.S. Environmental Protection Agency 2008b).

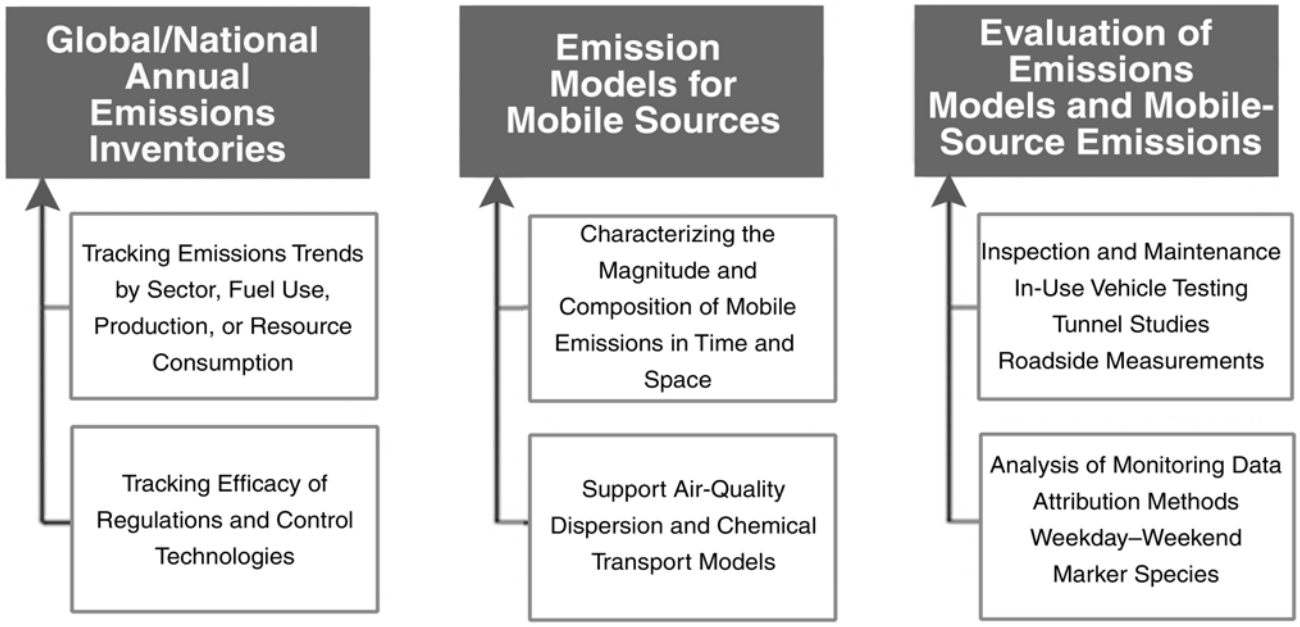


Figure 2.2. Building blocks in the development of on-road source emissions inventories. (Courtesy of Kenneth Demerjian)

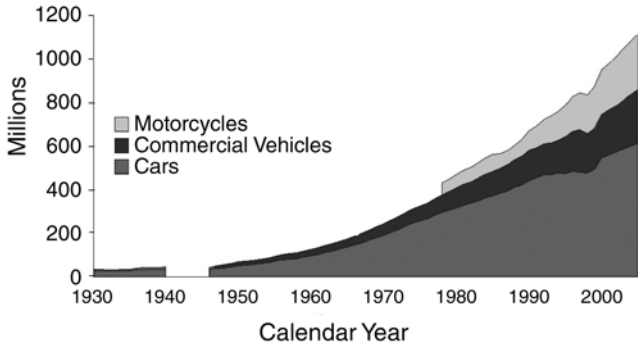


Figure 2.3. World motor-vehicle population by vehicle class. (Courtesy of Michael Walsh.)

In addition, the chapter reviews noncombustion sources of PM, such as tire and brake wear, and the application of methods used to quantify the contribution of pollution related to motor vehicles to ambient pollution in various cities. Lastly, methods for evaluating the motor-vehicle emissions through field measurements of in-use motor-vehicle emissions are reviewed and discussed. The potential role of atmospheric chemistry and fluid dynamics in local transformation processes that affect road-side exposures is also explored.

2.II. NATIONAL AND INTERNATIONAL TRENDS IN THE CHARACTERISTICS OF TRAFFIC

Around the world, the number of motor vehicles continues to increase in step with the gross domestic product (GDP) of nations. As a result, the control of motor-vehicle emissions will continue to be a major component of the challenge of regulating air pollution in urban centers. This section presents data on the worldwide motor-vehicle fleet, data by vehicle type and regions, and forecasts of the makeup of the fleet in years to come.

2.II.1 TRENDS IN THE WORLDWIDE MOTOR-VEHICLE FLEET

The principal factors leading to increases in the world's vehicle fleets are population growth, increased urbanization, economic improvement, and rapid expansion of metropolitan areas (often referred to as urban sprawl), especially in developing countries. The implications of urban sprawl for increasing exposure of populations to motor-vehicle emissions are discussed in Chapter 3. According to the United Nations, the world's population increased from approximately 2.5 billion people in 1950 to slightly more than 6 billion today and is projected to increase by an additional 50%, to approximately 9 billion, by 2050. Most of this growth will be in urban areas in developing countries.

The highest rates of annual GDP growth over the next two decades are forecast to be in China, East Asia, Central and Eastern Europe, and the former Soviet Union, with commensurate growth anticipated in the vehicle fleets in these regions. As a result, steady and substantial growth in the worldwide vehicle fleet can be anticipated, continuing the historical trends illustrated in Figure 2.3. The worldwide fleet exceeded 1 billion vehicles in 2002 and has continued to climb steadily since then. For our purposes, light- and medium-duty trucks are grouped with commercial vehicles.

Between 1980 and 1990, an average of 11 million cars and 23 million motor vehicles of all types (including cars, trucks, buses, motorcycles, and scooters) were added to the world's roadways per year. Between 1990 and 2000, the number of vehicles added has increased on average by 27 million per year, showing that, in absolute numbers, the rate of growth is actually increasing.

In 2005, about 60% of the world's cars and commercial vehicles were in Western Europe and North America; only about 20% were in Asia, the world's most populous region (Figure 2.4).

The number of motorcycles is forecast to approach 50 million per year by 2020; most of these will be in Asia. The impact of motorcycle emissions, while very significant in many Asian cities today, could change dramatically as a significant portion of the population in China (the country with the largest motorcycle population) shifts to electric motorcycles. See Appendix A (available on the HEI Web site) for information on trends in motor-vehicle types by region.

2.II.1.A. Diesel-Car Fleets Around the World

Because of their advantages in terms of fuel economy and durability, diesel cars are gradually increasing their share of the car market worldwide. Over the past four years, for example, diesel car sales have climbed from 21.1% to 22.4% of all new-car sales. Much of this growth in share has come from Europe, where more than one out of every two new cars is a diesel. European sales are high in large part because strong tax incentives favor diesel-fueled cars over gasoline-fueled cars (and in part because diesel-emissions standards are less stringent). However, trends vary widely elsewhere in the world, as described in Sidebar 2.1.

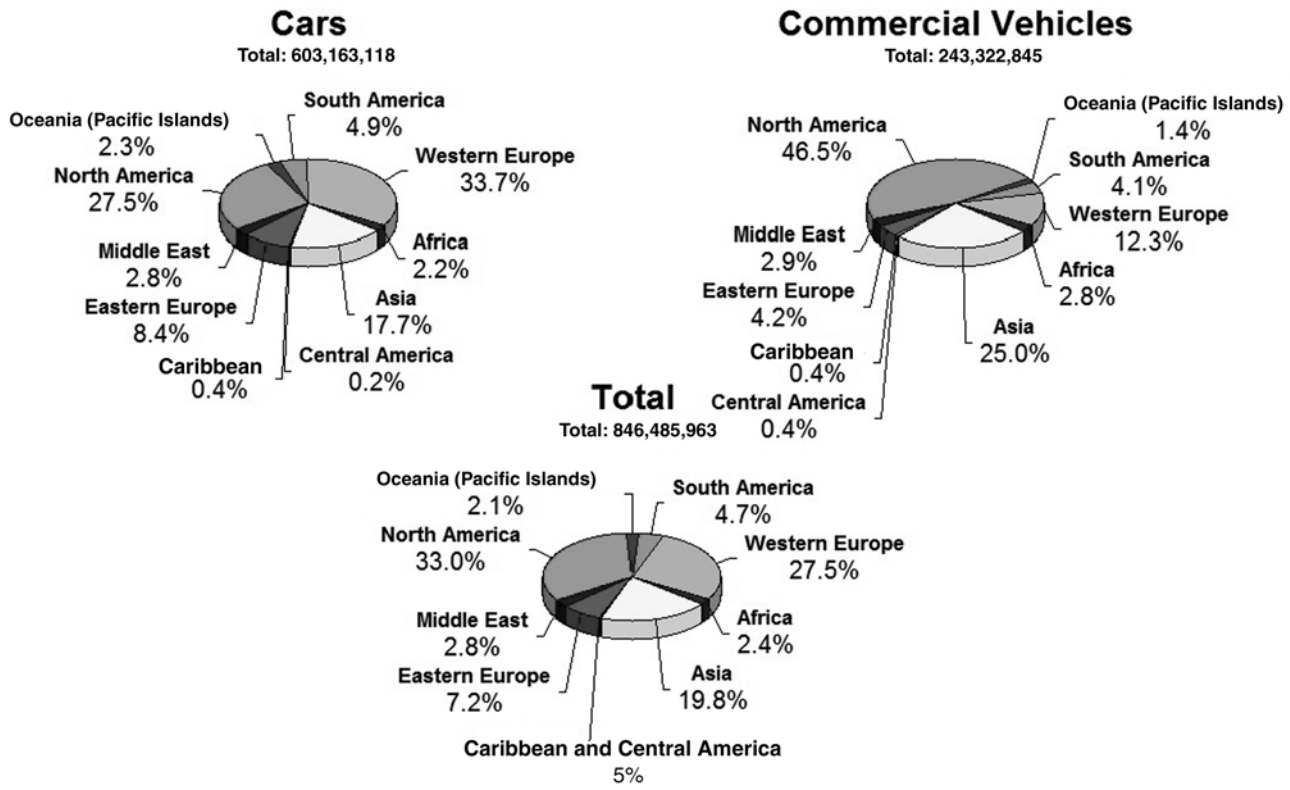


Figure 2.4. Cars, commercial vehicles, and total vehicles for 2005 by region. (Courtesy of Michael Walsh.)

Sidebar 2.1 Trends in Diesel Vehicles Around the World

United States At present, only a small fraction of new cars are diesels, but industry analysts expect this fraction to grow significantly in the future. Mercedes recently predicted that about 10% of its U.S. sales will be diesel by 2010. Ricardo, a consulting firm, forecasts that U.S. diesel-car sales will reach 1.5 million units by 2012. However, the relatively higher price per gallon of diesel compared with gasoline, among other factors, makes this growth forecast unlikely.

China Until recently, diesel cars were prohibited in China. As part of its negotiations to join the World Trade Organization, however, China agreed to allow diesel-car sales. Nevertheless, sales remain low, in part because of resistance from municipal environmental agencies. The Beijing Environmental Protection Bureau, for example, had been allowed by the State Council to prohibit new diesel cars until 2008, when the maximum permitted level of sulfur in diesel fuel was reduced to 50 parts per million. Otherwise, the State Council determined, diesel cars would exacerbate Beijing's already serious PM_{10} and ozone problems. Even with the low-sulfur fuel and the imposition of Euro 4 standards, Beijing discourages diesel cars because they emit higher levels of NO_x and PM than gasoline-fueled cars and would exacerbate the country's serious air pollution problems.

Hong Kong In past years, all taxicabs and a substantial fraction of cars in Hong Kong were diesels. However, the local Pollution Control Department used economic incentives to convert the taxicabs to run on liquid petroleum gas. Further, although gasoline-fueled cars are subject to European emissions standards, Hong Kong officials now require all new diesel cars to comply with the even more stringent California LEV 2 standards. Diesel fuel in Hong Kong has a maximum of 50-ppm sulfur.

India India heavily subsidizes diesel fuel, with the result that there are strong economic incentives to use it. Coupled with the emergence of relatively low-cost diesel cars, the market share of diesel vehicles has grown rapidly in the last few years and is now estimated at approximately 31% of all new-car sales and could exceed 50% by 2010. Without significant implementation of control technologies, such as diesel filter traps, this expected growth will likely result in a significant deterioration of air quality in Indian cities.

Brazil Diesel cars are banned in Brazil.

2.II.2 TRENDS IN MOTOR-VEHICLE SALES

Figure 2.5 shows that North and South America remain the largest market for cars, trucks, and buses, followed closely by Europe (including Western and Eastern Europe and Russia). Asia, including Oceania, is approaching 30% of the global market.

By 2020, Asia is expected to be the world's largest motor-vehicle market. Worldwide, cars, light trucks, and sport-utility vehicles (SUVs) will continue to constitute the largest fraction of the market, but overall growth is expected for all vehicle categories.

2.II.3 SUMMARY

The world fleet exceeded 1 billion vehicles in 2002 and is anticipated to increase at a higher-than-historical rate, given the forecast increases in GDP growth in China, East Asia, Central and Eastern Europe, and the former Soviet Union. Although North and South America currently represent the largest market for cars and commercial vehicles (approximately 37% of the world total), Asia is expected to surpass this mark by 2020. Motorcycle sales, predominantly in the Asian markets, are expected to increase to 50 million motorcycles per year by 2020, but motorcycle emissions might be moderated by a shift to electric-powered models. Diesel-fueled cars have increased their share of the world car market, probably because of their advantages in terms of fuel economy and durability.

Forecasts indicate significant increases in the worldwide motor-vehicle fleet commensurate with population growth, increasing urbanization, improving economies, and rapid expansion of metropolitan areas. This suggests that motor-vehicle emissions, in general, and traffic emissions, in particular, are likely to play an increasing role in pollutant exposures in urban environments unless countermeasures are adopted to substantially reduce emissions per vehicle-mile traveled (VMT). Experience in the developed countries has shown that aggressive pollution-control efforts can substantially reduce total motor-vehicle emissions and public exposure in spite of continuing growth trends.

In 2008 and 2009, the world has been in a deep economic recession, which has dramatically reduced new-vehicle sales. The recession could continue for some time. Based on past experience, however, it seems likely that vehicle sales will increase again once the global economy has recovered, and at least some are predicting a strong continuation of past growth trends (Sperling et al. 2009).

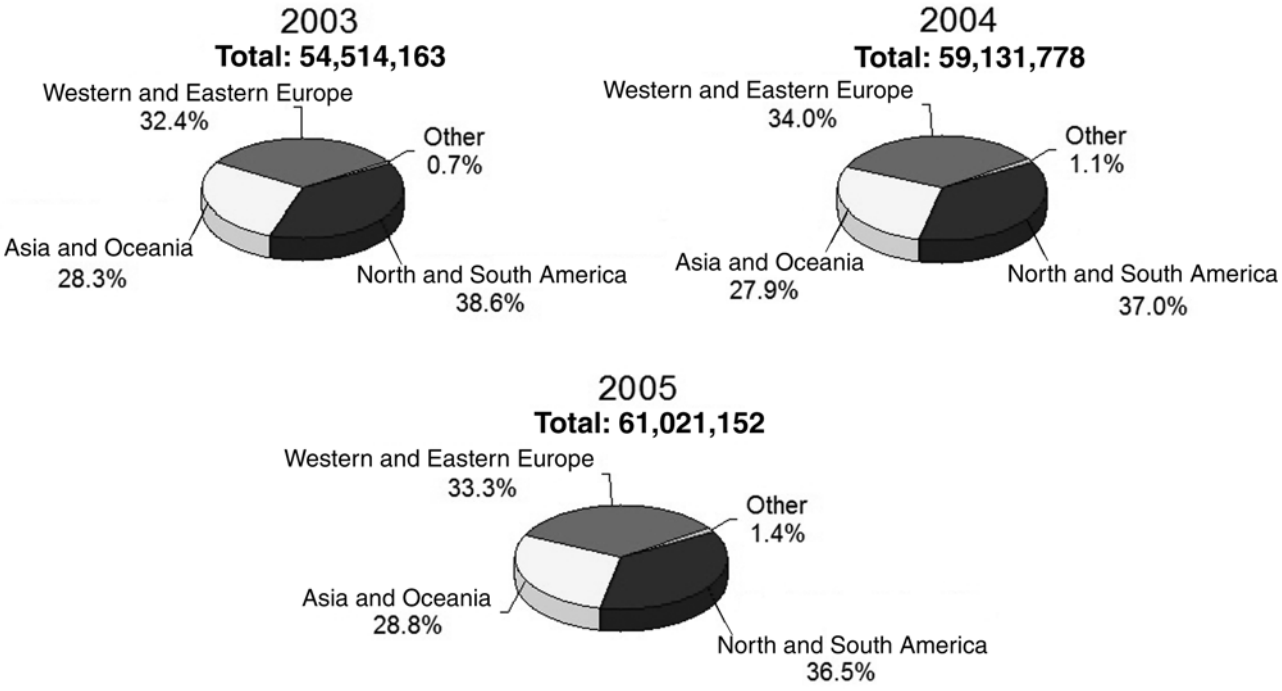


Figure 2.5. New-vehicle sales of cars and commercial vehicles for 2003, 2004, and 2005 by region. (Courtesy of Michael Walsh.)

2.III. REGULATION OF MOTOR-VEHICLE EMISSIONS

Motor vehicles emit large quantities of CO_2, CO, hydrocarbons (HC), NO_x, PM, and substances known as mobile-source air toxics (MSATs), such as benzene, formaldehyde, acetaldehyde, 1,3-butadiene, and lead (where leaded gasoline is still in use). Each of these, along with secondary by-products, such as ozone, can cause adverse effects on health and the environment. Growing vehicle fleets and increasing urbanization and traffic congestion have increased concerns about potential exposures to poor-quality air.

Concerns about the health effects of traffic-related pollution and air pollution in general have led to the introduction of emissions regulations and innovative pollution-control approaches around the world. As these measures are implemented, steady progress in reducing most air-pollution problems is being made. However, recognizing the likely continued growth in the vehicle fleet and the serious remaining problems in traffic-related air quality, the United States, European Union, Japan, and other countries are continuing to push for even stricter emissions controls in coming years.

Reducing the impact of motor-vehicle emissions on air quality requires a comprehensive strategy that typically includes four key components (shown in Figure 2.6): (1) emissions standards for new vehicles, (2) transportation planning and demand management, (3) specifications for clean fuels, and (4) inspection programs to ensure proper vehicle maintenance.

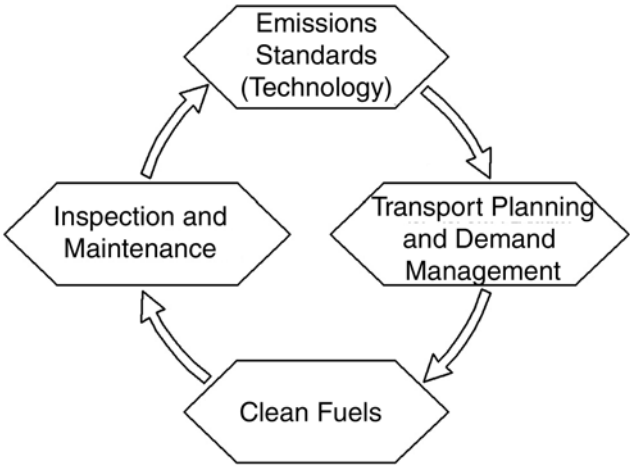


Figure 2.6. Elements of emissions-control strategy. (Courtesy of Michael Walsh.)

CO, PM, HC, and NO_x are regulated in emissions from both diesel and gasoline-fueled vehicles throughout the world. In the United States, in addition, the Clean Air Act requires the U.S. EPA to regulate or consider regulating MSATs by setting emissions standards for fuels, vehicles, or both. In 2007, the U.S. EPA finalized a new rule to reduce emissions of MSATs and defined eight "key" MSATs: benzene, 1,3-butadiene, acrolein, formaldehyde, acetaldehyde, polycyclic organic matter, naphthalene, and diesel exhaust. It also limited the amount of benzene in gasoline, limited HC emissions from passenger cars operating at cold temperatures, and tightened evaporative-emissions standards (U.S. EPA 2007a). These regulations will be phased in from 2010 to 2015 (for a complete list of MSATs and a more detailed discussion of the toxicity of MSATs and their regulations, see HEI Air Toxics Review Panel 2007). More than 30 years earlier, the U.S. EPA started to gradually phase out lead in gasoline (the first MSAT to be regulated). The removal of lead from gasoline around the world represents a major environmental success story. In addition to reducing ambient lead exposures and their related health consequences, removing lead from gasoline provides the opportunity to introduce catalytic-converter control technology for traffic emissions. Catalytic-converter control technologies reduce ozone precursors (such as volatile organic compounds [VOCs] and NO_x) and MSATs, thereby improving air quality with respect to multiple pollutants, including ozone, MSATs, and $PM_{2.5}$. As discussed in Sidebar 2.2, a majority of countries are now using lead-free gasoline and, with the introduction of emissions-control technologies, are beginning to reap the benefits of the resulting air-quality improvements. However, as noted in Sidebar 2.2, the replacement of lead with alternative metallic antiknock additives might prove to have health consequences as well.

As discussed in detail below, technologies and fuels that help control vehicle emissions must be treated in principle as a system by taking into account fuel additives, fuel reformulations, and naturally occurring trace elements (such as sulfur and certain metals) that can affect the performance of the technologies. The three leading regulatory programs in the world — in the United States, the European Union, and Japan — have all adopted this principle.

A number of countries also regulate fuel efficiency, or fuel consumption. The State of California has recently adopted a regulation controlling CO_2-equivalent emissions, including CO_2, methane, nitrous oxide (N_2O), and hydrofluorocarbons (the principal GHGs that contribute to climate change) (California Legislature 2002, 2006). The European Union has recently adopted a CO_2 regulation.

The implications of GHG-reduction strategies are discussed in Sidebar 2.3.

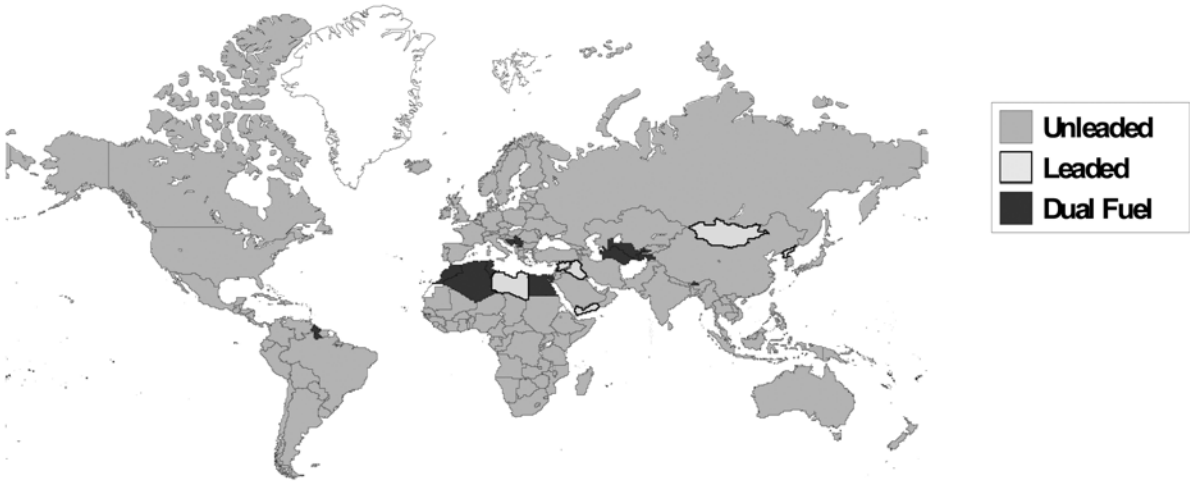
2.III.1 MOBILE-SOURCE EMISSIONS STANDARDS

Figure 2.7 shows, for selected vehicle categories, the percentage of cars, trucks, and buses affected by the emissions standards regulations on CO, PM, and NO_x, in the United States (or in connection with the North American Free Trade Agreement [NAFTA]), the European Union, or Japan, based on sales in these regions in 2005. About 60% of the world's fleet of passenger cars follow the European Union's regulatory standards, and almost 30% follow those of the United States (or NAFTA). The vast majority of diesel cars, more than 90%, follow the European Union's standards. More than 60% of light trucks follow the United States' standards; whereas more than 70% of heavy trucks follow the European Union's standards. Other than Japan, no country follows Japan's standards.

It is important to emphasize two points: (1) The emissions standards adopted by the United States and the European Union will determine the types of technologies used in, and the resulting emissions from, light- and heavy-duty vehicles around the world, which means that the standards should be sufficiently stringent to address the environmental problems for which they were designed; and (2) many developing countries lag the United States and the European Union by five or more years in implementing standards, although the lag time is narrowing. The following section provides details about the three leading

Sidebar 2.2 The Decreasing Use of Lead in Gasoline

The introduction of catalytic converters to treat exhaust gases from gasoline-fueled vehicles required the elimination of lead from gasoline. This change, which has occurred throughout most of the world, has resulted in dramatic reductions in the concentrations of ambient lead in most developing countries. The elimination of lead from gasoline suggests that this major source of lead in the environment is vanishing. As shown in Sidebar Figure 2.1, gasoline in Sub-Saharan Africa is now completely lead free. Although full verification remains problematic, it appears that only 17 countries (Afghanistan, Algeria, Bosnia-Herzegovina, Georgia, Iraq, Jordan, Macedonia, Mongolia, Montenegro, Morocco, North Korea, Palestine, Serbia, Tajikistan, Tunisia, Turkmenistan, and Yemen) still legally use leaded gasoline. Some countries are replacing lead with other metallic substitutes (to serve as antiknock additives), such as methylcyclopentadienyl manganese tricarbonyl (MMT) and dicyclopentadienyl iron (ferrocene), which are also potentially toxic, but precise data on their use are unavailable. Additional discussion of MMT can be found in Appendix B of this chapter (available on the HEI Web site).



Sidebar Figure 2.1. Worldwide distribution of leaded and unleaded gasoline in 2006. (Courtesy of Michael Walsh.)

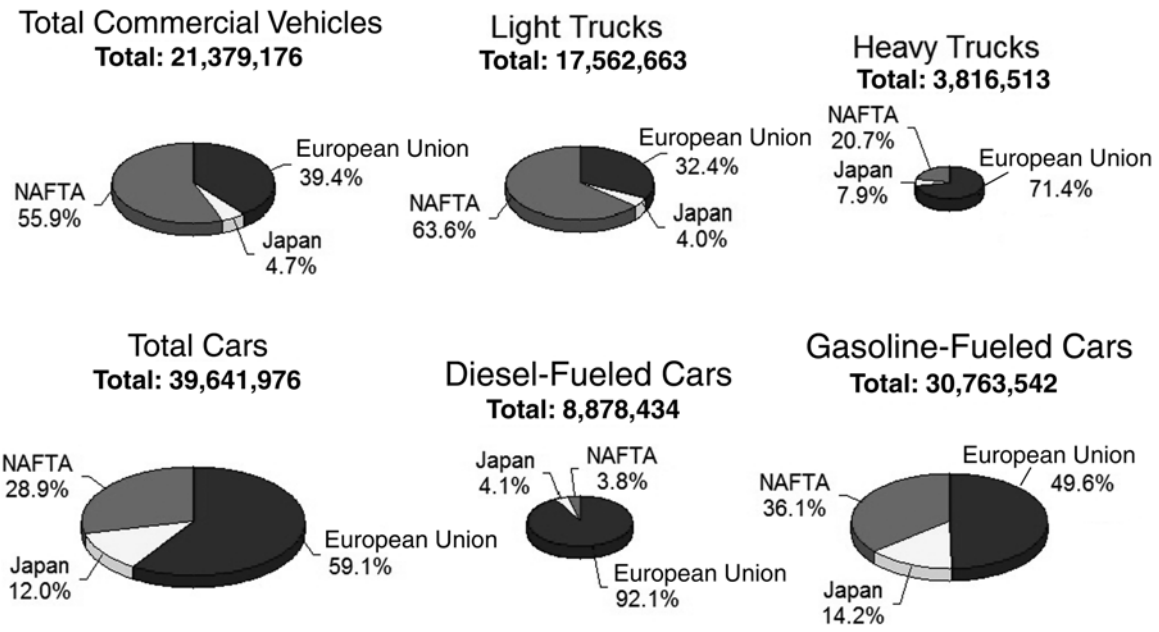


Figure 2.7. Vehicle sales for 2005 by vehicle class and regulatory authority. (Courtesy of Michael Walsh.)

Sidebar 2.3 Implications of GHG-Reduction Strategies for Motor-Vehicle Emissions

As nations consider actions to reduce emissions of GHGs from all sources, it is apparent that the transportation sector has a role to play. In developed countries, GHG emissions from the transportation sector grew by 16% between 1990 and 2006 (United Nations Framework Convention on Climate Change 2006). Considering the projected growth in vehicle numbers in developing countries, it is apparent that strategies to reduce GHG emissions from motor vehicles will be an important component of future strategies around the world to reduce GHG emissions from all sources.

There are three fundamental technology-based approaches to reducing GHG emissions from motor vehicles:

- Setting mandatory or voluntary GHG-emissions standards that force the development of control technologies;
- Shifting to lower-carbon fuels and advanced vehicle technologies; and
- Reducing the use of motor vehicles.

Examples of the strategies considered include (1) implementing mandatory Corporate Average Fuel Economy (CAFE) requirements or GHG-emissions standards for motor vehicles; (2) shifting to renewable, lower-carbon fuels; (3) mandating advanced vehicle technologies, such as battery-powered electric cars, hybrids, plug-in hybrids, and cars powered by fuel cells; (4) exploring approaches to reduce VMT, such as congestion pricing, expansion of bus service and other public rapid-transit systems, and additional taxes on vehicles and fuels. In some cases, these strategies will also reduce motor-vehicle emissions of CO, HC, and NO_x. Some of the strategies, such as the wider use of biofuels, remain untested in terms of their effects on emissions compared with petroleum-based fuels and might result in tradeoffs among emitted species. The wider use of alcohol-based fuels, for example, could result in lower emissions of CO and HC but potentially higher emissions of aldehydes (such as formaldehyde). Indirect effects caused by changes in land use (to grow the crops from which biofuels are made) will also be important in assessing the overall benefits or disadvantages of biofuels.

Around the world, nine governments of various nations, regions, and states have proposed, established, or are in the process of tightening their standards for motor-vehicle fuel economy or GHG emissions. These include the United States, the European Union, Japan, Canada, Australia, China, and South Korea (An et al. 2007).

Most industrialized nations apply emissions standards or fuel economy to new vehicles or have reached voluntary agreements with industry in order to reduce oil consumption or CO_2-equivalent emissions. However, the three largest automobile markets — the United States, the European Union, and Japan — approach these standards in quite different ways. Based on the methodology developed in a Pew report (An and Sauer 2004), the International Council on Clean Transportation

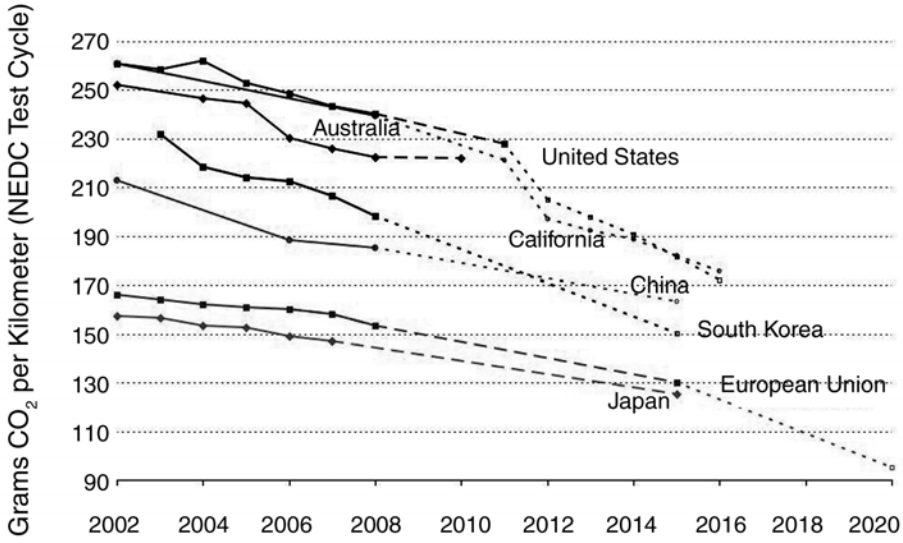
regulatory programs. Examples of emissions regulations adopted by other countries are provided in Sidebar 2.4.

2.III.1.A Emissions from Gasoline-Fueled Vehicles

For the past 40 years in the United States, California has consistently led the way in adopting more stringent emissions requirements for light-duty vehicles (i.e., cars and light trucks), which forced the development of new emissions-control technologies. The U.S. EPA has tended to follow California's lead, eventually adopting very similar standards for the country as a whole. The evolution of the California and federal standards for NO_x emissions from passenger cars are shown in Figure 2.8. Similar trends in emissions standards for HC, CO, and (for diesel vehicles) PM also occurred. Two-way catalytic converters were introduced on most new cars in the United States for the

Sidebar 2.3 (*Continued*) Implications of GHG-Reduction Strategies for Motor-Vehicle Emissions

recently updated figures to compare standards for fuel economy and GHG emissions normalized around appropriate metrics and vehicle-test cycles. According to these calculations, Japan now has the most stringent standards, and the United States has the most relaxed standards, in terms of fleet-average fuel economy or CO_2-equivalent rating.



Sidebar Figure 2.2. Actual and projected GHG-emissions standards for new passenger vehicles by country or region, 2002–2020. Solid lines indicate enacted standards; dashed lines indicate proposed or contested standards. Reprinted from ICCT 2009, with permission.

Sidebar Figure 2.2 (International Council on Clean Transportation 2009) shows global planning for significant improvements in fuel economy of vehicle fleets or GHG emissions over the coming decade. California has set the most significant goals — a 40% fleet-average improvement over 2002 standards — and after several years of delay has received a necessary waiver from the U.S. EPA. The Obama Administration has also proposed a joint rulemaking by the U.S. EPA and the Department of Transportation, which will achieve roughly equivalent standards to those of California by 2016 for the entire country. (California's requirement controls not only CO_2, but also methane, N_2O, and hydrofluorocarbons.) Japan anticipates that its new 2015 standards will deliver a 24% improvement. The European Union has adopted mandatory CO_2 standards, which will result in a level of 130 g/km by 2015 and 95 g/km by 2020, subject to a review in 2013.

China is in the process of developing its next generation of requirements, and India has begun work on fuel-economy requirements. South Korea has also announced its intention to tighten requirements.

But with regard to the effects of motor vehicles on climate change, it is clear that the overall growth in vehicle numbers in all categories, including aircraft and marine vessels, is overwhelming the world's control efforts to date.

Some of the efforts to address climate change have proven counterproductive to efforts to improve urban air quality. The rapid increase in diesel cars, for example, has been seen as significantly reducing CO_2 emissions compared to gasoline-fueled cars. However this rapid increase has been taking place in some instances in countries with relatively weak controls on PM emissions. On the one hand, the added PM exacerbates urban air-quality problems, resulting in serious adverse health consequences. On the other hand, a portion of the PM is black carbon, which has recently been identified as a potentially potent GHG, perhaps second only to CO_2 in the short term. As a result, diesel cars without advanced PM controls might slow down climate change only marginally, if at all, while exacerbating air pollution.

1975 model year; since 1981, every new gasoline-fueled car sold in the country has been equipped with a three-way catalytic converter. Catalytic converters were introduced in Japan in 1975 as well.

The European Union adopted its Euro 1 emissions standards that forced the introduction of catalytic converters for new gasoline-fueled cars in the early 1990s and has been gradually tightening the standards in stages: Euro 2 in 1996, Euro 3 in 2000, Euro 4 in 2005, Euro 5 in 2009, and Euro 6 in 2014 (European Parliament and the Council 2007). In the Euro 6 stage, the European Union will introduce a particle-number emissions limit for all diesel- and some gasoline-fueled cars to ensure that the absolute number of particles emitted is reduced along with their mass. The technology used to measure particle number in both light- and heavy-duty vehicles removes most of the volatile particles and excludes particles smaller than 20 nm. While the number-based standard was not determined in time to be incorporated in the Euro 5 regulations, the European Commission may impose it before Euro 6 requirements go into effect; some refer to this as Euro 5 1/2.

Controls to reduce the release of vapors from fuel, known as evaporative emissions, have also been in place since the early 1970s and have gradually become more stringent. These have been complemented in many countries by stage-2 vapor-recovery controls to reduce exposure to vapors during

Sidebar 2.4 Motor-Vehicle Emissions Regulations Around the World

Canada has adopted standards for vehicles and fuels that are virtually identical to, and on the same approximate schedule as, those of the United States.

Mexico has phased in Tier 1 standards for light-duty vehicles and is encouraging industry to phase in Tier 2 cars. A key determinant of the outcome of these discussions, and of the prospects for significant tightening of the standards for heavy-duty vehicles, is whether fuel quality will be improved. Mexico has also developed a detailed plan to phase in fuels that meet U.S. sulfur standards but on a somewhat later schedule.

Australia has harmonized its requirements with those of the European Union and will be largely on par with the European Union by the end of the decade.

The government of New Zealand, the last OECD country without emissions standards for new vehicles, adopted a rule that requires new and used light- and heavy-duty vehicles that enter New Zealand from January 1, 2005, to be built to the emissions standard that was current in Australia, the United States, Japan, or Europe at the date the vehicle was manufactured. In some cases, the rule allows for a transition period with less stringent emissions standards, depending on the timetable for the introduction of more stringent fuel specifications or production lead times needed for heavy-duty vehicles.

As noted earlier, China's new-vehicle sales are growing more rapidly than in any other country in the world. To deal with this rapid growth, China has already introduced Euro 2 standards for both light- and heavy-duty vehicles and has adopted a schedule to phase in Euro 3, Euro 4, and (for heavy-duty vehicles) Euro V standards between now and 2012. The major determinant of progress on emissions standards will be the schedule for improvements in fuel quality, especially reducing sulfur and MMT. Both of these issues are under intense discussion in China at the present time.

Thailand has decided to proceed to Euro 4 standards by the end of the decade. Agreement has been reached with the fuel industry to reduce sulfur concentrations in both diesel fuel and gasoline to a maximum of 50 ppm by 2010; discussions are ongoing about a possible reduction to a maximum of 10 ppm.

South Korea introduced Ultra-Low Emission Vehicle (ULEV) standards for gasoline-fueled cars and Euro 4 standards for diesel cars in 2006, and maximum sulfur concentrations for gasoline and diesel fuel have been reduced to 50 ppm and 30 ppm, respectively. The South Koreans are considering tighter emissions standards for the period after 2010.

Taiwan reduced the maximum sulfur concentrations in both gasoline and diesel fuel to 50 ppm in 2008. At the same time, it introduced 2004 U.S. standards for heavy-duty vehicles; the Euro IV standards for heavy-duty vehicles are deemed to be equivalent.

India has adopted Euro 2 standards for 2005 and Euro 3 for 2010. The major cities will be on a faster schedule, moving to Euro 4 by 2010. Currently, vehicles in 11 cities are required to meet Euro 3 standards: Agra, Ahmedabad, Bangalore, Chennai, Hyderabad, Kanpur, Kolkata (Calcutta), Mumbai (Bombay), New Delhi, Pune, and Surat. Vehicles in these cities will be required to meet Euro IV standards by 2010.

Brazil is phasing in U.S Tier 1 emissions standards at the present time and plans to jump to Tier 2 in 2009. Diesel cars continue to be banned throughout the country. For heavy-duty trucks and buses, Euro III was phased in from 2004 to 2006, and Euro IV was scheduled to be introduced in 2009. Fuel quality remains a difficult issue; for sulfur, a maximum of 50 ppm was required in the major cities by 2009. However, Petrobras did not meet this requirement. Recent agreements indicate that sulfur concentrations in fuel will be reduced to a maximum of 10 ppm by 2012 and that Euro V standards for diesel trucks will be introduced at that time.

Taiwan has traditionally had the world's most stringent new-vehicle standards for two- and three-wheelers. China, however, has recently adopted even tougher standards, which affect all new models introduced in 2008 and all motorcycles in 2009.

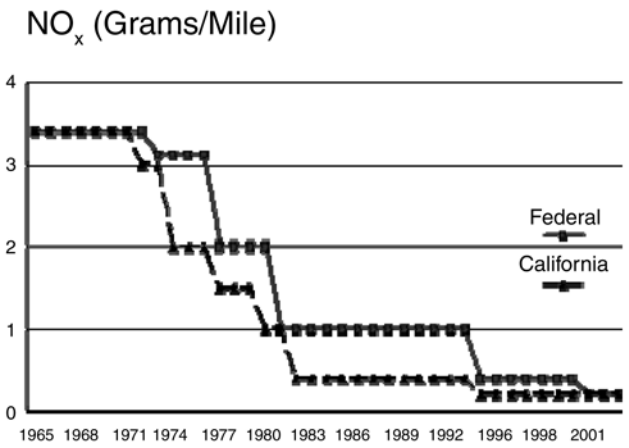


Figure 2.8. U.S. federal and California emissions standards for NO_x from passenger cars by year. (Courtesy of Michael Walsh.)

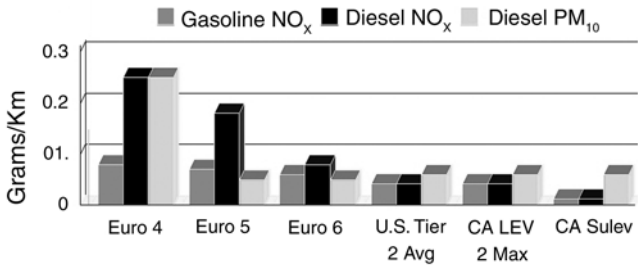


Figure 2.9. Emissions standards by pollutant for light-duty gasoline-fueled and diesel vehicles in the European Union, the United States, and California. (Courtesy of Michael Walsh.)

refueling. The United States has also introduced onboard vapor-recovery systems, which capture vapors during refueling and retain them in the vehicle to be burned as fuel.

In conjunction with the tightening of motor-vehicle-emissions standards, fuel-quality improvements were also mandated. In some cases the fuel modifications were necessary to make possible the introduction of the vehicle technologies required to meet the new standards. For example, the adoption of standards forcing the use of catalytic converters (such as the 1975 exhaust emissions standard in the United States or the Euro 1 standards for gasoline vehicles) necessitated the use of unleaded gasoline (see Sidebar 2.2 about lead in gasoline). Additional reductions in emissions have been achieved by decreasing the amount of sulfur and other toxic compounds (e.g., benzene) in gasoline (U.S. EPA 2000). In setting standards for new vehicles, policymakers must consider the close linkage between control technologies and fuel requirements and ensure that a fuel of appropriate quality will be available when the vehicle standards take effect. Both Europe and Japan have fuel-quality regulations similar to those of the United States.

2.III.1.B Emissions from Diesel-Fueled Vehicles

Light-Duty Vehicles Over the past decade, the United States and Japan have put stringent emissions standards in place for cars and trucks. Reductions in sulfur in diesel fuel are linked to U.S. Tier 2 light-duty-vehicle standards, which required gasoline-fueled and diesel vehicles to meet the same emissions standards for NO_x and PM starting in 2004 (U.S. EPA 2000). Conversely, the European Union has only recently completed the adoption of new light-duty-vehicle standards, Euro 5 and Euro 6, to go into effect in 2010 and 2015, respectively (European Parliament and the Council 2007). In contrast with the United States, the European Union continues to impose a substantially more relaxed NO_x standard for diesels than for gasoline-fueled cars, but it has pioneered the regulation of particle-number emissions, as noted above. NO_x and PM standards in the United States, California, and Europe are compared in Figure 2.9.

In the United States, the Tier 2 (U.S. EPA 2000) and Low Emission Vehicle II (LEV II) standards are gradually being phased in across the nation and in California, respectively. Low-sulfur gasoline (< 30 ppm) and near-zero-sulfur diesel fuel have been phased in smoothly. The U.S. EPA has also adopted near-zero sulfur in fuel requirements and very stringent standards for diesel engines used in off-road vehicles that will require the same degree of emissions control for most engine-size categories as the on-road standards. In addition, the U.S. EPA has recently adopted stringent standards for locomotives and marine vessels (U.S. EPA 2008a).

The European Union has been a leader in advancing the use of ultra-low-sulfur diesel fuel. Ultra-low-sulfur diesel fuel (< 10 ppm) already dominates fuel markets in several European Union countries; the Euro 4 directive limited sulfur to 50 ppm for both gasoline and diesel by 2005. The European Union further reduced sulfur in gasoline and diesel fuel to a maximum of 10 ppm starting in 2009 (European Parliament and the Council 2003).

Heavy-Duty Vehicles In the United States, the EPA's Heavy-Duty Diesel Rule (U.S. EPA 2001) established stringent, technology-forcing NO_x and PM standards for heavy-duty engines starting with the model year 2007, as well as a sulfur limit of 15 ppm for highway diesel fuel starting in 2006. The rule mandated very strict PM and NO_x source reduction for 2007 engines, and an even more stringent NO_x standard for 2010 engines. As can be seen in the

Table 2.1. Heavy-Duty Vehicle Emissions Standards in the European Union, Japan, and the United States and Canada

Region	Regulation and Year Implemented	Average Standard Values (g/kWh)	
		NO_x	PM
United States and Canada	2002–2004	2.7	0.13
	2007	1.6	0.013
	2010	0.27	0.013
European Union (transient cycle)	Euro III (2000)	5	0.2
	Euro IV (2005)	3.5	0.03
	Euro V (2008)	2	0.03
	Euro VI (2013)	0.4	0.01
Japan	2003–2004	3.38	0.18
	2005	2	0.027
	2009–2010	0.7[a]	0.01

[a] Japan has also adopted a "challenge value" of 0.23 g/kWh for NO_x, which will likely not be implemented until at least 2013.

Table 2.1, the NO_x and PM standards of the United States (and Canada) for heavy-duty vehicles are more stringent than those of the European Union and Japan, although Japan's "challenge value" for NO_x is quite close.

In Europe, Euro IV emissions standards for heavy-duty vehicles and engines have been in force since October 1, 2005 (European Parliament and the Council 1998); Euro V standards began being phased in on October 1, 2008 (European Parliament and the Council 2005). Separate but related fuel specifications preceded these new emissions standards as note above. As part of Euro VI, the European Commission has proposed to reduce emissions of NO_x by 80% and PM by 66% compared with Euro V values (European Parliament and the Council 2005). Euro VI will take effect on December 31, 2013, for new engines and in 2014 for all engines (see Table 2.1 for proposed emissions limits).

In addition to setting more stringent limit values, the Commission set provisions on off-cycle emissions, on-board diagnostics, durability of pollution-control devices, conformity of in-service engines and vehicles, and a particle-number limit value.

Japan mandated ultra-low-sulfur fuel (< 10 ppm sulfur) by 2007, and its domestic fuel industry responded by voluntarily introducing such a fuel two years ahead of schedule. In early 2005, the Japanese Central Environment Council (CEC) — an advisory body of the Ministry of the Environment — reached consensus on a next tier of standards for heavy-duty-diesel emissions to take effect in 2009–2010. The new standards will reduce NO_x and PM emissions by an additional 65% and 63%, respectively, compared with the 2005 standards. As can be seen in Table 2.1, Japan's PM standards for 2009–2010 are more stringent than those of Euro V and are comparable to those of the United States for 2007. Japan's NO_x standards for 2009–2010 NO_x are also more stringent than those of Euro V but less stringent than those of the United States for 2010. Japan has also set a "challenge value" for NO_x for 2009–2010, however, that is another 67% lower than its 2009–2010 standards; and would be comparable to the U.S. standard for NO_x in 2010. Japan has been monitoring technology developments closely in the last few years and will likely not implement the "challenge value" standard until at least 2013.

2.III.1.C Compliance Testing

It is important to note that direct comparisons of the emissions standards adopted by the United States, the European Union, and Japan are complicated by differences in the tests used to determine compliance. In the United States, the compliance test for light-duty vehicles, originally developed to represent typical driving during a trip to work in Los Angeles during the 1950s and 1960s, includes both a cold start (i.e., with the engine at ambient temperature of 68 to 75°F) and hot start (i.e., with the engine warm). More demanding test cycles were added later. In the European Union, the original compliance test represented lower-speed driving in Paris or Rome during the 1960s and 1970s and allowed the engine to be idled for 40 seconds before the start of the test, precluding measurements of cold-start emissions. Starting in 2000, the 40-second idle was eliminated in order to include cold-start emissions in the measurement. Subsequently, higher-speed steady-state modes were added as well as an alternative test cycle for low-powered vehicles. In Japan, standards were based on two compliance tests — a 10-mode hot-start urban test and an 11-mode cold-start test intended to simulate driving from the suburbs to the city.

In the United States, the European Union, and Japan, control technologies for gasoline-fueled vehicles have advanced to the degree that almost all of the exhaust emissions from a properly functioning vehicle are emitted during the cold-start portion of the test.

Compliance tests for heavy-duty vehicles and engines have also evolved over the past several decades. The United States initially used a 13-mode steady-state test but switched to a test with a transient cycle in the early 1980s just as Europe adopted the 13-mode test. In 2000, the European Union also added a test with a transient

cycle. Initially, Japan used a 6-mode steady-state test but after 1994 switched to a 13-mode test.

Extensive efforts led by the Economic Commission for Europe (ECE) have been underway for several years to develop a harmonized worldwide compliance test. These efforts appear to be close to resolution, at least for the European Union and the United States. Small differences in the weighting of the hot- and cold-start portions of the test as well as in the length of the soak time (the time between turning an engine off and then on again) are still being resolved.

2.III.2 CONTROL OF SULFUR CONTENT IN FUELS

Although many characteristics of gasoline and diesel fuels are important, lowering the amounts of sulfur in both have been singled out as a priority in many countries because of sulfur's potential for damaging or in some cases destroying advanced pollution-control equipment. Countries are appropriately reluctant to adopt emissions standards requiring advanced wall flow filters for diesel PM, for example, unless a fuel with a maximum sulfur content of 50 ppm is available. Maximum performance of these filters occurs with near-zero-sulfur fuel. NO_x-absorber technology is even more sensitive to sulfur and can only be used with fuels containing less than 10 or at most 15 ppm of sulfur.

Sulfur content in gasoline and diesel fuels is decreasing rapidly in countries that belong to the Organisation for Economic Co-operation and Development (OECD), and low-sulfur fuels are on the horizon in a number of developing countries as well.

The amount of sulfur in fuel is directly related to sulfur-dioxide (SO_2) emissions and affects emissions of total PM as well as CO, HC, and NO_x. Sulfur is also responsible for degrading the performance of catalytic converters in gasoline-fueled vehicles by mildly "poisoning" them.

In the oxygen-rich exhaust of diesel vehicles, several percent of the SO_2 formed during combustion is oxidized to sulfur trioxide (SO_3), which dissolves in the water vapor present to form sulfuric acid (H_2SO_4) vapor. H_2SO_4, along with elemental carbon, forms very small (so-called ultrafine) particles in diesel exhaust.

According to the U.S. EPA, approximately 2% of the sulfur in diesel fuel is converted to direct PM emissions. More details about the effects of control technologies and fuel composition on emissions can be found in the next section.

Figure 2.10 summarizes the sulfur content of gasoline for on-road vehicles in use in 2005, 2008, and (projected) 2010 worldwide; it shows (1) that more than 80% of all gasoline sold in 2005 had a maximum of 500 ppm sulfur and (2) that by 2010, assuming "business as usual", almost 70% of all gasoline will have a maximum of 50 ppm sulfur.

Figure 2.11 summarizes the sulfur content of diesel fuel for on-road vehicles in use in 2005, 2008, and (projected) 2010 worldwide; it shows (1) that more than 75% of all diesel fuel sold in 2005 had a maximum of 500 ppm sulfur and (2) that by 2010, assuming "business as usual," approximately 65% of all diesel fuel will have a maximum of 50 ppm sulfur.

2.III.3 INSPECTION AND MAINTENANCE

Vehicles that are properly tuned tend to run more cleanly than vehicles that are out of tune. Modern vehicles equipped with advanced pollution controls are even more dependent on properly functioning components to keep pollutant emissions low. Minor malfunctions in the air–fuel mix or the spark-management system can significantly increase emissions. Major malfunctions in pollution-control components can cause emissions to skyrocket. A relatively small number of vehicles with serious malfunctions frequently cause the majority of vehicle-related pollution problems. Unfortunately, it is rarely obvious which vehicles fall into this category, as the emissions themselves might not be noticeable, and pollution-control malfunctions do not necessarily affect vehicle drivability. Effective vehicle-inspection programs based on periodically subjecting vehicles to a short test can identify these problem cars and, by requiring a retest after maintenance or repair, ensure their proper performance. The combination of inspection (I) and remedial maintenance (M) has become known as I/M programs. Targeted I/M programs can contribute substantially to reduction of the pollution caused by such vehicles. Onboard diagnostic technology can also play a critical role in ensuring in-use compliance as such systems become more widespread around the world.

2.III.4 SUMMARY

Progress in the reduction of emissions of PM, CO, HC, and NO_x from gasoline- and diesel-fueled motor vehicles has been significant in the leading industrialized countries, and more stringent control requirements to further reduce NO_x emissions from diesel vehicles are starting to be phased in. These reductions have been achieved through a comprehensive strategy that involves emissions controls, cleaner fuels, and vehicle-inspection programs. However, the numbers of vehicles and VMT are expected to continue to grow rapidly in the future, especially in developing countries, offsetting these reductions at least to

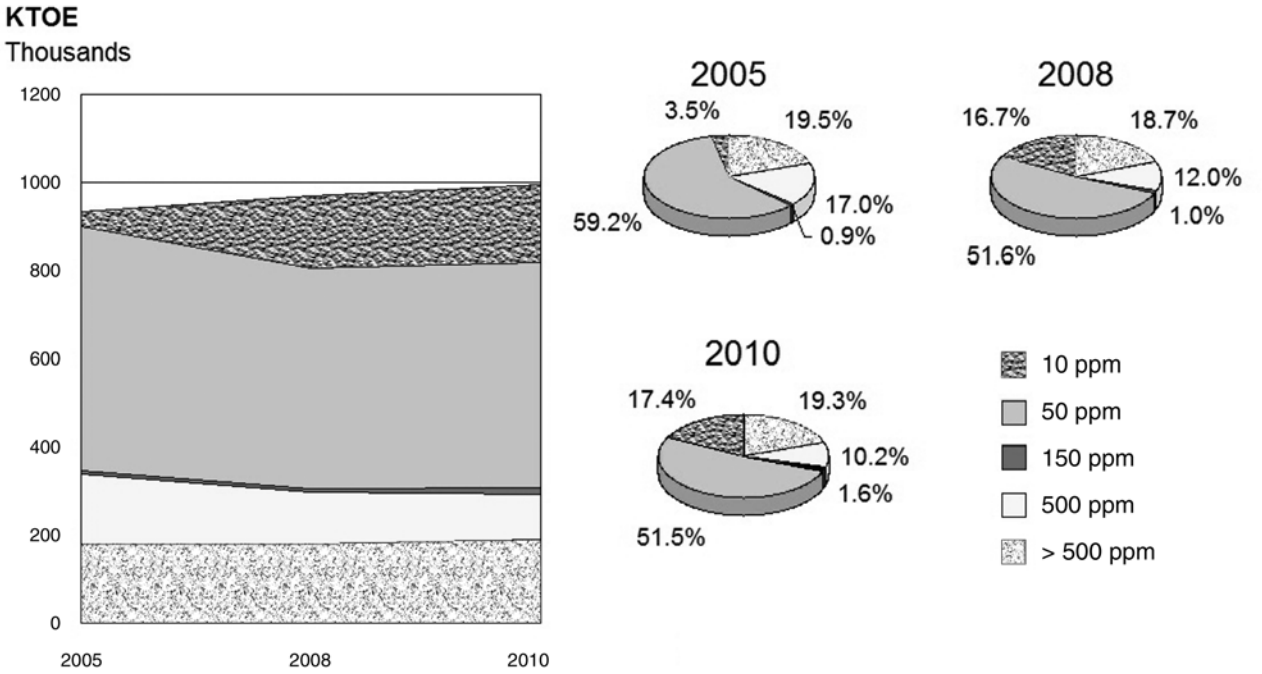


Figure 2.10. Sulfur content (in ppm) of on-road gasoline worldwide for 2005, 2008, and (projected) 2010. (KTOE = kilotons of oil equivalent.) (Courtesy of Michael Walsh.)

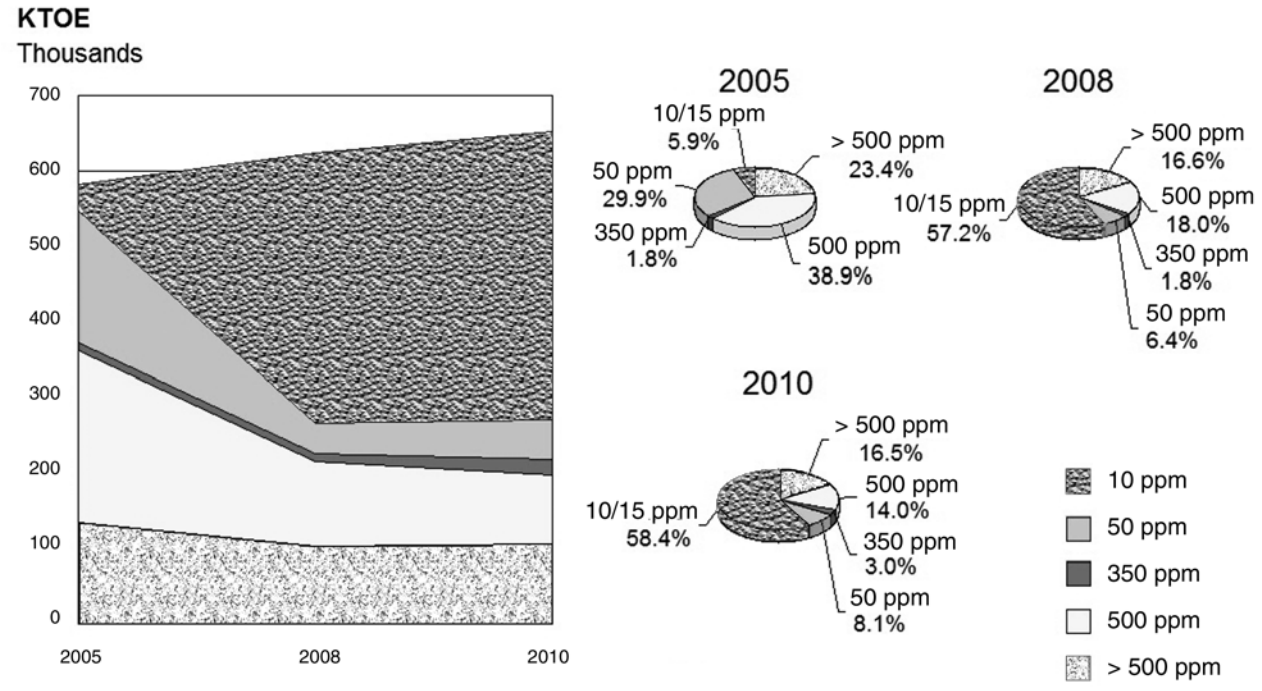


Figure 2.11. Sulfur content (in ppm) of on-road diesel fuel worldwide for 2005, 2008, and (projected) 2010. (KTOE = kilotons of oil equivalent.) (Courtesy of Michael Walsh)

some extent and posing a significant challenge to air-quality regulators.

Many of the developing countries that are industrializing more rapidly are moving to tighten their vehicle-emissions requirements to improve urban air quality. China, for example, the country with the highest rate of growth in numbers of vehicles, has already introduced country-wide vehicle-emissions standards comparable to those of the European Union in the mid-1990s and will implement 2005 European Union standards in 2010. South Korea, India, Thailand, Brazil, Chile, and Mexico, among others, are also moving toward state-of-the-art vehicle and fuel requirements. Several developing countries have also taken measures designed to reduce GHG emissions.

Technologies are now available or emerging that, in combination with clean fuels, can lower CO, HC, NO_x, and PM emissions from on-road vehicles per mile driven to a very small fraction of what they once were. The principal challenge now is to get these technologies adopted around the world. Over the next decade, similar controls for off-road vehicles (such as construction equipment and agriculture vehicle) and fuels will increasingly be implemented. Several factors are driving these trends:

- Continued growth in the manufacture of vehicles (especially in China and other parts of Asia) and their concentration in urban areas where pollution concentrations remain high;
- Growing evidence from health studies that show adverse effects of air pollution at lower and lower concentrations; and
- Advances in vehicle technology and clean fuels that are making it possible to achieve lower and lower emissions rates at reasonable costs.

2.IV. EFFECTS OF CONTROL TECHNOLOGIES AND FUEL COMPOSITION ON EMISSIONS

2.IV.1 GASOLINE-FUELED VEHICLES

Gasoline is a complex mixture of volatile HC used as a fuel in spark-ignition engines. The pollutants of greatest concern from gasoline combustion are CO, HC, NO_x, lead, and certain toxic HC, such as benzene. The production of each of these can be influenced by the composition of the gasoline used by the vehicle.

As previously mentioned, the use of catalytic converters to treat exhaust gas from gasoline-fueled vehicles required the elimination of lead from gasoline. Other factors that have been determined to reduce exhaust and evaporative emissions and their photochemical reactivity are (roughly in order of effectiveness) sulfur content, vapor pressure, distillation characteristics, light-olefin content, and aromatic content (Sawyer 1992). A detailed discussion of fuels and their relationship to emissions-control technologies is provided in Appendix B of this chapter (available on the HEI Web site).

Modern gasoline engines use computer-controlled intake-port fuel injection with feedback control based on an oxygen sensor that precisely meters the quantity and timing of fuel delivered to the engine. Control of in-cylinder mixing and the use of high-energy ignition promote nearly complete combustion. Three-way catalytic converters reduce emissions of CO, HC, and NO_x by more than 90%. Engines that are designed to warm up rapidly minimize emissions from cold starts. On-board diagnostic (OBD) systems monitor the performance of emissions systems and identify component failures. Vehicles that can go in excess of 160,000 km with minimal maintenance are now common in many countries.

2.IV.2 DIESEL-FUELED VEHICLES

Diesel vehicles with no exhaust after-treatment system emit relatively small amounts of CO, and exhaust and evaporative HC but large amounts of NO_x and particulates. Modest to significant degrees of NO_x control can be achieved by delaying fuel-injection timing and adding exhaust-gas recirculation. Very-high-pressure, computer-controlled fuel injection can also be timed to reduce PM emissions. However, modifying engine variables to simultaneously reduce NO_x and PM is difficult and limited, because the optimal settings for one pollutant frequently increase emissions of the other, and vice versa. Reformulated diesel fuels, with lower sulfur and aromatics and increased cetane number, can effectively reduce NO_x and PM emissions from diesel vehicles (U.S. EPA 2001).

Attaining very low emissions of NO_x and PM requires exhaust after-treatment. As mentioned earlier, certain technologies are especially sensitive to sulfur in fuel so that sulfur content needs to be less than 50 ppm. Lean-NO_x catalysts, selective catalytic reduction, NO_x-storage traps with periodic reduction, filter traps with periodic burn-off, and oxidation catalysts with continuous burn-off are evolving technologies that are being phased in at various rates around the world. Japan, for example, tends to lead the world in the widespread use of PM filters on new diesel vehicles; Europe tends to lag. A new type of combustion technology, the homogeneous-charge compression-ignition engine, provides another approach to reducing NO_x and PM and is receiving significant attention. It has been introduced in some engines for at least some engine-operating conditions. Reformulated fuel with

reduced sulfur and aromatics and increased cetane number can also effectively reduce NO_x and PM.

In spite of the tremendous improvements in vehicle emissions per mile driven resulting from the vehicle and fuel standards adopted by many countries, the continued growth in VMT has offset many of these gains. As a consequence, motor vehicles remain a major pollution source in most large cities, and for some pollutants in some cities they are the dominant source. The next section will review the contributions of motor vehicles to air pollution.

2.V. CONTRIBUTIONS OF THE TRANSPORTATION SECTOR TO EMISSIONS OF CRITERIA POLLUTANTS

Figure 2.12 shows estimates of emissions of the criteria pollutants CO, NO_x, VOCs, and SO_2 in the United States from the transportation sector (namely, on-road and off-road vehicles, referred to as highway and nonhighway vehicles in the U.S. EPA's National Emissions Inventory), industrial processes, fuel combustion, and miscellaneous sources. As can be seen, the transportation sector is a major contributor of CO, NO_x, and VOCs. The percentage contribution of these three criteria pollutants by this sector is even greater in major metropolitan areas. In the New York metropolitan area, for example, on-road and nonroad vehicles together account for 98%, 65%, and 43% of total CO, NO_x, and VOC emissions, respectively (New York State Department of Environmental Conservation 2009). Estimates of primary emissions of PM_{10} and $PM_{2.5}$, which have recently been added to emissions inventories, indicate that on-road vehicles contributed 0.9% of total PM_{10} and 2.1% of total $PM_{2.5}$ emissions in 2007 (U.S. EPA 2008b). If the contribution of paved road dust is included, the total PM_{10} contribution from motor vehicles would be

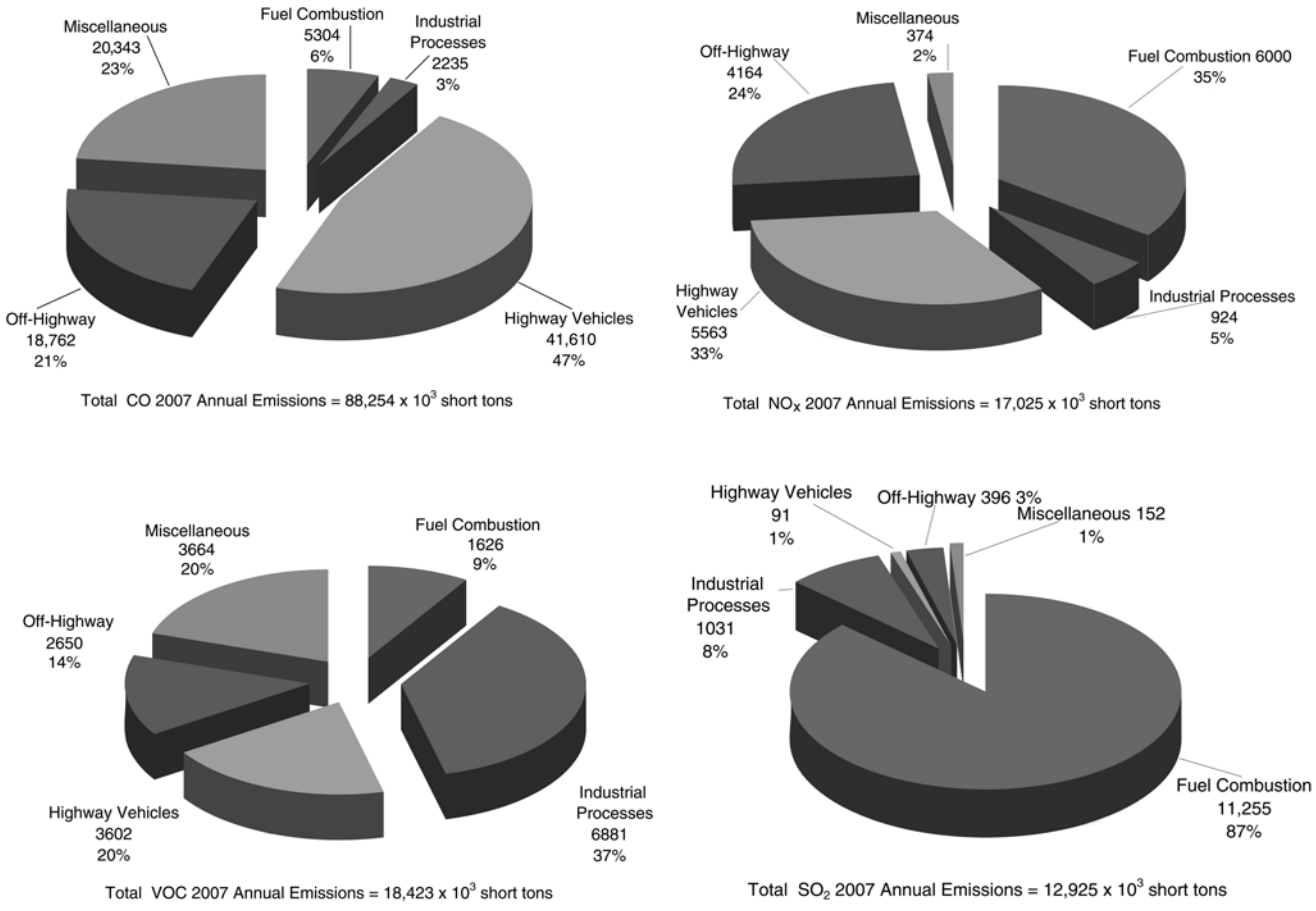


Figure 2.12. Distribution of total annual emissions of the criteria pollutants CO, NO_x, VOCs, and SO_2 for 2007 by source, in units of 1000 short tons per year. Sources are fuel combustion (electric utilities, industrial production, and other processes), industrial processes (metals processing, chemical and allied product manufacturing, storage and transport, petroleum and related industries, solvent utilization), transportation (highway vehicles and off-highway equipment), and miscellaneous (waste disposal and recycling and other sources). Data from 2005 NEI database projected to 2007 (U.S. Environmental Protection Agency 2008b).

approximately 16% (based on the average of the 2005 and 2008 road-dust data), and the $PM_{2.5}$ portion of those emissions would be 2.3%. Resuspended road dust is discussed in more detail below in Section VII. It should be noted that estimates of PM emissions are highly uncertain and have had very limited field valuation and verification.

Both the transportation sector's contribution to emissions of the ozone precursors VOCs and NO_x and the importance of these precursors in ozone mitigation are well known and have been under study for several decades. Less well understood are the compound-specific contributions of exhaust emissions to local air quality. The compounds of interest include formaldehyde, acetaldehyde, and 1,3-butadiene (in the case of VOCs); metals, such as transition metals; and specific particle-size ranges, such as $PM_{0.1}$ (also referred to as ultrafine PM). Although the overall magnitude of the emissions of criteria pollutants is an important factor in meeting National Ambient Air Quality Standards (NAAQS), it must be noted that specific emissions components and the proximity of their sources to populations can be as important or more important than the magnitude of the emissions. This will be discussed in more detail in the next chapter.

The chemical composition of motor-vehicle emissions is quite complex and varies with the type of engine (spark ignition or diesel), fuel (gasoline, diesel, compressed natural gas, or biofuels), and control technology being used. Hundreds of organic compounds have been identified in motor-vehicle emissions; Table E.1 of Appendix E in this chapter (available on the HEI Web site) provides an example of a detailed compilation. Most of these compounds were measured at the emissions source, and many have not been specifically observed in ambient air. Dilution and the chemical and physical lifetimes of many compounds likely drive their concentrations below the analytical detection limits of typical ambient-air-pollution monitors. Detailed quantification of the composition of VOC or PM emissions by source type is a significant challenge, given the large number of engine types, changing technologies, and emissions controls that need to be considered. The development of composition profiles of emissions by source type has been the method of choice and is discussed later in Section 2.VI.3. Composition profiles and estimates of particle-number concentrations (which are typically dominated by particles less than 0.05 µm in diameter) are important factors in the modeling of on-road and near-road pollutant exposures, as discussed in Chapter 3. Particles less than 0.05 µm in diameter contribute negligibly to the mass of PM and would introduce significant measurement challenges if a particle-number emissions standard were to be implemented.

In the case of NO_x emissions, the fractional contribution of NO_2 is not well documented and might be altered by the introduction of new emissions-control strategies. California has found that because its NO_x-emissions standards have been sufficiently stringent, overall NO_2 concentrations have continued to decline even though the NO_2 fraction of total NO_x might have increased, especially for diesel vehicles. In Europe, although NO_x concentrations have been declining, the NO_2 fraction of roadside NO_x has been on the rise (Carslaw 2005). The source of this change is likely the introduction of advanced PM-emissions controls (such as filter traps) on diesel vehicles, which power a large fraction of the European fleet and might further raise future NO_2 concentrations. A few in-use vehicle studies have shown that exhaust emissions include other nitrogen compounds, such as ammonia (NH_3), nitrous acid (HONO), nitrous oxide (N_2O), and hydrogen cyanide (HCN), and that emissions of these compounds can be enhanced in cars equipped with three-way catalysts (Behrentz et al. 2004; Heeb et al. 2004, 2006; Baum et al. 2007).

2.VI. QUANTIFYING EMISSIONS FROM MOTOR VEHICLES

The quantification of motor-vehicle emissions is a critical factor in estimating their impact on local air quality and traffic-related exposures. Although the most important determinants of emissions from an individual vehicle are the technology mandated by emissions standards and the fuel quality mandated by fuel regulations, other factors related to the use of the vehicle, even beyond the total miles traveled, can also have an impact. Historically, emissions data have been limited to criteria pollutants and are derived from emissions models that depend critically on input data that are difficult to compile at a level of substantial spatial and temporal detail. The emissions models that will be needed and the technical challenges that will have to be addressed to meet the demand for high-quality estimates of traffic-related exposures are discussed in this section. In addition, several non-criteria pollutants that are associated with traffic-related exposure but are not currently estimated in emissions models are identified. Information about these pollutants will help distinguish the profiles of emissions from different sources or vehicle types in traffic-influenced environments. The future impacts on traffic-related exposures resulting from anticipated changes in the mix of vehicles, fuels, and emissions controls are also discussed.

Modeling the impact of on-road motor vehicles on air quality involves the characterization of travel activities, estimation of vehicle emissions, and consideration of the atmospheric transport, dispersion, chemistry, and deposition of

pollutants. In this section, selected models that are used to develop motor-vehicle-emissions inventories are described.

2.VI.1 MODELS USED TO ESTIMATE TRAVEL ACTIVITY

Characterization of the nature and extent of travel activity is essential for estimating emissions from motor vehicles. The key determinants of emissions in a region are the vehicle volume and speeds, total number of VMT per day, number of trips per day, and types of vehicles operating. Detailed characterization of travel activity is needed to develop the spatially and temporally resolved emissions inventories that are required by regional- and local-scale air-quality models.

2.VI.1.A Traffic Data

The most widely used method of measuring the magnitude of vehicle travel and roadway use in an area is to count traffic volume at selected locations along the roadways. Traffic volume is defined as the number of vehicles passing a given location on a given roadway during a specified period of time. Traffic volumes are routinely measured on major roadways in many parts of the world. Most traffic counts do not identify the types of vehicles operating on the roadway; however, special weigh-in-motion counters are used at selected locations to count vehicles by the number of axles and by weight class (but not by fuel type).

In the United States, the Federal Highway Administration (U.S. FHWA) requires state departments of transportation to collect and annually report traffic volumes on all state highways. It also requires counts of traffic volumes on selected highways for 13 vehicle classes reflecting the number of tires and axles as well as whether the vehicles are single- or multiple-unit trucks. Traffic volumes on highways and arterials are often measured continuously with high time resolution. In contrast, data on traffic volumes on rural and urban collector and local roads are usually sparse and are often collected only for special study periods. Traffic volumes are often reported as annual averages. Day-specific, seasonal, weekday, and weekend traffic volumes are reported less frequently or not at all. Annual traffic counts and VMT data are available to the public in the High Performance Monitoring System database maintained by the U.S. FHWA.

The distribution of traffic over time is important because the VMT, vehicle mix, and vehicle speeds vary by time of day. Agencies commonly report this distribution for traffic at selected locations. One-hour maximum traffic volumes are frequently two or more times greater than daily average volumes.

Vehicle speed is also important in estimating vehicle emissions. "Spot speed" at specific locations is commonly measured on many roadways. However, these instantaneous measurements can differ from the type of data needed for estimating emissions, which are the average speed over a given length of a roadway that reflects delays encountered by vehicles. These latter data are often collected in travel-time surveys. In special studies, vehicles have been equipped with global-positioning systems and data loggers to collect vehicle speeds, travel times, trip lengths, and day-of-week usage for periods of more than a week (Wolf et al. 2001; Huai et al. 2006). The collected data can be linked with transportation-network data from a geographic information system (GIS) to calculate speeds on specific road segments.

Surveys of trip origins and destinations are used to collect data on actual travel activity, which is important for developing forecasting models as well as policies and strategies for accommodating growth in travel. Home interviews are used to collect data on travel within a metropolitan area. Roadside surveys are used to collect data on through-trips and travel within and beyond a given area. These surveys provide a variety of information that cannot be obtained from traffic counts, such as trip starts and trip ends in traffic zones, and trips between two specific traffic zones.

2.VI.1.B Roadway-Location Data

Roadway-location data are needed to develop emissions inventories and to analyze the impact of traffic-related emissions on human health. These data are also needed for roadway-proximity estimates (often used in epidemiologic studies as surrogates of exposure to traffic-related air pollution [see Chapter 3]) and are sensitive to the spatial accuracy of the location data. Roadway-location data are available from the U.S. Census Bureau (2008) and other government agencies in the United States, but the degree of their spatial accuracy varies and might not be suitable for certain applications. More accurate and up-to-date roadway-location data are available from commercial vendors that supply digital maps for the global-positioning systems used in motor vehicles.

2.VI.1.C Travel-Demand Models

Travel-demand models were developed to make long-range forecasts of traffic volumes on roadway systems. For such models, a region is divided into travel-activity zones, and a roadway system is represented as a series of links and intersection nodes. Major roadways are represented explicitly; travel on local roads between zones is estimated in the aggregate (or using surrogate roads). The output of travel-demand models is frequently used to determine VMT per day and the number of trips per day for inventories of emissions

from on-road vehicles. Travel-demand models generally comprise four steps, including trip generation, trip distribution, mode choice, and traffic assignment (Deakin and Harvey 1993). The steps are sequential, and each step involves one or more submodels.

In best-practice analyses, demographic and socioeconomic forecasts and survey data are used in a preliminary step, before trip generation, to estimate the number of households with no workers, one worker, or two or more workers and the conditional proportion of households with no cars, one car, or two or more cars per household, given the number of workers per household. Daily trip generation is estimated for various trip purposes, including home-based work, home-based social or recreational activity, home-based school, other home-based activity, and non-home-based activity. Trip generation is estimated using linear-regression models that incorporate workers per household, household income, employment density, retail employment, service employment, vehicles per household, and household size. School trips might be divided into grade-school, high-school, and college trips, with trip generation dependent on school-population age and enrollment.

Trip distribution, the second step in developing a travel-demand model, frequently employs use of a gravity-flow model that includes a blend of peak and off-peak travel times. The gravity-flow model predicts a table of mean zone-to-zone travel times for each trip purpose. Fixed adjustment factors are applied to specific trip interchanges to account for variations in trip making not adequately explained by the gravity-flow model.

The third step, mode choice, employs statistical models to forecast travel mode by trip purpose. For home-based work trips, for example, it is common for a best-practices model to subdivide trips into bicycle, walk, and motorized modes. The next step subdivides the motorized trips by one-person auto, two-person auto, three-person auto, and transit modes. The transit trips are further divided into auto-access trips and walk-access trips. Mode choices for other trip purposes are less numerous and less nested. Survey data and statistical models are used to assign the time of trips to peak and non-peak traffic periods.

A variety of methods are used for traffic assignment, the fourth step in developing traffic-demand models. The object of this step is to achieve transportation-system equilibrium while maintaining internal consistency. Miller (1997) describes the static-user, dynamic-user, optimal-user, and stochastic-user equilibrium models as well as the process of incremental capacity-restrained assignment. Some applications incorporate feedback on travel speed into steps two and three (the trip distribution and mode choice), and iteratively refine the fourth step, travel assignments. Many analyses do not incorporate feedback or equilibration of demand with supply.

Deakin and Harvey (1993) have identified a variety of limitations in the current practice of travel-demand modeling (see Sidebar 2.5). Despite these concerns, the outputs of travel-demand models for traffic volume, trip origin, and trip destination are recommended by the U.S. EPA for use in compiling urban motor-vehicle-emissions inventories. They are considered superior to VMT estimated from traffic counts and roadway-geometry data.

2.VI.2 MODELS FOR ESTIMATING MOTOR-VEHICLE EMISSIONS FACTORS

2.VI.2.A MOBILE6

MOBILE6 is version 6.0 of MOBILE, a computer model developed by the U.S. EPA to predict emissions from on-road motor vehicles that was first released in 1978 as MOBILE1. It is the most widely used factor model of its kind. Modified versions of MOBILE are used throughout the world to estimate emissions factors. MOBILE6, the current basic version of the model, estimates emissions of HC, CO, and NO_x in grams per mile. More recent versions (MOBILE6.1 to MOBILE6.3) (*www.epa.gov/otaq/m6.htm*) also estimate emissions of PM, sulfur oxides, ammonia, air toxics, and selected GHGs. MOBILE6 is designed to include all types of on-road (also known as on-highway) vehicles, including light-duty cars and trucks, heavy-duty trucks, motorcycles, and buses. It also includes data suitable for predicting average fleet-emissions rates in the United States (excluding California) from 1987 to 2051. A similar model, the Emissions Factors model (EMFAC), is available for California. MOBILE6 relies heavily on U.S. Federal Test Procedure emissions data obtained as part of the new U.S. vehicle-certification program. To estimate total on-road emissions in a given area (typically a county), vehicle-emissions factors from MOBILE6 are combined with traffic-activity data, such as hourly VMT, roadway type, and area type (e.g., rural or urban). The model is commonly used to generate regional or aggregated data for use in emissions inventories for state implementation plans, determinations of transportation-plan conformity, analyses of emissions trends, environmental-impact statements, hot-spot analyses, and U.S. EPA rulings.

MOBILE6 estimates emissions for eight vehicle classes subdivided into 28 vehicle-technology classes. It considers both exhaust and evaporative emissions, including four exhaust modes (cold start, hot start, hot stabilized, and idle emissions) and six evaporative modes (diurnal, hot soak, running losses, resting losses, refueling losses, and crankcase emissions). It incorporates the U.S. federal vehicle-emissions standards (including the pre-control, Tier 0, Tier 1, Tier 2, and LEV standards). The most important additions

Sidebar 2.5 The Limitations of Travel-Demand Modeling

The current generation of travel-demand modeling has the following limitations:

- Key variables for predicting travel behavior, such as household income, parking and auto-operating costs, and the number of workers per household, are omitted.
- Trip-generation variables other than auto ownership and income (such as household size, which would be a good predictor) are omitted.
- Trip attractions are inadequately represented.
- In trip-distribution models, variables for the accessibility of public transit and walking are omitted.
- Peak and off-peak information by trip type and market segment is lacking.
- Socioeconomic variables affecting travel behavior are simplistically represented.
- Non-work travel is simplistically characterized and modeled.
- In many regions, the collection of data to develop and maintain adequate travel models (such as the regular collection of data on land use, land-use regulations, and monitoring surveys and networks) is insufficient.
- The characterization of travel in the travel-demand models for subsequent use in air-quality models is limited to estimates of peak and off-peak traffic on a typical weekday with school in session.
- Transportation models designed to address transportation-system capacity issues rather than air-quality issues are limited in six ways:
  1. They are not rigorously evaluated against observational data for the baseline period.
  2. They do not provide the hourly temporal resolution needed for air-quality analyses.
  3. They do not provide seasonal and weekday–weekend differences in travel estimates.
  4. They do not provide accurate distributions of speed by link.
  5. They do not distinguish accurately between traffic patterns for light-duty and heavy-duty vehicles.
  6. They do not provide traffic outputs for specific small- and moderate-size collector roads.

(Source: Deakin and Harvey 1993)

to MOBILE6 in recent years have been the new, lower emissions in the 2007 and 2010 standards for heavy-duty diesel trucks and the incorporation of the impact of NO_x "defeat devices." (These built-in devices cause engines from several manufacturers to produce lower emissions in certification tests than in typical in-use conditions. Typical in-use NO_x-emissions rates for heavy-duty trucks made between 1988 and 2000 are 4% to 29% higher than indicated by engine-certification data.) The model adjusts its emissions estimates to account for fuel characteristics, operating parameters, environmental parameters, and local control programs. The basic equations, methodology, and variables used to estimate the average emissions rate of a given class of vehicles are summarized in Sidebar 2.6.

Emissions estimates for heavy-duty vehicles are determined using data from engine-certification tests and data on energy use. Before installing heavy-duty engines in vehicles, manufacturers "certify" (test) a limited number of engines on dynamometers. Emissions rates are measured as the mass of a pollutant emitted per unit of work done by the engine, i.e., expressed as grams per brake-horsepower–hour (g/bhp-hr). Emissions factors (in g/bhp-hr) are converted to grams per mile using conversion factors that account for brake-specific fuel consumption, fuel density, and fuel economy. Temperature corrections are applied for gasoline vehicles. Speed corrections are applied for both gasoline and diesel vehicles.

MOBILE6 incorporates algorithms to adjust emissions rates for light-duty vehicles for the estimated effects of I/M programs. It splits the vehicle population into "normal emitters" and "high emitters." The default I/M effectiveness for modern vehicles equipped with OBD II on-board diagnostic equipment is 85% identification of high emitters, 90% repair rate for identified vehicles, and after-repair emissions level equivalent to normal-emitter level (or 1.5 times the certification standard, whichever is higher).

MOBILE6 does not use idling-vehicle emissions data directly to estimate idle-emissions rates. Instead, it estimates idle emissions from the emissions rates it calculates for vehicles traveling at 2.5 mph, its lower speed category.

MOBILE6's estimates of the evaporative and other non-exhaust emissions from gasoline-fueled vehicles include (1) the diurnal "breathing losses" that occur as the fuel tank heats up during the day, (2) the resting losses that

Sidebar 2.6 The Basic Equation of Emissions Factor Models

$$\left[\begin{matrix}Fleet\ Avg\\ Emissions\ Rate\end{matrix}\right]_{Veh\ Class} = \sum_{Age}\left[\begin{matrix}Travel\\ Fraction\end{matrix}\right] \times \left(\left[\begin{matrix}Base\\ Emissions\\ Rate\end{matrix}\right] + \left[\begin{matrix}Tampering\\ Offset\end{matrix}\right] + \left[\begin{matrix}Aggressive\\ Driving\end{matrix}\right] + \left[\begin{matrix}Air\ Condi-\\ tioning\end{matrix}\right]\right) \times \left[\begin{matrix}Temperature\\ adjustment\end{matrix}\right] \times \left[\begin{matrix}Speed\\ adjustment\end{matrix}\right] \times \left[\begin{matrix}Fuel\\ adjustment\end{matrix}\right]$$

The basic equation used in emissions factor models includes the summation of a set of variables performed over the 25 model years prior to the year of interest.

The travel fraction is the portion of VMT contributed by vehicles of various ages in the vehicle class. This is estimated from data on vehicle registration and mileage accumulation. Because registration data do not specify engine type, the proportion of diesel and gasoline-fueled vehicles is estimated from vehicle sales.

Base emissions rates in grams per mile (or grams/bhp-hr for heavy-duty vehicles) for running emissions, and grams per start for trip-start emissions are developed from Federal Test Procedure data modeled as a linear function increasing with vehicle mileage. The base emissions rate is a function of vehicle type, model year, and technology type and is obtained from tests on a chassis dynamometer for light-duty vehicles and trucks, an engine dynamometer for heavy-duty vehicles, and a chassis dynamometer for motorcycles on various urban driving cycles (the LA4 driving cycle [designed to represent city-driving conditions], for example, is used for light-duty vehicles). The proportion of high-emitting light-duty vehicles increases with vehicle age. Trip-start emissions are converted to grams per mile using data on average trips per day and miles per day.

The tampering offset is based on in-use data and is applied for pre-1996 vehicles that lack onboard diagnostic systems.

The factor for aggressive driving is incorporated because the Federal Test Procedure data for the LA4 driving cycle lacks real-world accelerations that add off-cycle emissions. It is based on supplemental Federal Test Procedure data for post-1999 light-duty vehicles.

The air-conditioning factor is calculated for full usage, scaled down by an estimated air-conditioning demand factor based on temperature and humidity adjustment. Depending on the pollutant being estimated, the air-conditioning factor is a function of speed, vehicle class, or emitter category. It is based on supplemental Federal Test Procedure data for post-1999 light-duty vehicles.

The temperature adjustment is applied to the emissions rates and defined at 75°F. A temperature is based on test data compiled for temperatures ranging from 20°F to 95°F. Temperature effects are a function of technology (such as carburetion versus fuel injection).

The speed adjustment is based on vehicle-test data for alternate test cycles and is applied for freeways, ramps, arterials, and local roadways. Vehicle-emissions rates are a nonlinear function of speed, and the nature of their dependence on speed varies widely by pollutant.

Federal Test Procedure tests of gasoline-fueled vehicles are run with Indolene (a standardized gasoline used by researchers that is non-oxygenated and free of additives, with a Reid vapor pressure of 9.0 psi and relatively low sulfur). The fuel adjustment is applied to account for differences between Indolene and conventional fuel and for the Reid vapor pressure as a function of temperature, oxygen content, and sulfur content.

The resulting estimates of emissions rates from the various classes of vehicles are combined to determine the fleet-average emissions rate for a given region and year. The emissions factors for each vehicle class are weighted according to the fraction of the total VMT that they represent, as shown here:

$$\left[\begin{matrix}Fleet\ Avg\\ Emissions\\ Rate\end{matrix}\right] = \sum_{Veh\ Class}\left[\begin{matrix}VMT\\ Mix\end{matrix}\right]_{Veh\ Class} \times \left[\begin{matrix}Fleet\ Avg\\ Emissions\\ Rate\end{matrix}\right]_{Veh\ Class}$$

The final VMT mix is calculated using MOBILE6 modeling software by applying average annual mileage-accumulation rates for each vehicle class to estimates of class sizes. The default VMT mix for 2010, for example, is 35.4% light-duty gasoline-fueled cars, 51.7% light-duty gasoline-fueled trucks, 0.2% light-duty diesel trucks, 3.6% heavy-duty gasoline-fueled trucks, 8.6% heavy-duty diesel trucks, and 0.5% motorcycles.

result from vapor permeation and liquid leaks through various parts of the evaporative-control system, (3) hot-soak losses that occur after the vehicle has been turned off, resulting from evaporation of fuel in the engine and fuel-delivery system, (4) running evaporative losses that occur as the vehicle is being operated over the road, (5) refueling losses that are a result of vapor space displacement and spillage, and (6) crankcase losses that are primarily the result of defective positive-crankcase-ventilation systems. The modeled evaporative-emissions rates are based on U.S. evaporative standards and vehicle-certification evaporative-test results. Evaporative emissions are modeled by subdividing the fleet by type of fuel-delivery technology and by whether vehicles have passed or failed purge-and-pressure testing. As with exhaust emissions, MOBILE6 also includes data for "gross liquid leakers," vehicles with excess evaporative emissions. Composite emissions rates by vehicle age are determined as a weighted sum of the emissions rates from vehicles that passed or failed purge-and-pressure testing. The proportion of vehicles that failed and of vehicles that are gross liquid leakers increases with vehicle age. Estimates of evaporative-emissions are adjusted to account for the local Reid vapor pressure (a measure of fuel volatility) and ambient temperature. Estimates of hot-soak emissions are adjusted for the estimated distribution of soak time. Running losses are also corrected for speed and trip length, as longer trips result in more fuel heating and higher running losses. MOBILE6 calculates the diurnal losses for each hour of the day, given hourly temperature data. It also converts all evaporative-emissions rates to grams per mile using data on average trips per day, miles per day, and miles per gallon.

MOBILE6 has a number of issues and limitations that are of concern. These are a subset of more general concerns about modeling motor-vehicle emissions (see below). A detailed and extensive list of these concerns can be found in the MOBILE review conducted by the National Research Council (2000). Seven specific concerns about MOBILE6 are listed below.

1. It assumes that an equal number of vehicles travel uphill and downhill and does not account for the effect of roadway grade (i.e., on speed and load) on emissions, which can be large because of the nonlinearity of emissions with speed and load.
2. It uses only one variable, average vehicle speed, to represent vehicle-operating modes. Operating modes, such as idle, steady-state cruise, and degree of acceleration and deceleration, can have a large effect on emissions, independent of vehicle speed. MOBILE6's simple adjustment for aggressive driving, for example, is insufficient to address this issue.
3. Its characterization of emissions from high emitters is based on sparse data and is highly uncertain. High emitters contribute a disproportionate amount of emissions and need better characterization.
4. Its method of estimating PM emissions, independently of vehicle speed, load, or ambient temperature, is overly simplistic. The PM in tire-wear and brake-wear emissions is constant for each vehicle class. Emissions of resuspended fugitive dust from vehicle travel on paved and unpaved roads are not included in estimates of PM emissions, even though they are often the largest contributor to emissions of PM_{10}.
5. Its estimates for emissions of MSATs are based on estimated fractions of VOCs or PM rather than on detailed data on the individual MSATs.
6. It is only suitable for estimating emissions for aggregated vehicle activity on an urban and regional basis. The spatial and temporal scales inherent in MOBILE6 have limited capability in supporting modeling of emissions on a mesoscale or instantaneous emissions on a microscale.
7. Its estimates are of unknown accuracy and degree of uncertainty. Few evaluation studies have been performed. This is surprising, given MOBILE6's age and its important role in air-quality management and policy making. The lack of performance evaluation studies is a major shortcoming. Testing MOBILE6's ability to estimate actual in-use vehicle emissions is feasible using data from state emissions-inspection testing, remote sensing, roadside-pullover inspections, tunnel studies, ambient air-quality monitoring, and air-quality models.

2.VI.2.B Other Motor-Vehicle Emissions Models

Other models of motor-vehicle emissions have been developed, and some are summarized in this section.

The EMFAC model was developed by the California Air Resources Board to estimate fleet-average emissions rates for California vehicles (California Air Resources Board 2007). Because vehicles sold in California have to meet stricter emissions standards than vehicles sold in other states, the California Air Resources Board developed EMFAC, which uses data on California vehicle certification and activity. EMFAC was developed in parallel with MOBILE and takes the same overall approach using data specific to vehicles traveling on California roads (Shah et al. 2006).

Singer and Harley (1996) developed a fuel-based method for calculating inventories of motor-vehicle emissions. In this method, emissions factors are normalized to fuel consumption and expressed as grams of pollutant emitted per gallon of fuel burned (rather than per mile of

vehicle travel). Fleet-average emissions factors are calculated from measured on-road emissions of a large, random sample of vehicles. The model was demonstrated in Southern California by remote-sensing measurements of CO emissions from more than 70,000 in-use vehicles. The potential benefits of this method are that fuel-consumption data might be more accurate than VMT, and the resulting estimates of vehicle-emissions rates are based on in-use measurements rather than certification-test data and deterioration factors. Potential difficulties in applying the method are that it requires many remote-sensing measurements and that not all pollutants of interest can be measured remotely with adequate sensitivity.

A new model called the Motor Vehicle Emissions Simulator (MOVES) is being developed by the U.S. EPA to address new analysis and modeling needs that cannot be met by MOBILE6. The MOVES model consists of a suite of software packages or modules designed to estimate emissions for on-road and non-road sources. It covers a broad range of pollutants and supports multiple scales of analysis, from fine spatial and temporal scales to annual national emissions inventories. Its capabilities are similar to those of the U.S. EPA's MOBILE6 and NONROAD models. (NONROAD estimates emissions for off-road mobile sources, such as logging, agricultural, and construction equipment; aircraft; and recreational vehicles.) MOVES also estimates modal emissions to support microscale traffic analyses. An important feature of MOVES (as opposed to MOBILE6) is that it uses in-use emissions data. It is also designed to facilitate testing against real-world data much more easily than MOBILE6 was. A description of the model and the MOVES software, as well as a demonstration version, are available (*www.epa.gov/otaq/models/moves*). The U.S. EPA intends to replace MOBILE6 and NONROAD with MOVES.

2.VI.3 ISSUES AND LIMITATIONS IN MODELING MOTOR-VEHICLE EMISSIONS

The principal limitations of modeling motor-vehicle emissions are the degree of quality of the traffic information and of the accuracy of the emissions models. As noted above, traffic-count data and the outputs of travel-demand models lack the spatial and temporal resolution desired for detailed traffic characterization. Traffic and emissions models are not subjected to comprehensive evaluation to assess their accuracy and degree of uncertainty. Uncertainties in the data and in associated assumptions in models of motor-vehicle emissions have not been explicitly quantified and remain the major challenges in improving estimates of motor-vehicle emissions. In the absence of such uncertainty estimates, confidence levels have been suggested by emissions experts based on the current state of knowledge (NARSTO, 2005). This approach provides qualitative insight in setting priorities to reduce uncertainty in emissions estimates from sources having the greatest impact on aggregate emissions.

Concerns for discrepancies between real-world vehicle emissions and model estimates remain because of the lack of evaluation data and the slow rate of model improvements after the discovery of model biases.

The development of profiles of the composition of emissions by vehicle type within the mobile-source emissions category is necessary to support emissions-based air-quality models and source-attribution models for estimating traffic-related exposures. The development of profiles of the species composition of VOCs or PM from motor-vehicle emissions by vehicle type is a significant challenge, given the many vehicle types, changing technologies and fuels, and emissions controls that must be considered. Emissions characterization from laboratory dynamometer testing (see Fujita et al. 2007, for example) remains the principal method of developing speciation profiles for emissions from various engine and vehicle types.

The profiles by vehicle types developed over the past several decades provide the fundamental data used in emissions models. SPECIATE 4.0 (U.S. EPA 2006) is the current version of the U.S. EPA's database-management software package that provides access to a repository of speciation profiles of total organic compounds and PM from air-pollution sources; it can be queried to provide speciated emissions for air-quality models, input to chemical-mass-balance receptor models, and verification of profiles derived from multivariate receptor models. The California Air Resources Board has developed an interactive data-access Web site (*http://arb.ca.gov/ei/speciate/interopt06.htm*) that provides downloadable speciation profiles.

2.VI.4 SUMMARY

Quantifying emissions from motor vehicles requires the collection of fundamental data on traffic over space and time, including, for example, traffic counts, vehicle types, travel speeds, fuel types, and emissions controls. The amount of resources required for collecting such data can be prohibitive and has stimulated the use of travel-demand models, which forecast traffic volumes on roadway systems based on estimates of trip generation, trip distribution, mode choice, and traffic assignment. Although a variety of limitations have been identified in current travel-demand models, VMT estimates from these models are considered superior to VMT estimates from traffic-count data for the development of regional emissions inventories. Data on local traffic counts and roadway locations might be more

appropriately used when data on small-area variations in traffic and vehicle emissions are needed to analyze traffic-related health effects.

Computer models used to estimate emissions from on-road vehicles have evolved over three decades and now provide estimates of emissions rates in grams per mile for total HC, CO, NO_x, PM, SO_2, NH_3, selected air toxics, and GHGs. The large number of parameters and complex algorithms used in these models suggest the presence of significant uncertainties and limitations in the resulting emis-sions estimates. In addition, emissions models do not account for the effects of roadway grade, operating mode (other than average speed), and high emitting vehicles.

Emissions estimates for PM and air toxics are limited and need to be better characterized to reduce their high uncertainty. The quality of the speciation profiles used to apportion the chemical composition of emissions to specific source types is a contributing factor to the uncertainty in species-specific emissions estimates, especially in that many profiles have not been updated for a decade or more and might not reflect changes in technology that have affected various motor-vehicle classes.

Given the pivotal role that emissions models play in the generation of regional or aggregated data for use in emissions inventories for state implementation plans, determinations of transportation-plan conformity, analyses of emissions trends, environmental-impact statements, hot-spot analyses, and U.S. EPA rulings, the extent of the evaluation and verification of these models by means of actual field measurements has been quite limited. This represents a major shortcoming that should be considered when evaluating the results from an emissions-based model and the local impact of motor-vehicle emissions on air quality and human exposure.

2.VII. EMISSIONS FROM TIRE WEAR, BRAKE WEAR, AND RESUSPENDED ROAD DUST

Tire wear, brake wear, and resuspended road dust are sources of noncombustion emissions from motor vehicles. Although these emissions are not regulated in the way exhaust emissions are, they need to be considered in assessing the impact of motor vehicles on human health. As tailpipe-emissions controls become more effective, PM emissions from noncombustion sources will make up a larger proportion of vehicle emissions. Furthermore, emissions from these sources contain metals and condensed organic compounds that might contribute to the health effects of motor-vehicle emissions.

Particles from tire wear are mechanically generated by the rolling shear of tire tread against the road surface. The rate of tire-tread wear is quite variable; the average tread wear for a single passenger tire ranges from 0.006 g/km to 0.09 g/km, depending on the type of road conditions (e.g., asphalt or concrete), driving conditions (e.g., acceleration, abrupt deceleration, speeding, or turning), and tire conditions (e.g., tire type, tire pressure, or vehicle load). Most of these particles are coarse; less than 10% are fine (Rogge et al. 1993). Tire-wear particles consist primarily of organic material, including various styrene-butadiene-rubber polymers, natural rubber, *n*-alkanes ranging from C19 to C41, *n*-alkanoic acid (primarily stearic acid), and PAHs (Rogge et al. 1993).

Modern brake pads are made of non-asbestos materials; about one-third of this material becomes airborne PM as the brakes wear. The rates of PM emissions from brake wear range from 5.1 mg/mile to 14.1 mg/mile (3.2 to 8.8 mg/km) for modern light-duty cars and trucks (Garg et al. 2000) (wear rates were measured in milligrams per stop and converted to equivalent continuous emissions rates using the average life of the brakes). Higher rates are expected for heavy-duty vehicles. Brake wear generates smaller particles than other noncombustion emissions processes, such as the resuspension of road dust. Testing a variety of modern brake materials on a brake dynamometer showed that the PM_{10} mass from brake wear consisted of 27% coarse particles ($PM_{10–2.5}$), 35% fine particles ($PM_{2.5–0.1}$), and 38% ultrafine particles (Garg et al. 2000). These researchers also found that about 18% of the mass was carbonaceous material (primarily organic carbon). Aluminum, barium, calcium, copper, manganese, molybdenum, potassium, phosphorus, silicon, strontium, sulfur, titanium, vanadium, and zirconium accounted for most of the remaining mass. The elemental composition of brake particles varies with the brake material. In tunnel studies, Lough and colleagues (2005) found elements from brake wear in the tunnel dust and determined that antimony, barium, calcium, and copper were important components of $PM_{2.5}$ in that environment.

In addition to PM emissions from exhaust, tire wear, and brake wear, significant PM emissions are contributed by road dust that is resuspended by vehicles traveling over it on paved or unpaved roads. The dust is pulverized on the roadway and then resuspended by turbulence in the vehicles' wake. Over time, equilibrium is established between the amount of dust deposited on and resuspended from a road.

Road-dust emissions are often an important source of PM_{10} in urban emissions inventories and in the atmosphere in general. These dust particles are mechanically

generated from crustal materials (local soils). The analysis of samples of paved-road dust showed that coarse particles, consisting of approximately 85% to 95% PM_{10}, ranged in size from 2.5 μm to 10 μm; on average, less than 25% of the PM_{10} mass consisted of particles with diameters of less than 2.5 μm (Cowherd Jr and Donaldson 2005). Road dust includes a combination of mineral oxides commonly found in soils (Gillies et al. 2001) plus organic constituents from vehicle exhaust, such as polycyclic aromatic hydrocarbons (PAHs) (Smith et al. 1995); elements from tire wear and brake wear (Rogge et al. 1993); platinum-group elements from catalytic converters (Gómez et al. 2002; Whiteley and Murray 2003); and allergens (Miguel 1999). In a study of dust collected in two tunnels in Wisconsin, Lough and colleagues (2005) found that the most abundant elements (measured by X-ray fluorescence and inductively coupled plasma–mass spectrometry) in road dust as percentages of total PM_{10} mass were iron (average 4.5% ± 1.7%), calcium (4.2% ± 0.9%), silicon (3.9% ± 0.8%), sodium (2.2% ± 0.8%), magnesium (1.1% ± 0.2%), sulfur (0.84% ± 0.26%), aluminum (0.69% ± 0.24%), and potassium (0.41% ± 0.10%). Other less abundant elements measured in road dust included barium, zinc, copper, antimony, lead, manganese, nickel, arsenic, cadmium, and chromium.

Emissions rates for road dust are influenced by many factors. For paved roads, the most important factors are believed to be vehicle speed, average daily traffic volume, the number of lanes and volume per lane, the fraction of heavy vehicles (buses and trucks), and the presence or absence of curbs, storm sewers, and parking lanes (Midwest Research Institute 1993). Weather and the condition of the roadway surface can also be important (Lough et al. 2005). For unpaved roads, emissions rates are known to vary with the volume of traffic and the fraction of silt (particles smaller than 75 μm in diameter) in the road-surface material (Cowherd Jr 1974). Cowherd and colleagues (1974) developed empirical equations to estimate emissions rates for road dust in grams per mile on paved and unpaved roads based on the silt loading (the mass of silt-size material per unit area of travel surface), average vehicle weight, particle-size class, and frequency of days with measurable ($P > 0.01$ inch) precipitation or soil-material moisture content. The equations were incorporated into the U.S. EPA's AP-42 guidance document for emissions calculations (U.S. EPA 2007c) and are widely used.

The emissions rates were statistically derived from measurements of differences in upwind and downwind concentrations of PM_{10} and its chemical constituents obtained near industrial roadways with various silt loadings and at difficult heights using the chemical-mass-balance approach. However, inferring emissions rates from such measurements at several heights and locations using the mass-balance approach is problematic and uncertain. The resulting emissions rates were parameterized in terms of silt loading and vehicle weight. The rates are strong functions of silt loading, which can vary from 0.03 g/m^2 to 400 g/m^2, and is rarely measured on roads — especially limited-access roads, which have the highest traffic volumes. A cross-validation study of estimates for dust from paved roads conducted by the U.S. EPA (1993) showed that 50% of the data differed from the predicted values by factors of more than three; the 90% confidence interval for the ratio of predicted-to-observed values was a factor of eight for a core data set and 9.5 for a larger set. The results suggest order-of-magnitude uncertainties in the estimates routinely made for resuspended road dust.

Several other methods of estimating dust emissions from paved roads have been investigated. In addition to the mass-balance approach using PM-concentration profiles taken by Cowherd and colleagues, three groups of researchers used dispersion models to fit measurements of the tracer sulfur-hexafluoride and PM_{10} concentrations and to infer PM_{10}-emissions rates (Clairborn et al. 1995; Kantamaneni et al. 1996; Venkatram et al. 1999). Fitz and colleagues measured PM concentrations in a roadway with instrument probes located on the front of a moving vehicle and on a trailer towed behind the vehicle (Fitz and Bufalino 2002; Fitz et al. 2005). Data from these investigations showed a wide range in variability in emissions factors for road dust and suggested that more investigation is needed to characterize these emissions accurately.

In summary, the emissions from tire wear, brake wear, and resuspended road dust should not be overlooked in assessments of vehicles emissions and their effects on human health. Noncombustion emissions make up an increasingly large proportion of total vehicle emissions, and they contain chemical compounds, such as trace metals and organics, that might contribute to human health effects.

2.VIII. SOURCE APPORTIONMENT OF MOTOR-VEHICLE EMISSIONS

Receptor models and air-quality dispersion models have been used to estimate the contributions of various types of sources, including motor vehicles, to ambient air pollution. In this section, we focus on multivariate receptor models, which use measured concentrations to estimate the contributions of sources at specific receptors (i.e., monitoring sites). (Air-quality dispersion models are discussed in Section IV of Chapter 3.) Receptor models have

been developed and applied to estimate air-pollution source apportionment for more than 30 years (Miller et al. 1972). They are best suited to assess the source contribution of pollutants that are complex mixtures of chemical constituents, such as PM and VOCs, where differences in the composition of pollutants from different types of sources can be exploited.

The fundamental principles of receptor modeling are that mass conservation can be assumed and that a chemical-mass-balance analysis can be used to identify and apportion sources of airborne PM or VOCs. Receptor modeling requires measurement data for a large number of chemical constituents over a number of samples. The mass balance can be written to account for all m species in the n samples as contributions from p independent source types.

$$x_{ij} = \sum_{p=1}^{P} g_{ip} f_{jp} + e_{ij}, \quad (1)$$

where x_{ij} is the measured concentration of the jth species in the ith air sample, g_{ip} is the contribution of the pth source type to the ith air sample, f_{jp} is the concentration of the jth species in material emitted by source type p, and e_{ij} is the portion of the measurement that cannot be fitted by the model.

A variety of approaches have been implemented to solve this equation. A key feature distinguishing the approaches is whether the source emissions profile (f) is known. The chemical-mass-balance model uses measured source emissions profiles for the suspected source types and solves for the mass contributions using effective-variance least-squares regression (Watson et al. 1984). It has been used extensively for source apportionment of PM and has been found to apportion major categories of primary sources effectively when the source emissions profiles were known with certainty and were sufficiently distinct from one another (Chow and Watson 2002). Typically, the chemical-mass-balance model is able to distinguish contributions from four to eight types of sources, including motor vehicles. It is only rarely able to distinguish reliably between contributions of resuspended road dust and of other types of fugitive-dust sources (Watson et al. 1994). Its ability to separate primary PM contributions of diesel and gasoline-fueled vehicles is enhanced when individual particle-phase organic compounds, such as PAHs, are included (Schauer et al. 1996, 2002; Schauer and Cass 2000; Zheng et al. 2002; Fraser et al. 2003; Fujita et al. 2007). Secondary aerosols from all types of sources emitting SO_2, NO_x, or VOCs are often reported as a separate "source contribution" (of SO_4, NO_3, or secondary organic aerosol) even though the model cannot distinguish the different types of sources contributing the secondary aerosols (e.g., power plants or motor vehicles). Uncertainty in the local source profiles and changes in source profiles between source and receptor locations caused by atmospheric processes often limit the ability of the chemical-mass-balance model to account adequately for the observed mass concentrations.

Recently, applications of the chemical-mass-balance model to $PM_{2.5}$ source apportionment have been extended by incorporating SO_2, CO, and NO_2 gas-to-particle ratios in $PM_{2.5}$-source data (Marmur et al. 2005, 2006, 2007), which can help identify (and separate) sources that have fairly similar $PM_{2.5}$-emissions composition and significantly different gaseous emissions. Results for Atlanta, Ga., indicated that this extended model is able to separate the $PM_{2.5}$ contributions of exhaust from gasoline-fueled and diesel vehicles more accurately than the chemical-mass-balance model without the gas-to-particle ratios. It also more accurately quantified the contribution of primary $PM_{2.5}$ emissions, i.e., $PM_{2.5}$ emitted directly into the atmosphere, of coal-fired power plants to ambient $PM_{2.5}$ than did the conventional chemical-mass-balance model.

Most other receptor models employ various types of factor analysis to solve Equation 1 for both the source profiles and the contributions over a set of samples. Principal-component analysis, absolute principal-component analysis, and confirmatory factor analysis have been applied to PM (Hopke et al. 1976; Koutrakis and Spengler 1987; Hopke 1999). Additional efforts have focused on two newer factor-based approaches: the UNMIX model developed by Henry (Henry 1991, 2000) and the positive matrix factorization (PMF) model developed by Paatero and Hopke (Paatero 1997, 1999). These two newer models put constraints on the possible solutions (e.g., non-negative source impacts) to achieve physically meaningful results. UNMIX uses principal-component analysis to reduce the dimensionality of the data space and additional constraints derived from "looking at the edges of the data." Various forms of the PMF model exist, including PMF2, PMF3, the flexible multilinear engine, and the expanded multilinear engine. PMF uses explicit least-squares analysis instead of the implicit least-squares analysis used by the other models. PMF and UNMIX have been widely applied to estimate PM source contributions and, to a lesser extent, VOC source contributions. Their ability to distinguish exhaust factors from diesel and gasoline-fueled vehicles is improved when temperature-resolved carbon fractions (Lee et al. 2003; Maykut et al. 2003; Kim and Hopke 2004, 2005; Kim et al. 2004; Liu et al. 2006) or individual particle-phase organic compounds (Larsen and Baker 2003; Lee et al. 2004) are included. It is important to

recognize that the results are a set of distinct chemical-composition profiles and contributions associated with the profiles. Analysts must evaluate, based on their knowledge of measured source composition, whether the profiles represent one or more specific types of sources.

Receptor models have been applied in many locations to estimate source contributions to ambient PM. Tables C.1 through C.4 in Appendix C of this chapter (available on the HEI Web site) list representative studies in which the contributions of motor vehicles to PM in urban areas have been estimated. Almost all PM source-apportionment studies in urban areas have identified a contribution from motor vehicles. Some have distinguished between motor-vehicle exhaust and resuspended road dust. Many source-apportionment studies for cities in the U.S. (Table C.1) have made separate estimates for the contribution of exhaust from diesel and gasoline-fueled vehicles. Few studies of regions outside the U.S. (Table C.2) also report separate contributions from diesel and gasoline-fueled vehicles. A number of recent studies have focused on apportioning the contributions from diesel- and gasoline-fueled vehicles to primary organic PM or PAHs (Table C.3). None of the models distinguished between emissions from off-road and on-road vehicles, which is probably an important distinction for understanding total diesel-vehicle emissions.

Receptor models yield a wide range of results for $PM_{2.5}$ and PM_{10}. The results summarized in Table C.1 indicate that, in U.S. cities, motor-vehicle contributions range from 5% in Pittsburgh, Pa., under conditions with very high secondary aerosol, to 49% in Phoenix, Ariz., and 55% in Los Angeles, Calif. Variations within cities can be large. Analyses for a suburban location in Los Angeles, for example, estimated that only 10% of $PM_{2.5}$ was from motor-vehicle exhaust. Estimates of diesel-vehicle contributions to $PM_{2.5}$ in the U.S. ranged from 1% in Baltimore, Md., to 32% in Los Angeles. The same studies estimated contributions from gasoline-fueled vehicles ranging from 0% in Missoula, Mont., to 33% in Phoenix. The contribution of diesel and gasoline-fueled vehicles varies widely within cities and between cities. Outside the United States, estimates of the contribution of motor-vehicle exhaust to $PM_{2.5}$ range from 6% in Beijing, China, to 53% in Barcelona, Spain (Table C.2). Estimates of the contribution of motor-vehicle exhaust to PM_{10} range from 4% in northern Chinese cities to 48% in Madrid, Spain, and even 63% on a roadside in Thessaloniki, Greece. Differences in the models and quality and extent of the input data also affected these results.

A number of PM-source-apportionment studies have intercompared receptor models by applying them to a common set of data (Maykut et al. 2003; Ito et al. 2004; Marmur et al. 2005, 2006; Buset et al. 2006; Hopke et al. 2006; Yuan et al. 2006; Brook et al. 2007; Chen et al. 2007) (see Table C.4). Hopke and colleagues (2006) reported on one of the largest intercomparison of these studies, which used $PM_{2.5}$ data from Washington, D.C., and Phoenix, Ariz. The study involved eight research groups. Each research group applied one or more of eight models (UNMIX, PMF2, multilinear engine, principal-component analysis, absolute principal-component analysis, expanded multilinear engine, confirmatory factor analysis, and targeted factor analysis). The number and nature of source profiles derived by the various groups and models were not consistent. The number of source types identified ranged from 3 to 10 in Washington and 4 to 8 in Phoenix. The names used by the groups to describe the source categories varied widely. Nevertheless, traffic (or motor vehicles) was identified as a source type in all of the analyses. The estimates of traffic contributions to $PM_{2.5}$ were more variable for Phoenix (27–59%) than for Washington (8–23%); however, all of the models estimated that traffic was the largest contributor to $PM_{2.5}$ in Phoenix and the second or third largest contributor in Washington, D.C. The contribution of emissions from diesel-fueled vehicles was distinguished from those of gasoline-fueled vehicles in 4 of 9 cases that made use of data from Washington and 7 of 11 cases that made use of data from Phoenix.

The estimates of contributions from diesel and gasoline-fueled vehicles made by the various models were poorly correlated. The research groups agreed that better data are needed to distinguish accurately between emissions of diesel and gasoline-fueled vehicles. Despite differences in naming conventions, many similar source profiles were identified in the comparisons of models. Crustal (soil), sulfate, oil, and salt profiles were most unambiguously identified and highly correlated across research groups and models. The contribution estimates were especially similar across research groups for traffic and secondary sulfate in Phoenix, and for traffic and secondary nitrates in Washington ($r = 0.9$), and to a lesser extent for secondary sulfate in Washington ($r = 0.75$). Overall, the results from these intercomparisons showed improved performance among the models relative to previous intercomparison studies (Hopke 1991).

Other intercomparison studies in Toronto, the San Joaquin Valley in California, New York, and Hong Kong reported fairly similar estimates from the PMF, UNMIX, multilinear-engine, and principal-component-analysis models. Studies in Seattle, Wash., and Atlanta, Ga., however, reported large differences between estimates from the PMF and chemical-mass-balance models, the UNMIX and chemical-mass-balance models, and the chemical-mass-balance model and the chemical-mass-balance model with the Lipschitz global optimizer (Maykut et al. 2003; Marmur et al. 2006).

There are a number of issues in connection with the use of receptor models for source apportionment. Reff and colleagues (2007) reviewed existing methods of applying the PMF model to PM and noted that few publications reported the procedural decisions and the selection of model parameters in enough detail for other researchers to be able to evaluate, reproduce, or compare results across studies. Few publications explain the criteria for the selection of the pollutant species used in the modeling, how the number of source factors was selected, or how uncertain the results were. Inconsistencies exist in the handling of data below the limits of detection, in the ways PM mass is apportioned among sources identified by the PMF model, and in the way uncertainties are estimated in results. Reff and colleagues made recommendations for detailed documentation of the methods used in PMF modeling and for the areas in which research was needed to improve and standardize PMF modeling. Many of these issues apply to other multivariate models as well.

The ability of receptor models to distinguish motor-vehicle emissions from other types of emissions accurately and then to identify and distinguish the components of motor-vehicle emissions from each other is a major issue for traffic studies. PM contributions from motor vehicles, for example, are first distinguished from those of other sources; the relative contributions from diesel and gasoline-fueled vehicles are then estimated (primarily on the basis of organic carbon [OC] and EC data). The availability of data on temperature-resolved fractions of carbonaceous species has proved to be very helpful in distinguishing these sources (Chow et al. 2005; Kim and Hopke 2005; Brown et al. 2007; Buzcu-Guven et al. 2007). However, difficulties arise because wood smoke and secondary organic aerosols are richer in organic carbon than in elemental carbon, much like emissions from gasoline-fueled vehicles. In a study in Phoenix, Ariz., Brown and colleagues (2007) distinguished wood smoke from emissions from diesel and gasoline-fueled vehicles using a two-step PMF-modeling process and estimates of potassium not derived from soil (used as a marker for wood smoke). Buzcu-Guven and colleagues (2007) also identified a general motor-vehicle profile and a separate diesel profile in the Midwestern United States using PMF, but the general mobile-source factor (with high concentration of organic carbon [OC] and high OC/EC ratios) may have included contributions from anthropogenic and biogenic secondary organic aerosols.

The U.S. Department of Energy's Gasoline/Diesel PM Split Study was conducted to identify unique compounds that can be used to separate the contributions of diesel and gasoline-fueled vehicles (Fujita et al. 2005; Lawson et al. 2005). As more ambient measurements are made with relevant organic tracers, the prospects for more accurate source apportionment of emissions from these two sources will improve. Distinguishing the motor-vehicle contribution to road dust from that of other fugitive dust sources, such as construction and agricultural activities, can be problematic because the profiles of the chemical constituents are collinear. As a result, neither emissions inventories nor receptor models can accurately describe the contribution of motor vehicles to road dust (Watson and Chow 2000).

Interpretation of the factors predicted by receptor models is also an issue, because it is the most subjective and least quantitative aspect of modeling. To select their sources, researchers most frequently search libraries of PM-source composition for profiles and enrichment ratios similar to those in their source factors. There is no guarantee that a receptor model's factor represents just one source type. Analysis of spatial and temporal patterns in the source contributions can assist in identification (e.g., wood smoke during cold winter months and secondary organic aerosols in summer, when photochemical activity is high) (Ramadan et al. 2000; Liu et al. 2005). Auxiliary analyses, such as back-trajectory analysis and dispersion modeling, can be used in conjunction with receptor modeling to help identify specific sources corresponding to the predicted factors (Watson et al. 2002; Kim et al. 2003; Held et al. 2005; Kim and Hopke 2005; Marmur et al. 2006; Lane et al. 2007). Associations between the contribution factors and meteorologic data or other air pollutants (such as NO_x, ozone, NH_3, or CO) have also been examined. The use of multiple auxiliary analyses such as these can increase confidence in factor identification.

In summary, a large number of multivariate receptor models have been developed and applied to estimate source contributions of pollutants in urban and rural areas. These include models that do not require a priori knowledge of source composition profiles and models that use data on both gaseous and particulate species. Improvements in models and measurement databases have enhanced the ability of the models to distinguish sources such as motor vehicles from other sources; however, accurate estimation of the separate contributions of diesel and gasoline-fueled vehicles to ambient PM continues to be a challenge.

2.IX. METHODS FOR MEASURING MOTOR-VEHICLE EMISSIONS

Up to this point, most of the discussion has focused on trends in motor-vehicle fleets, regulations, and control technologies as well as on models that estimate motor-vehicle emissions and their contribution to ambient air pollution. However, the actual measurement of motor-

vehicle emissions is critically important for validating the models (because we have learned over the years that models can be significantly biased in their estimates of emissions [National Research Council 2000; NARSTO 2005]) and for estimating human exposure to traffic-related pollutants. Demonstrating the validity of emissions models and the efficacy of regulatory controls introduced over the past three decades remain two of the greatest challenges to air-quality researchers. This section discusses field-measurement approaches that have been used in recent years to address specific elements of the characterization, quantification, and tracking of motor-vehicle emissions.

2.IX.1 CHARACTERIZATION OF EMISSIONS FROM IN-USE ON-ROAD VEHICLES

2.IX.1.A Mobile Instrumented Laboratories

Mobile instrumented laboratories designed for performing vehicle-chase studies to characterize in-use emissions are becoming commonly available (Cocker 3rd et al. 2004; Kittelson et al. 2004; Kolb et al. 2004; Westerdahl et al. 2005). With an instrumented trailer towed behind a truck, direct measurements of on-road truck emissions can be performed (Kittelson et al. 2001; Morawska et al. 2007). An extendable inlet probe from the trailer collects samples of exhaust gases and aerosols at various stages of plume dilution. A feature of studies using these instrumented trailers is that emissions samples can be obtained from vehicles over prescribed drive cycles, speed profiles, or other operational variables of interest and then directly compared with emissions characterizations made with laboratory chassis dynamometers.

2.IX.1.B Vehicle-Chase Studies

The feasibility of deploying mobile laboratories that follow closely behind motor vehicles to sample their exhaust plume and measure various gas-phase and aerosol constituents has been demonstrated (Canagaratna et al. 2004; Cocker 3rd et al. 2004; Westerdahl et al. 2005; Kittelson et al. 2006). These "vehicle-chase studies" have been described in detail in Canagaratna and colleagues (2004) and typically entail having a mobile lab follow a target vehicle at a distance of approximately 3 to 15 meters while the vehicle moves through city traffic or quiet neighborhoods (or, if the target vehicle is a bus, while it makes stops to pick up or discharge passengers). Instantaneous measurements of PM or selected exhaust gases, and their correlations with CO_2 used as the exhaust-plume tracer, are fundamental to the experimental design.

The application of this method has been quite successful and has demonstrated (1) that a mobile lab is a viable means of measuring the PM mass, gases, and chemical species in emissions from a large number of in-use on-road motor vehicles (Canagaratna et al. 2004; Kolb et al. 2004); (2) that compressed natural gas (CNG)-fueled buses and diesel-fueled buses equipped with Continuously Regenerating Technology (CRT), a technology from Johnson Matthey aimed at reducing PM that utilizes an oxidation catalyst and a particulate filter in series, show significant reductions in PM emissions compared with standard diesel buses (Canagaratna et al. 2004); (3) that, although comparisons of PM-emissions measurements from vehicle-chase studies and dynamometer tests are consistent on average, the real-world, in situ measurements (in chase studies) suggest significantly more variation in emissions than dynamometer tests do (Canagaratna et al. 2004); (4) that buses fueled by CNG emit significant amounts of methane that are likely the result of engine misfiring and could require additional controls (such as exhaust-gas recirculation or oxidation catalyst) (Herndon et al. 2005); (5) that buses fueled by CNG emit significant amounts of formaldehyde and could require additional controls (such as oxidation catalyst) (Herndon et al. 2005); and (6) that the CRT system on diesel-fueled buses significantly increases the ratio of NO_2 to NO_x, which might have to be addressed in the long term (Shorter et al. 2005).

The ratios of nonrefractory-PM emissions to CO_2 emissions, calculated and categorized by vehicle type, from two vehicle-chase studies (Herndon et al. 2005) that used an aerosol mass spectrometer are summarized in Figure 2.13. Nonrefractory PM includes most organic carbon and inorganic components.

The height of each bar denotes the average emissions ratio calculated over the chase events representing the particular vehicle class. The vehicle classes were broadly categorized as MTA (New York City Metropolitan Transit Authority) buses, non-MTA buses, and other heavy-duty vehicles. The MTA class was further divided into buses with a Detroit Diesel Corporation 6V-92 engine, buses with a Detroit Diesel Corporation Series 50 engine, buses with continuously regenerating technology, and buses fueled by compressed natural gas. The non-MTA class consisted of passenger buses used in the city that are operated by companies other than the MTA. The class of other heavy-duty vehicles consisted of trucks as well as school and charter buses. The figure also shows emissions ratios calculated for a "dirty car" (i.e., a car emitting a large amount of blue smoke) and for mixed traffic in a few tunnels. Samples from the occasional bus fueled with compressed natural gas showed low PM emissions compared with the diesel buses equipped with a CRT system. Additional findings from the vehicle-chase studies are summarized in Sidebar 2.7.

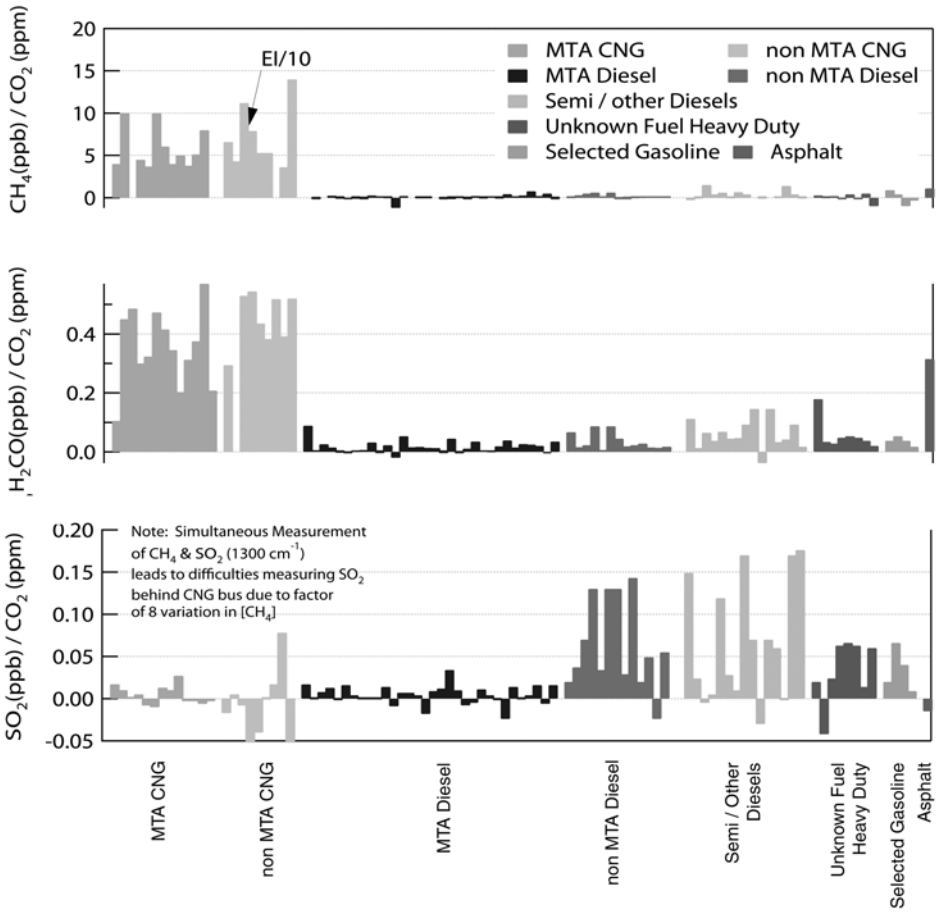
Sidebar 2.7 Findings from Vehicle-Chase Studies

Sidebar Figure 2.3 shows the emissions of methane, formaldehyde, and sulfur dioxide from a variety of vehicle types measured in individual chase-study events (Herndon et al. 2005).

The results indicate that the CNG-powered buses emitted considerable amounts of methane per CO_2 compared with the diesel buses. There is also evidence that a significant fraction of these emissions occurred as a result of engine misfiring, as also noted in dynamometer tests (Lanni 2003). Increased methane without concomitant CO_2 increases was found in nine of the 21 chases of CNG-powered buses, suggesting that these buses emitted approximately 0.5% of their carbon as unburned fuel during normal operation.

Formaldehyde emissions were one-tenth of methane emissions on a per-molecule basis. The general finding that CNG-powered buses emit high concentrations of formaldehyde (Sidebar Figure 2.3) has also been made in chassis-dynamometer studies by Lanni and colleagues (2003) and Kado and colleagues (2005). In a study by Ayala and colleagues (2002), formaldehyde emissions were greatly reduced in the presence of an oxidation catalyst, suggesting a possible remedy for this potentially toxic emissions product from CNG-fueled vehicles.

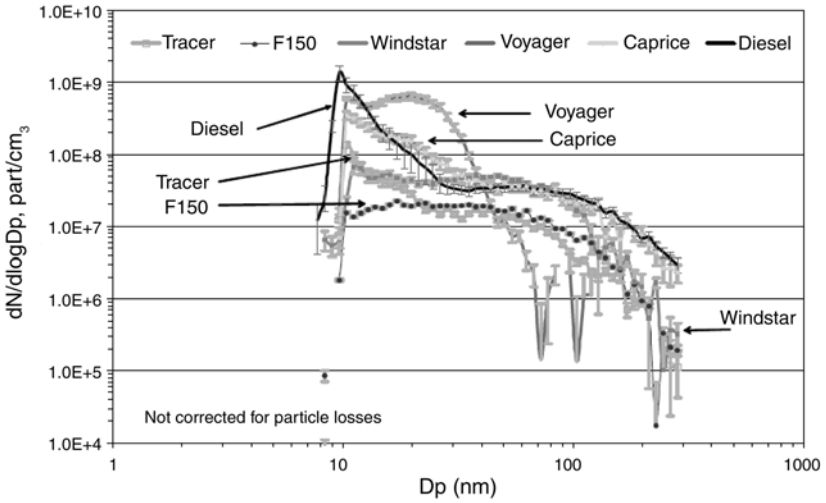
Chase studies have also reported that NO_2 slip associated with continuously-regenerating-trap (CRT) control technologies in diesel-fueled vehicles results in ratios of NO_2 to NO_x in exhaust-plume fractions of 50% or more on average (Shorter et al. 2005).



Sidebar Figure 2.3. Molar emissions ratios for methane (CH_4) (top panel), formaldehyde (H_2CO) (middle panel), and sulfur dioxide (SO_2) (bottom panel) of individually "chased" vehicles. The classes of vehicles, from left to right, are: New York City Metropolitan Transit Authority buses fueled by compressed natural gas (MTA CNG), non-MTA buses fueled by CNG (non MTA CNG), MTA buses fueled by diesel (MTA Diesel), non-MTA buses fueled by diesel (non MTA Diesel), tractor-trailers and other heavy-duty trucks (Semi/other Diesel), heavy-duty vehicles powered by unknown fuels (Unknown Fuel Heavy Duty), selected gasoline-fueled vehicles (Selected Gasoline), and asphalt-paving fumes (Asphalt). Results for SO_2 when chasing CNG-powered buses are presented but are not considered valid because of spectral-line masking of SO_2 at high methane concentrations. Bars represent individual in situ measurements. Reprinted from Herndon et al. 2005, with permission of the American Chemical Society.

Sidebar 2.7 (*Continued*) Findings from Vehicle-Chase Studies

Kittelson and colleagues (2006) have performed vehicle-chase studies to characterize particle-size distributions in emissions from in-use diesel and gasoline-fueled vehicles and have demonstrated the production of significant quantities of nanometer-scale particles by both engine types as shown in Sidebar Figure 2.4.



Sidebar Figure 2.4. Average size distribution of PM in emissions from various on-road diesel- and gasoline-fueled vehicles during acceleration, with the standard deviation of the mean corrected for background and dilution ratio. Vehicles, from left to right, are: 1995 Mercury Tracer passenger car, 1999 Ford F-150 pickup truck, 1998 Ford Windstar minivan, 1989 Dodge Voyager minivan, and 1984 Chevrolet Caprice passenger car, and a diesel-fueled vehicle. Data on diesel size distribution from Kittelson et al. 2002. Reprinted from Kittelson et al. 2006, with permission of Elsevier.

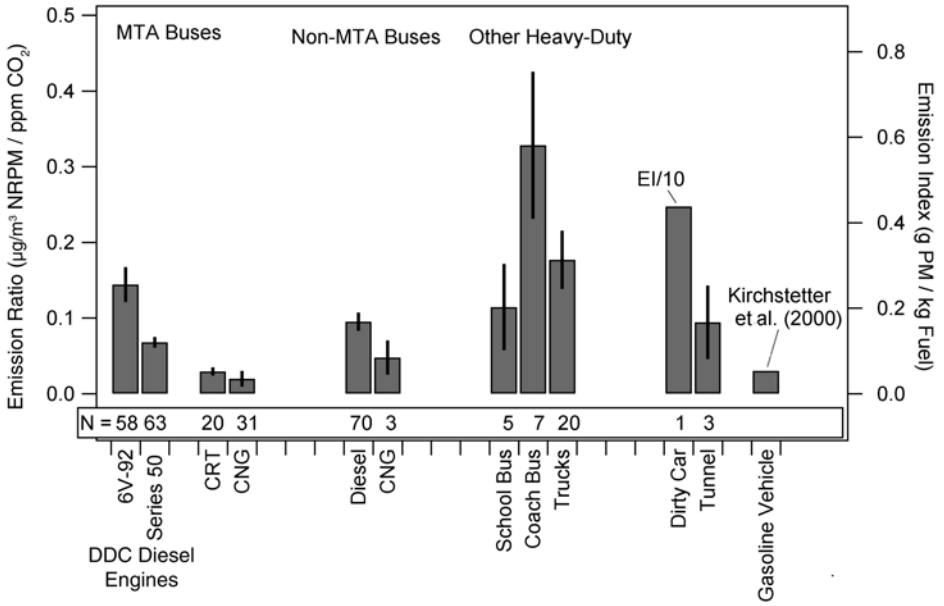


Figure 2.13. Classification of average nonrefractory-PM (NRPM) emissions by vehicle class in two New York City vehicle-chase studies. The bars represent average emissions ratios (of NRPM to CO_2) and the corresponding emissions index (g PM per g fuel) calculated for the chase events for each vehicle class. The error bars represent ± 1 standard error of the mean. (MTA = New York City Metropolitan Transit Authority; EI = emissions index; CRT = continuously regenerating technology; CNG = compressed natural gas; and DDC = Detroit Diesel Corporation. See text for additional details on vehicles classes and engine types.) Reprinted from Canagaratna et al. 2004, with permission of the American Association for Aerosol Research.

2.IX.2 TUNNEL STUDIES

Over the years, the measurement of selected gaseous and particle-species concentrations in roadway tunnels has yielded detailed source characterizations for diesel and gasoline-fueled vehicles under real-world in-use conditions. In addition, tunnel studies have been used to demonstrate the efficacy of emissions-control strategies (one of the stages in assessing accountability, i.e., linking regulatory actions to human-health responses) and to assess emissions models and their potential biases.

Although tunnel studies provide a more realistic representation of exhaust dilution than laboratory studies do, they are still not completely representative of the dilution and mixing of emissions that occur on roadways and have other limitations as well. For example, they do not consider effects of cold starts or of the full range of driving cycles and speed profiles of vehicles operating on highways. Moreover, although tunnels can have grades that affect power loads and emissions, the modeled emissions factors are based on an assumption of no grade. With these limitations, only a portion of the results from emissions models can be assessed. Nevertheless, tunnel studies provide valuable real-world evaluations of emissions models as well as a unique opportunity to track and demonstrate the progress made over time by the implementation of emissions-control strategies.

Table D.1 in Appendix D of this chapter (available on the HEI Web site) summarizes selected tunnel studies performed over the past decade and their key findings. Some of the information obtained from these studies includes (1) the particle size and chemical composition (including gaseous components) of emissions from in-use gasoline-fueled cars and light- and heavy-duty diesel vehicles, (2) estimates of emissions factors for criteria pollutants from diesel and gasoline-fueled motor-vehicle fleets, (3) assessments of the effects of road grade on emissions, (4) estimates of metals in emissions from brake wear, (5) estimates of emissions of non-criteria pollutants (such as carbonyls, PAHs, hydrocarbons [e.g., alkanes, alkenes, and aromatics], and nitrous acid), (6) estimates of emissions of resuspended dust, and (7) observational datasets that can be used to test and evaluate models of motor-vehicle emissions and to track historical trends of such emissions.

2.IX.3 ADVANCES IN MEASUREMENT TECHNOLOGIES AND ROADSIDE MEASUREMENTS

It has been almost two decades since the first open-path (i.e., across-road) remote-sensing systems using dispersive infrared (IR) spectroscopy were demonstrated for monitoring in situ on-road CO emissions (Bishop et al. 1989; Stedman 1989; Stephens and Cadle 1991). The systematic application of open-path infrared- or light-absorption-monitoring techniques such as these have proven to be of value in monitoring motor-vehicle emissions, tracking the progress of national programs to control motor-vehicle emissions, and identifying the shortcomings of those programs (Bishop and Stedman 2008). More information about remote sensing and its application is presented in Sidebar 2.8.

Similar technologies have been applied for the monitoring of HC and NO (Zhang et al. 1993, 1996b; Guenther et al. 1995; Popp et al. 1999). The remote-sensing techniques have been further refined with the advent of tunable diode

Sidebar 2.8 Across-Road Remote Sensing to Detect High Emitters

Remote-sensing devices were developed in the 1980s to measure exhaust emissions from in-use vehicles without interfering with the vehicles' activities (Bishop et al. 1989; Stedman 1989; Lawson et al. 1990; Zhang et al. 1993; Guenther et al. 1995; Zhang et al. 1996a; Zhang et al. 1996b). The technology is almost invisible to the vehicle operator and uses a beam of light to instantaneously determine the pollutant concentrations in emissions from the vehicle as it passes by. Infrared and ultraviolet light is directed across the road and passively reflected back to detectors that monitor light intensity at characteristic wavelengths. The amount of characteristic light absorbed by the detectors is translated into the exhaust concentration of the three gaseous pollutants CO, HC, and NO_x. Across-road remote sensors to measure PM emissions are still under development. Today's remote-sensing systems are commonly situated on one-way, single-lane roadways, such as freeway on-ramps, to minimize interference from multiple vehicles in the light path. The systems usually include video cameras to record vehicles' license-plate numbers for identification purposes and to make it possible to establish their make, model, and year. Several systems of this kind are commercially available (e.g., AccuScan 4600, Environmental Systems Products, East Granby, Conn., *www.esp-global.com*).

In its evaluation of vehicle I/M programs, the National Academy of Sciences found roadside remote-sensing was a useful screening tool to identify vehicles likely to pass or fail conventional I/M tests and recommended increased use for assessing the effectiveness of vehicle-emissions and I/M programs (National Research Council 2001). Many states (such as Texas, Colorado, and California) have implemented

lasers and light-detection and -ranging (LIDAR) technology (Nelson et al. 1998; Jimenez et al. 2000; Mazzoleni et al. 2004). The refinements help to provide more precise fast-response measurements, which in turn allow for better resolution of the vehicles sampled and an expanded list of chemical compounds monitored. Open-path remote sensing has been particularly effective for sampling large portions of the in-use motor-vehicle fleet.

For example, studies by Mazzoleni and colleagues (2004) sampled vehicles in Las Vegas using two commercial vehicle-emissions remote-sensing open-path systems: an ultraviolet LIDAR optical system for measuring PM opacity and a system for measuring gases (CO, HC, NO_2, and CO_2) by infrared or ultraviolet light absorption. More than 40,000 gasoline-fueled vehicles were sampled over a three-year period (2000–2002), and emissions distributions were developed. Figure 2.14 illustrates a significant skewness in the distributions of observed CO and PM emissions. The

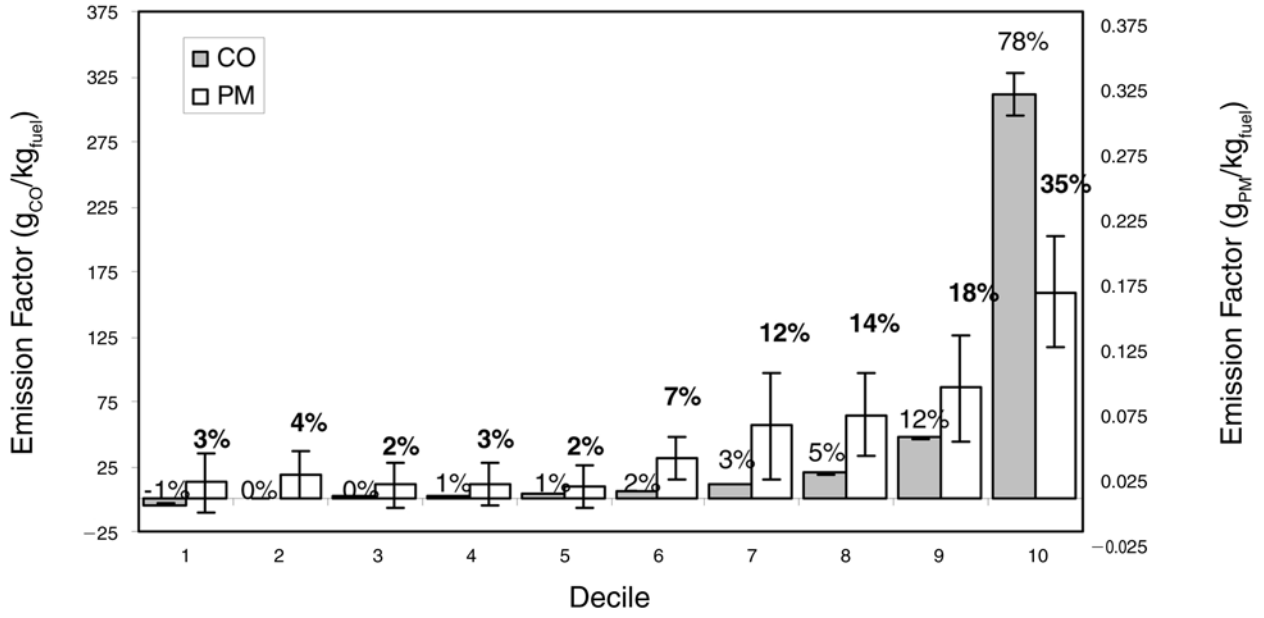


Figure 2.14. Skewed contributions of CO and PM emissions factors from gasoline-fueled vehicles by decile, from lowest to highest CO emitters, in a study in Las Vegas in 2002. Reprinted from Mazzoleni et al. 2004, with permission of the Air and Waste Management Association.

Sidebar 2.8 (*Continued*) Across-Road Remote Sensing To Detect High Emitters

remote-sensing programs to help identify high-emitters for early repair or low-emitting "clean" vehicles to exempt them from scheduled inspections at test facilities.

One such program is the High Emitter Repair or Scrap (HEROS) program created by California's South Coast Air Quality Management District (2007). The rationale for the program was that light-duty vehicles are major contributors of air pollutants in the South Coast Air Basin. Studies showed that the highest-emitting 10% of these vehicles were contributing well over 50% of the light-duty fleet's total emissions of ozone and PM-forming pollutants (Lawson et al 1996), emphasizing the need to identify and repair or scrap the high emitters to ensure further emissions reductions in the fleet. The goal of the HEROS program is to identify high emitters using remote-sensing technology and to solicit their owners' voluntary participation (by offering incentives, such as free or reduced-cost vehicle-emissions testing and repairs) to reduce emissions from such vehicles. Remote sensing was incorporated into the program because it is a cost-effective and proven technology for monitoring a large fraction of a fleet. Using three roadside testing systems, HEROS collected almost 3 million valid readings in 2007–2008, yielding approximately 1 million unique vehicle-emissions measurements (corresponding to approximately 10% of the fleet in the air basin) at locations throughout the basin. Locations and sampling times at each location were chosen to ensure that a representative sample of the light-duty vehicle fleet was taken. High emitters were identified using a combination of the remotely sensed vehicle-exhaust data, past history of vehicle emissions in biannual testing, vehicle age, and vehicle weight.

analysis showed that vehicles in the group with the highest 10% of sampled emissions ("high emitters") contributed more than 76% of the CO, more than 42% of the HC, more than 45% of the NO, and more than 80% of the PM. Earlier studies have reported similar contributions from high CO emitters (Beaton et al. 1995). The implications of these findings are important for policies aimed at reducing emissions and suggest the need for some form of routine monitoring of on-road emissions in conjunction with an I/M program. Similar measurement datasets for heavy-duty diesel vehicles are not available, and contributions of emissions from high emitters in this fleet remain to be determined.

Many roadside measurement studies have been designed principally to evaluate dispersion models applied to describe the dispersion of pollutants near roadways (defined as line sources, see Chapter 3 for details) and to address specific issues associated with motor-vehicle pollution. These field studies typically involve the deployment of measurement platforms downwind of a road (based on the prevailing wind direction) to measure the concentration gradient of emitted species (Carr et al. 2002; Sturm et al. 2003; Carslaw 2005; Imhof et al. 2005; Carslaw et al. 2006). The development of fast-response real-time instrumentation for the measurement of trace gases and the determinations of the composition of aerosols as well as size distributions (Kolb et al. 2004) has provided new opportunities for characterizing in-use on-road motor-vehicle emissions, as described above in detail. New portable emissions-monitoring systems provide another option for the measurement of these emissions (Unal et al. 2004; Cadle et al. 2008).

2.IX.4 SUMMARY

Evaluating models of motor-vehicle emissions and tracking the efficacy of regulatory actions to control them remain significant challenges for researchers studying air-quality control. The limited number of roadside monitors has made it difficult to track both the effectiveness of emissions controls and the national trends in motor-vehicle emissions of CO, VOCs, NO_x, and PM species. New measurement technologies and monitoring platforms, such as instrumented vans, have expanded opportunities to characterize in-use on-road emissions and to evaluate emissions factors. The deployment of instrumented vans to chase and sample the exhaust plume of targeted vehicles, for example, has been shown to be effective in characterizing gas- and particle-phase exhaust emissions of a variety of heavy-duty vehicles (fueled by diesel, compressed natural gas, or gasoline). In addition open-path across-road measurements of vehicle exhaust (mainly of CO) have proven quite effective in sampling large numbers of vehicles and in assessing the performance of I/M programs, the validity of emissions models, and the relative contribution of high emitters.

Tunnel studies, although typically limited by the speed ranges represented, do nonetheless provide useful data for evaluating the validity of emissions models under such conditions and for assessing long-term trends in motor-vehicle emissions and the effectiveness of regulatory emissions controls.

To date, most characterization studies of on-road vehicle emissions have provided data meant to better quantify emissions factors for criteria and non-criteria pollutants emitted by in-use motor vehicles. These studies have also supplied information about the sources of uncertainty likely to affect the validity of emissions models. Field experiments, which could validate on- and off-road vehicle emissions, have not occurred in part because of the many degrees of freedom associated with the multiple source types, ranges of operation, and the spatial and temporal distribution of the sources in the environment.

A particular challenge to many of the techniques that measure in-use motor-vehicle emissions is posed by the transient nature of cold-start emissions. The newer techniques that make roadside fast-response measurements and employ across-road remote-sensing techniques could be used to sample a significant number of cold-starting vehicles if properly deployed (for example, vehicles leaving parking lots) and thereby address this challenge.

The application of advanced measurement technologies for on-board emissions characterization, on-road in situ emissions measurements, and across-road remote sensing of motor-vehicle emissions in conjunction with the application of advanced vehicle identification and tracking suggest that researchers can now conduct well-designed field experiments for validating models of motor-vehicle emissions and need to await only the necessary interest and commitment of resources to move forward.

2.X. PHYSICAL AND CHEMICAL TRANSFORMATION PROCESSES IN THE VICINITY OF THE ROADWAY

Historically, CO, PM, VOCs, and NO_x have been the chemical constituents of primary interest in studies of motor-vehicle emissions. In particular, VOCs and NO_x are studied because of their role as oxidant precursors and because of the health consequences of exposures to the high concentrations of CO and the NO_2 portion of NO_x found near roadways. Dispersion and land-use regression models applied to estimate concentration gradients in the vicinity

of roadway emissions sources as well as the subsequent exposure assessments are discussed in Chapter 3. Studies characterizing the gas- and particle-phase species on or near roadways indicate the presence of complex chemical mixtures that vary in time and space, by source type (such as gasoline or diesel fuel), and in relation to the chemical composition of the local background in which they occur (Harrison et al. 1998; Zhu et al. 2004). Systematic chemical characterization of roadside environments remains limited. Even so, the U.S. EPA has identified more than a thousand chemical compounds in mobile-source emissions that might pose potential health risks and thus be considered MSATs.

The master list of MSATs (see Appendix E on the HEI Web site) is partitioned by source (such as gasoline exhaust, evaporative emissions from gasoline, diesel exhaust, and evaporative emissions from diesel fuel) and includes estimates of the sources' respective emissions factors. Exposure estimates for many MSATs are sufficiently low that their study will require models that take microscale dispersion of emissions in space and time into account and also an understanding of the MSATs' chemical and physical transformations. Chemical transformations of MSATs can reduce concentrations of the primary emitted toxic species, thereby mitigating exposure, but other chemical transformations can result in the formation of secondary products that are potentially more toxic than their precursors, thus possibly increasing the toxicity of the exposure. Chemical and physical transformations include, but may not be limited to, gas-phase oxidation and nitration processes, aerosol nucleation and growth, and gas–particle interactions (such as gas adsorption–desorption on particles and gas–particle partitioning).

The relevant chemistry associated with our understanding of pollutant exposures on and within 500 m of roadways is discussed in the following section.

2.X.1 TRANSFORMATION PROCESSES OF GASES AND PARTICLES

The chemical transformations of VOCs and NO_x that take place in the atmosphere are critically important to understanding the production of oxidants and other secondary products and their potential health consequences. Figure 2.15 shows a schematic of the photochemical oxidation cycle, which includes the key processes that link precursor emissions (such as VOCs, NO, and SO_2) to the formation of photochemical oxidants and secondary particles.

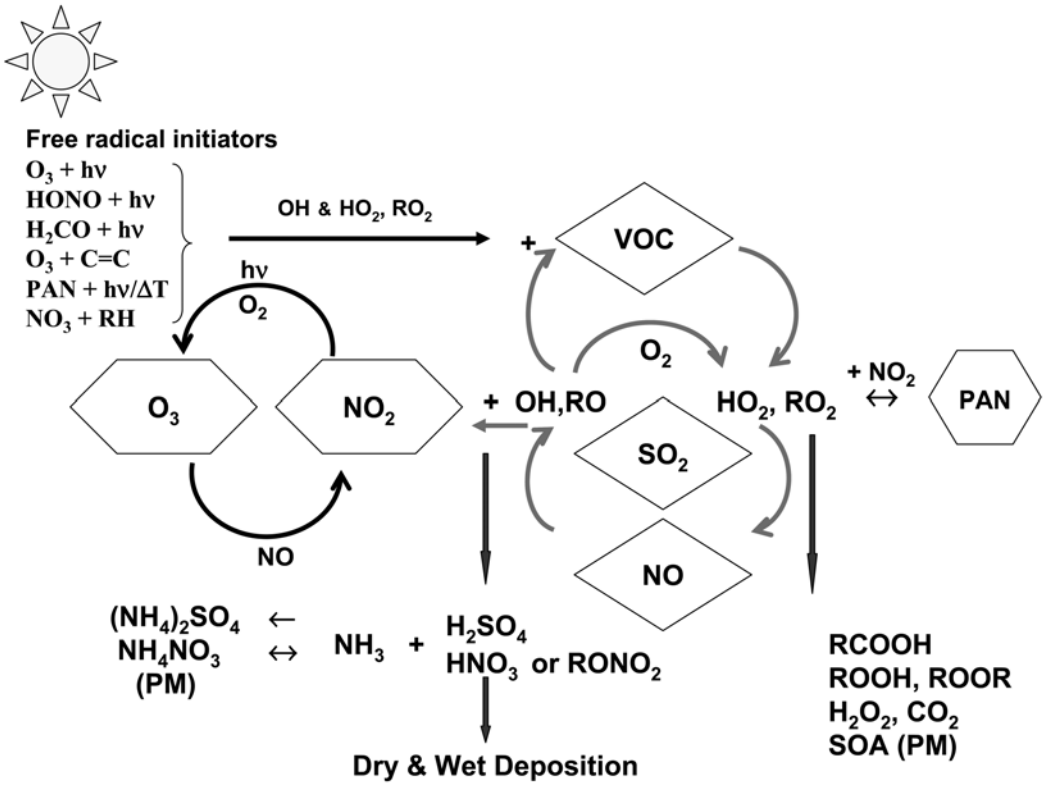


Figure 2.15. Schematic of the photochemical oxidation cycle. Adapted from Demerjian 1986.

Chemical and physical processes on and near roadways typically involve (1) reactions of primary emitted gases with entrained oxidants (i.e., ozone and hydroxyl radicals) in the mixing of exhaust with ambient air, (2) aerosol dynamics affecting the primary emitted particles, or (3) new particle production from chemical reactions during plume dilution. The spatial dispersion of line-source emissions, such as those from motor vehicles on a roadway, is complicated and depends on many factors, including wind speed, wind direction relative to the roadway, atmospheric stability, roadway elevation, and the surrounding terrain (Sharma et al. 2004). The effects of these factors generally limit observations of the influences on line-source emissions to distances of approximately 500 m from the line source. Concentration gradients downwind of line sources have traditionally been modeled using the Gaussian plume approximation (see Chapter 3 for more detail). Under typical daytime convective conditions, a line-source plume disperses at distances of 500 m or greater from the source and blends with the urban background atmosphere such that its contribution is indistinguishable from other source contributions. However, under stable atmospheric conditions, which typically occur at night, the concentration gradient of line-source plumes can be significantly greater than that of daytime plumes (which appear to be limited to 500 m) (Zhu et al. 2006) and thus cannot be discounted as a potentially important component in estimating exposures under these atmospheric conditions. Pasquill (1971) found that, under the unstable atmospheric conditions typical of daytime hours, Gaussian plume approximations of dispersion at a 500-m distance from the source have horizontal and vertical dispersion coefficients of σ_h = 90 m and σ_v = 70 m, respectively, whereas under moderately stable atmospheric conditions the approximations of dispersion at a 2-km distance have dispersion coefficients of σ_h = 70 m and σ_v = 20 m.

Experimental models of the effects of emissions at a microscale level of detail (distances of less than 50 m) have considered the treatment of turbulent vehicle-wake effects that depend on such factors as the vehicle size, speed, and exhaust-exit point (Eskridge et al. 1979; Eskridge and Hunt 1979; Eskridge and Rao 1986; Bäumer et al. 2005; Dong and Chan 2006). Models have also been used to study special cases of high-concentration exposures, such as those associated with street canyons or "hot spots" of congestion, with some success (Vardoulakis et al. 2003; Unal et al. 2004; Tsai et al. 2005). In most cases, these models predicted the concentrations of the primary pollutants emitted but not the subsequent chemical transformations, although it is possible to include first-order chemical transformations of primary emissions components under certain specific assumptions in the models. Physicochemical plume models that use simulations of large eddies are computationally feasible, but the application of such models is probably still many years in the future.

Chemical and physical transformations of components of vehicle-exhaust emissions also occur in the initial stages of dilution, and subsequent mixing with the surrounding air. Exhaust plumes, which contain CO_2, H_2O, CO, NO, NO_2, HC, semivolatile organic compounds, inorganic material, and PM, exit tailpipes at relatively high temperatures and concentrations, conditions that provide the opportunity for chemical reactions and condensation processes. Figure 2.16 shows schematics of possible in-plume transformations during the initial stages of exhaust dilution, in the first tens of seconds, and of transformations likely to occur during the plume-entrainment stage, up to several minutes later.

As exhaust plumes mix with (or entrain) background air, it is possible that the chemical reactions are "diffusion limited," meaning that the rate of the chemical reaction is faster than the rate of bringing the materials together, such that the reaction rate is limited by the diffusion rate. An example of a diffusion-limited reaction occurs during the entrainment of background ozone into a plume of NO where rate of NO_2 formation depends on the rate of turbulent mixing (i.e., diffusion) in the first tens of seconds after exiting the tailpipe. This phenomenon is thus very localized and only likely to affect exposures that occur within about 10 m of the source.

In addition to the many gas-phase chemical reactions described above, that might occur between emissions constituents during the early stages of exhaust dilution, phase transitions (i.e., changes from gas to particle and vice versa, resulting in the production and loss of particle-number concentrations) can also occur. Phase transitions are likely the result of the interaction of primary emitted elemental carbon and sulfuric acid cores. These two chemical constituents interact with semivolatile organic compounds (such as unburned lubrication oil) at exhaust temperature, a temperature sufficient to condense these constituents during the earliest stages of dilution (tens of seconds). As the chemical constituents equilibrate at ambient conditions, they might coagulate or re-volatilize as the exhaust plume dilutes (hundreds of seconds) and, in turn, affect the chemical composition of local primary and secondary organic aerosols (Robinson et al. 2007) as well as local particle-number concentrations (Zhu et al. 2002). It should be noted again that the rate of turbulent mixing depends on the stability of the atmosphere, and more stable conditions accentuate local chemical and physical transformation processes.

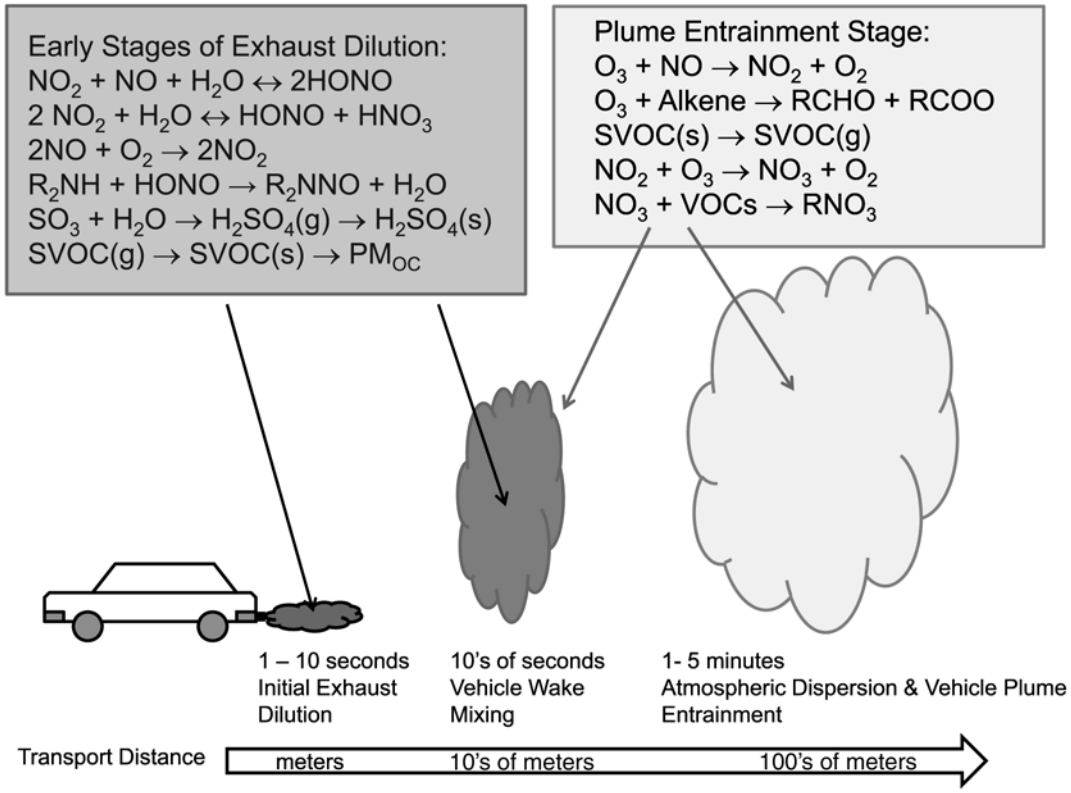


Figure 2.16. Schematic of the possible chemical transformation of motor-vehicle emissions in the early stages of dilution and plume entrainment. (Courtesy of Kenneth Demerjian.)

2.X.2 SUMMARY

The characterization of pollutants and their chemical and physical transformations on and near roadways is very complex and has been limited by the availability of instrumentation suitable to support the needed characterization. The study of the effects of exposure to pollutants near roadways remains somewhat nascent and has been limited to criteria pollutants thus far. The transformation processes that occur both in the earliest stages of exhaust dilution and later during plume entrainment can produce toxic gases, semivolatile compounds, and particle-associated chemical constituents. This suite of chemical constituents is not typically measured in roadside environments and must be the focus of future efforts that take advantage of new fast-response measurement technologies.

2.XI. SUMMARY AND CONCLUSIONS

Characterizing and quantifying emissions from motor vehicles are the keys to assessing human exposure to traffic-related air pollution. Figure 2.17 illustrates the principal elements linking emissions characterization to emissions models and to human exposure described in this chapter.

Concerns about the health effects of pollution related to motor vehicles have led to new emissions regulations and innovative pollution control around the world. There has been considerable progress in reducing the emissions of CO, HC, PM, and NO_x from gasoline- and diesel-fueled motor vehicles in the major industrialized countries. Stringent requirements to further reduce NO_x emissions from diesel vehicles are being phased in. Forecasts indicate a significant increase in the worldwide motor-vehicle fleet commensurate with population growth, increasing urbanization, improving economies, and rapid expansion of

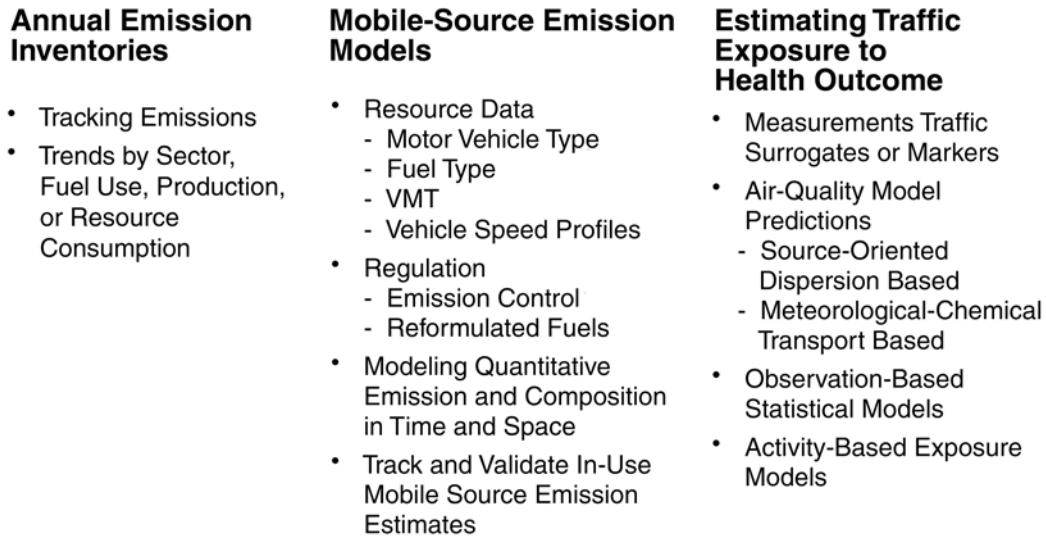


Figure 2.17. Major elements linking emissions and exposure. (Courtesy of Kenneth Demerjian.)

metropolitan areas. These increases will offset at least in part the progress made by emissions regulations and continue to pose a considerable challenge to regulators charged with maintaining air quality. Thus the location of motor vehicles with respect to the population must be taken into account when estimating trends in human exposure.

Motor vehicles are a major contributor of all criteria pollutants (except SO_2). In addition to PM emissions from exhaust, tire wear, and brake wear, significant PM emissions are contributed by road dust that is resuspended by vehicles traveling on paved and unpaved roads. The composition of tire wear and brake wear, although not fully characterized, includes styrene and butadiene polymers, *n*-alkanes (C19–C41) from tires, and a variety of trace metals from brake linings. Road dust includes a combination of mineral oxides commonly found in soils, organic constituents from vehicle exhaust, elements from tire wear and brake wear, platinum-group elements from catalytic converters, and allergens. Road-dust emissions are often an important source of PM_{10} in urban-area emissions inventories and the atmosphere. Data on primary emissions of PM_{10} and $PM_{2.5}$, which have recently been added to emissions inventories, indicate that in 2007 motor vehicles contributed 2.1% of the total $PM_{2.5}$ emissions and 0.9% of the total PM_{10} emissions. If the contribution of PM_{10} emissions from paved roads is included, the total PM_{10} contribution from motor vehicles would be about 16%. Although recent progress in emissions characterization looks promising, PM-emissions estimates remain highly uncertain and have had very limited field valuation and verification.

Quantifying emissions from motor vehicles requires the compilation of fundamental, detailed traffic data distributed in space and time, including, for example, traffic counts, vehicle types, travel speeds, fuel types, and emissions controls. Resource requirements for collecting these data can be prohibitive and have led to the use of travel-demand models, which forecast traffic volumes on highway networks based on estimates of trip generation, trip distribution, mode choice, and traffic assignment. Although a variety of limitations in current travel-demand models have been identified, VMT estimates made using these models are considered superior to estimates made using data on traffic counts and roadway locations.

Computer models that predict emissions from on-road motor vehicles have evolved over three decades and provide estimates of emissions rates in grams per mile for total HC, CO, NO_x, PM, SO_2, NH_3, selected air toxics, and GHGs. The large number of parameters and complex algorithms used in these models suggest the presence of significant uncertainties and limitations in the resulting emissions estimates. Among the issues raised are that the emissions models do not account for the effects of roadway grade and operating mode (other than average speed), and that they poorly quantify the contribution of high-emitters.

Emissions estimates for PM and air toxics are limited and need to be better characterized to reduce their high uncertainty. The quality of the speciation profiles used to apportion the chemical composition of emissions by

source type is a contributing factor to the uncertainty in species-specific emissions estimates, especially because many profiles have not been updated for a decade or more and might not reflect the changes in technology that have affected various types of sources.

The extent of the evaluation and verification of emissions models by means of actual field measurements has been quite limited, considering the pivotal role they play in the generation of regional or aggregated data for use in emissions inventories for state implementation plans, determinations of transportation-plan conformity, analyses of emissions trends, environmental-impact statements, hotspot analyses, and U.S. EPA rulings. Additional evaluation and verification of mobile-source emissions models will improve accuracy and reduce uncertainties with regard to the contributions of these emissions in air-quality simulations and exposure models.

Emissions from tire wear, brake wear, and resuspended road dust should not be overlooked in assessments of vehicles emissions and their impact on human health. With the introduction of combustion controls, these noncombustion emissions are becoming an increasingly large proportion of total vehicle emissions, and they contain chemical compounds, such as trace metals and organics, that might contribute to human health effects.

Receptor models and air-quality dispersion models have been used to assess the contributions of different types of sources, including motor vehicles, to ambient pollution in urban and rural areas. The receptor models include models that do not require a priori knowledge of source-composition profiles and models that use data on both gaseous and PM concentrations. The application of receptor models shows a wide range of results for $PM_{2.5}$ and PM_{10}. The results in U.S. cities, summarized in Table C.1 of Appendix C (available on the HEI Web site) show that motor-vehicle contributions range from 5% in Pittsburgh, Pa., under conditions with very high secondary aerosol, to 49% in Phoenix, Ariz., and 55% in Los Angeles, Calif. Outside the United States, estimates of the motor-vehicle contribution to $PM_{2.5}$ range from 6% in Beijing, China, to 53% in Barcelona, Spain (as shown in Table C.2 of Appendix C). Estimates for PM_{10} range from 4% in northern Chinese cities to 48% in Madrid, Spain, and even 63% near a roadside in Thessaloniki, Greece. Differences in the models and in the quality and extent of the input data also affected these results. Overall, improvements in models and measurement databases have enhanced the ability of the models to separate sources such as motor vehicles from nonvehicular sources; however, accurate estimation of the separate contributions of diesel and gasoline-fueled vehicles to ambient PM remains challenging.

Evaluating emissions models and tracking the progress and efficacy of emissions controls remain significant challenges to air-quality researchers. The limited numbers of roadside monitors have made it difficult to track the effectiveness of emissions controls and the national trends in motor-vehicle emissions of CO, VOCs, NO_x, and PM. New measurement technologies and monitoring platforms have expanded opportunities to characterize in-use on-road vehicle-exhaust emissions and to evaluate emissions factors. The deployment of instrumented vans to chase and sample the exhaust plume of targeted vehicles has been shown to be effective in characterizing gas- and particle-phase exhaust emissions from a variety of heavy-duty vehicles (fueled by diesel or compressed natural gas) or gasoline-fueled vehicles. In addition, open-path across-road measurements of vehicle exhaust components (mainly of CO) have proven quite effective in sampling large vehicle populations and assessing the performance of I/M programs, emissions models, and the contributions of high emitters.

Tunnel studies, although typically limited by the speed profiles represented, have nonetheless provided useful data for evaluating the efficacy of emissions models and for assessing long-term trends in motor-vehicle emissions.

Historically the chemical constituents of motor-vehicle emissions that have been of primary interest are CO, PM, VOCs, and NO_x. VOCs and NO_x are of interest principally because of their role as oxidant precursors. Measurement studies of the gas- and particle-phase chemical environments on and near roadways indicate the presence of complex chemical mixtures that vary in time and space, by source type, and in relation to the chemical composition of the background atmosphere in the region in which they are found.

The characterization of pollutants and their chemical and physical transformations on and near roadways has been limited by the availability of instrumentation needed to support characterization studies. The transformation processes that occur in the early stages of exhaust dilution, as well as in plume entrainment, can produce toxic gaseous, semivolatile, and particle-phase chemical constituents. Some of these constituents (such as HNO_2, HNO_4, semivolatile organic compounds, and $PM_{0.1}$) are not typically measured in roadside environments and must be the focus of future measurement efforts, taking advantage of a new generation of advanced fast-response measurement technologies.

Finally, the availability of advanced measurement technologies for on-board emissions characterization, on-road in situ emissions measurements, and across-road remote sensing of emissions in conjunction with advance methods

for vehicle identification and tracking suggests that well-designed field experiments for emissions-model verification are now possible and await only the necessary interest and commitment of resources to move forward.

Assessment of the impact of emissions from motor vehicles in general, and from traffic, on air quality and human exposure is critically dependent on the quality of the estimates of motor-vehicle emissions in time and space. Improving the quality of motor-vehicle-emissions inventories is fundamental to advancing air-quality modeling and exposure-assessment techniques, which are the subject of Chapter 3.

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2.XIII. APPENDICES AVAILABLE ON THE WEB

APPENDIX A. Global Trends in Motor Vehicle Types by Region and Pollution Controls

APPENDIX B. Fuel Composition Changes Related to Emissions Controls

APPENDIX C. Summary of Source Apportionment Studies in the Past Decade

APPENDIX D. Summary of Tunnel Studies in the Past Decade

APPENDIX E. Subset of U.S. EPA Master List of Mobile-Source Air Toxics

ABBREVIATIONS AND OTHER TERMS

CEC	Japanese Central Environment Council
CNG	condensed natural gas
CO	carbon monoxide
CO_2	carbon dioxide
ECE	Economic Commission for Europe
EMFAC	Emissions Factors model
GDP	gross domestic product
GHGs	greenhouse gases
GIS	geographic information system
H_2SO_4	sulfuric acid
HC	hydrocarbons
HNO_2	nitrous acid
I/M	inspection and remedial maintenance
LIDAR	Light Detection and Ranging
MOVES	Motor Vehicle Emissions Simulator
MSAT	mobile-source air toxics
N_2O	nitrous oxide
NAAQS	National Ambient Air Quality Standards
NAFTA	North American Free Trade Agreement
NH_3	ammonia
NMHC	nonmethane hydrocarbon
NO_x	nitrogen oxides
OBD	on-board diagnostic
OECD	Organisation for Economic Co-operation and Development
OC	organic carbon
PAH	polycyclic aromatic hydrocarbon
PEMS	portable emissions monitoring systems
PM	particulate matter
$PM_{0.1}$	ultrafine PM, ≤ 0.1 μm in aerodynamic diameter
$PM_{2.5}$	PM ≤ 2.5 μm in aerodynamic diameter
PM_{10}	PM ≤ 10 μm in aerodynamic diameter
PMF	positive matrix factorization
SO_2	sulfur dioxide
SO_3	sulfur trioxide
U.S. EPA	U.S. Environmental Protection Agency
U.S. FHWA	U.S. Federal Highway Administration
VMT	vehicle-miles traveled
VOCs	volatile organic compounds

Chapter 3

Assessment of Exposure to Traffic-Related Air Pollution

CONTENTS

CONTENTS (*CONTINUED*)

Chapter 3

Assessment of Exposure to Traffic-Related Air Pollution

3.I. INTRODUCTION

In the course of their daily activities, individuals come in contact with a variety of air contaminants in several microenvironments. Time spent in these environments results in personal exposures that relate to both chronic and acute health effects, particularly for sensitive individuals. Air-pollutant exposures are chemically, physically, and biologically complex, and the air pollutants derive from a vari-ety of sources. Motor vehicles represent a major source of air pollutants that have a substantial impact on ambient air exposures, indoor air exposures, and personal exposures.

Pollutants from motor vehicles number in the thousands and include toxic, mutagenic, and carcinogenic compounds that vary greatly in their physical and chemical properties. Pollutants from vehicle emissions are related to vehicle type (e.g., light- or heavy-duty vehicles) and age, operating and maintenance conditions, and exhaust treatment. Resulting ambient concentrations are determined by emission rates in combination with vehicle-use conditions, including traffic characteristics, meteorologic conditions, road dust, and topography. Traffic-related emissions contribute to both primary and secondary ambient pollutant concentrations against a background of similar contaminants emitted from stationary (point and area) sources. Traffic-related emissions also contribute to pollutant concentrations found in microenvironments.

Traffic-related pollutants affect ambient air quality on a wide range of spatial scales, from local roadsides and urban scales to broadly regional background scales. As illustrated in Figure 3.1 (Stein et al. 2007), the highest direct exposures to traffic-related emissions are likely to occur at the local scale, that is, in a vehicle traveling in traffic or on a roadside out to a few hundred meters. At greater distances ("urban scale"), traffic emissions are likely to be well mixed with emissions from other sources and are more difficult to apportion. These air pollutants migrate indoors through ventilation and infiltration and thus contribute to indoor exposures. The populations potentially at greatest health risk are people who either spend a considerable amount of time in traffic (such as taxi or truck drivers, commuters, and school children) or who live or work near busy roads. Sensitive subgroups such as people with asthma may be at even greater risk in these microenvironments.

Motor vehicles are a complex source of pollutants that pose significant challenges to assessments of exposures and human health effects. The components of the mix of traffic-related air pollutants that could be associated with health outcomes might not be known and might be different for different health outcomes. Thus, it is not practical or feasible in epidemiologic studies to measure all components of the traffic air-pollutant mix. A widely used approach to characterize traffic pollution is to employ individual pollutants (also known as tracers or marker compounds) or direct measures of traffic as surrogates to represent exposures to the source. The identification of surrogates is a reasonable compromise in apportioning the contribution of traffic emissions to ambient air pollution and for use as a traffic-exposure measure in epidemiologic studies. Surrogates can also help in the assessment of spatial and temporal distributions of ambient pollution related to motor vehicles, individual exposures, and exposures in epidemiologic studies as well as in the development of cost-effective traffic-mitigation control strategies.

Two broad categories of surrogates have been used for assessing the contribution of traffic emissions to ambient air pollution and for estimating exposure to air pollution from traffic in epidemiologic studies: (1) measurement of traffic-related pollutants and (2) direct measures of traffic itself. The most commonly used surrogates include carbon monoxide (CO*), nitrogen dioxide (NO_2), benzene, particulate matter (PM) mass and number, and elemental carbon (EC) also known as black carbon (BC) or black smoke (BS).

Direct measures of traffic itself include self-reported traffic intensity, distance to the nearest road, traffic volume within buffers, and sophisticated models of traffic exposure incorporating numerous other parameters (such as meteorologic variables and data on land use, emissions, or traffic). Additional factors such as time–activity patterns influence personal exposure, but these are not often included in the models.

Central air-pollutant monitoring stations, such as those established by the U.S. Environmental Protection Agency (U.S. EPA) for monitoring criteria pollutants, have been placed to measure population exposures on the urban or regional scales and have produced short- and long-term data on the temporal variability of selected air pollutants. Although the measurements at these stations are impacted by traffic-related pollutants, the stations are not able to capture local-scale perturbations caused by such pollutants. Practices for siting monitors vary between countries, with

* A list of abbreviations and other terms appears at the end of this chapter.

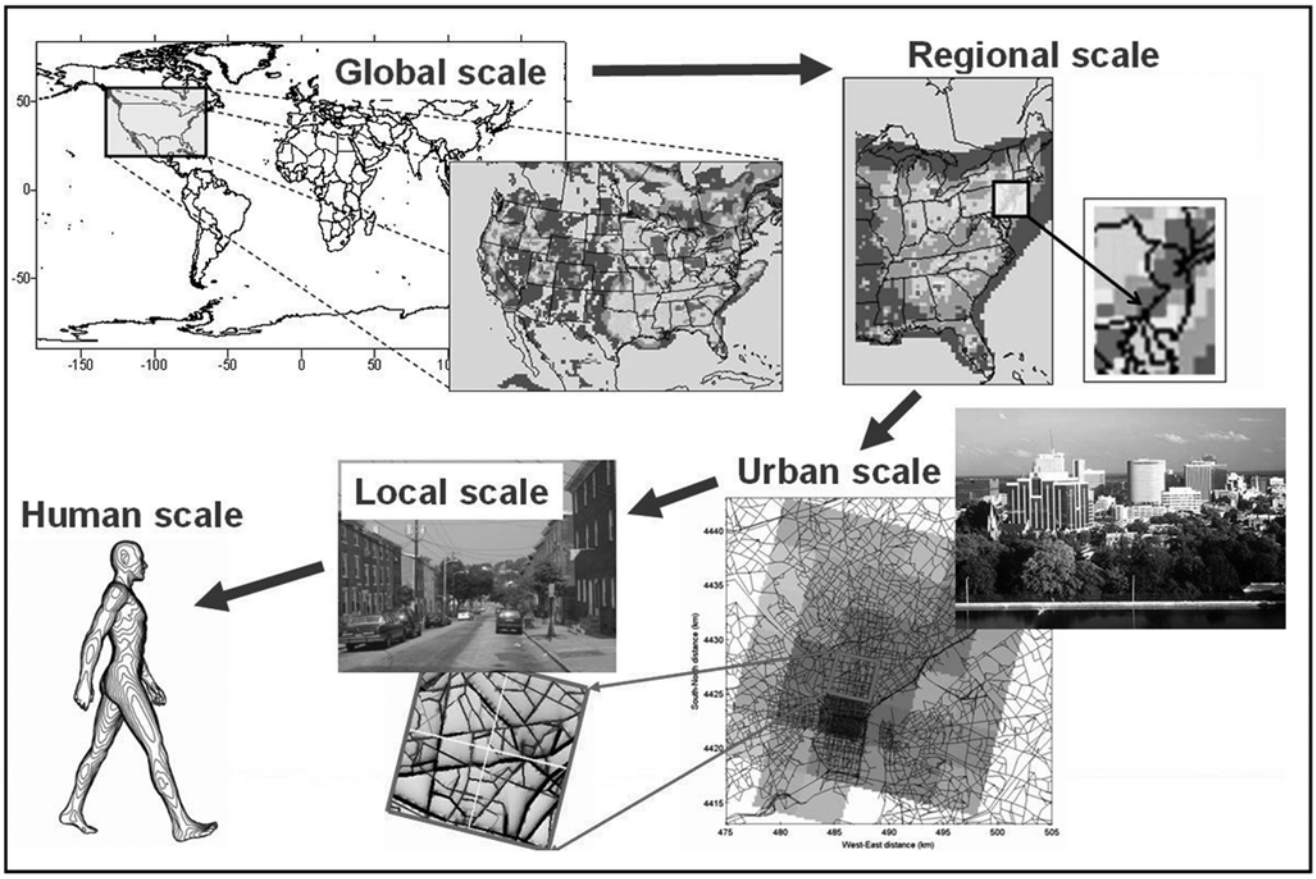

Figure 3.1. Graphic representation of the scales used in modeling emissions from traffic. (Reprinted from Stein et al. 2007, with permission of Elsevier.)

some countries in Europe using roadside monitors, which may capture small-area influences from traffic. Differences in monitoring practices complicate international comparisons of ambient conditions and exposures.

In assessing the role of vehicle emissions on ambient pollutant concentrations and ultimately individual exposures, it is important to account for the temporal impact of the emissions, particularly on the local scale. In addition, the contribution of vehicle emissions locally has to be considered within the context of background pollutant concentrations. Although vehicle emissions are likely to contribute substantially to local, urban, and regional (background) pollutant concentrations, their contribution to pollutant concentrations at each geographic scale is difficult to assess. This was demonstrated in a recent study in Hong Kong (So et al. 2007) in which long-term variations in $PM_{2.5}$ ($PM \leq 2.5$ µm in aerodynamic diameter) and its chemical constituents were measured at three sites: a roadside (with heavy diesel traffic), a residential area, and a rural area (with no roads, residences, commercial sites, or industry). Annual concentrations of EC, used as an indicator of motor-vehicle emissions, were highest at the roadside site (approximately 17 µg/m^3); concentrations at residential and rural sites were lower by 67% and 88%, respectively, than those at the roadside. The study demonstrated that concentrations of vehicle emissions are likely to be highest nearest roadways but probably have an impact on air-pollution concentrations over a wide geographic region.

Assessing exposure of the population to traffic-related air pollution is complicated by several factors, including the fact that there is no single metric of traffic, that traffic pollutants vary spatially, and that other non-traffic sources contribute identical pollutants to ambient and indoor air. Epidemiologic studies have relied on various surrogates of traffic emissions, many of which are criteria pollutants and are monitored by the U.S. EPA and similar agencies elsewhere. One limitation of pollutants measured at central monitors is the lack of spatial resolution necessary to capture both the temporal and spatial variability of pollutants from local-scale traffic. This poses a significant challenge for assessing traffic exposures in long-term epidemiologic studies of populations directly affected by traffic emissions. A few studies have employed both personal and stationary monitors to provide better local estimates of exposure to traffic-related air pollutants. The methods used in these

studies have limited application to epidemiologic studies because of the cost, respondent burden, limitations in monitoring methods, pollutant averaging times, and other factors. A number of modeling techniques have been developed for estimating traffic-pollutant exposures that hold promise for use in large epidemiologic studies of traffic-related air pollution.

This chapter focuses on characterization of local-scale exposure to traffic-related air pollutants on and near roadways and in epidemiologic studies. The emphasis is on primary traffic-generated pollutants* and not the more broadly dispersed secondary pollutants (such as ozone) that are derived from the atmospheric transformation of gases and PM components over time and space. The term "roadways" is used in this report to indicate any type of highway, expressway, major or local road, or any other structure designed to convey automobiles. The studies reviewed often distinguish between types of roads on the basis of the traffic volume using a variety of terms, in part based on national usage preferences, but there is no widely agreed-upon definition for each road type. In general, highways, freeways, and motorways are assumed to be the roadways with the highest traffic volumes; major roads have intermediate levels of traffic volumes; and local arterials have lower volumes.

Commonly used surrogates of traffic exposure and modeling approaches (e.g., land-use regression [LUR] or proximity models) are reviewed and assessed for their appropriateness as indicators of traffic exposure and for use in health-effects studies. For a recent review of the mobile-source air toxics not considered in this report, see *Special Report 16, Mobile-Source Air Toxics: A Critical Review of the Literature on Exposure and Health Effects* (HEI Air Toxics Review Panel 2007).

In addition, issues associated with assessing traffic-related air-pollution exposures in epidemiologic studies and models for assessing traffic exposures are discussed. Traffic-exposure issues associated with epidemiologic studies include exposure misclassification, limitations of using central monitors, approaches to better understanding local-scale traffic variations, changes in land use (such as urban sprawl), and environmental justice. The traffic models reviewed are those developed to predict local exposures to traffic-related pollutants and include proximity-based, interpolation, land-use-regression, dispersion, and hybrid individual-exposure models.

* This term is used for pollutants emitted directly from the tailpipes of motor vehicles and their rapidly formed near-source physical and chemical transformation products.

3.II. MEASURES OF TRAFFIC AND TRAFFIC-RELATED POLLUTANTS

This section presents results of measurements of traffic-pollution surrogates (pollutants and direct measures of traffic) at different spatial scales and describes their use in epidemiologic studies. The pollutants covered are CO, NO_2, PM mass and number, EC (also known as BS or BC), benzene, and, in a few studies, other air toxics. Because PM from combustion sources spans a large range of sizes, a brief summary of how it is classified is provided here. An explanation of the definition of EC follows.

Historically, PM in ambient air has been categorized for regulatory purposes into two fractions based on the split in the mass-weighted size distribution at around 2.5 μm: PM_{10} (PM ≤ 10 μm in aerodynamic diameter) and $PM_{2.5}$, a subset of PM_{10}. PM greater than 2.5 μm and less than 10 μm ($PM_{2.5–10}$) is referred to as *coarse particles*. A third fraction is defined by the number distribution and contains a large number of small particles that contribute very little to the total mass, but are present in high numbers. This fraction, which is a subset of $PM_{2.5}$, is commonly referred to as *ultrafine PM* (UFP) and is defined as PM ≤ 0.1 μm in aerodynamic diameter ($PM_{0.1}$). The concentration of UFP in ambient air is reported as the number of particles per unit volume rather than the mass per unit volume as is done for PM_{10} and $PM_{2.5}$. $PM_{0.1–2.5}$ is referred to as *fine particles*.

PM is also divided into two categories based on formation processes during exhaust dilution: *nucleation mode PM* (generally < 0.05 μm) and *accumulation mode PM* (> 0.05 μm). Nucleation events also occur in the atmosphere during specific meteorologic and air-quality conditions. An example of on-road PM size distribution by number, volume (an indirect measure of mass), and mass and by modes is illustrated in Figure 3.2 (for a more detailed description of particle formation and ambient-air regulations see U.S. EPA 2004).

One component of PM that has been explored as a surrogate for exposure to traffic-related air pollution is EC (or BC or BS). There are no universally recognized physical or chemical definitions or reference measurement methods for EC. Instead, this indicator of combustion soot (or carbon black) is defined operationally by the measurement, temperature protocol, and optical monitoring methods used in individual studies. There are more than 15 published methods of measuring EC; some of the methods differ by up to a factor of two. Likewise, the published definitions of atmospheric EC range from (1) graphitic material but not graphite, diamond, or fullerene; to (2) a complex three-dimensional polymer with the capability of transferring electrons; to (3) "soot" formed when oxygen-to-carbon ratios during combustion are less than one. Fortunately,

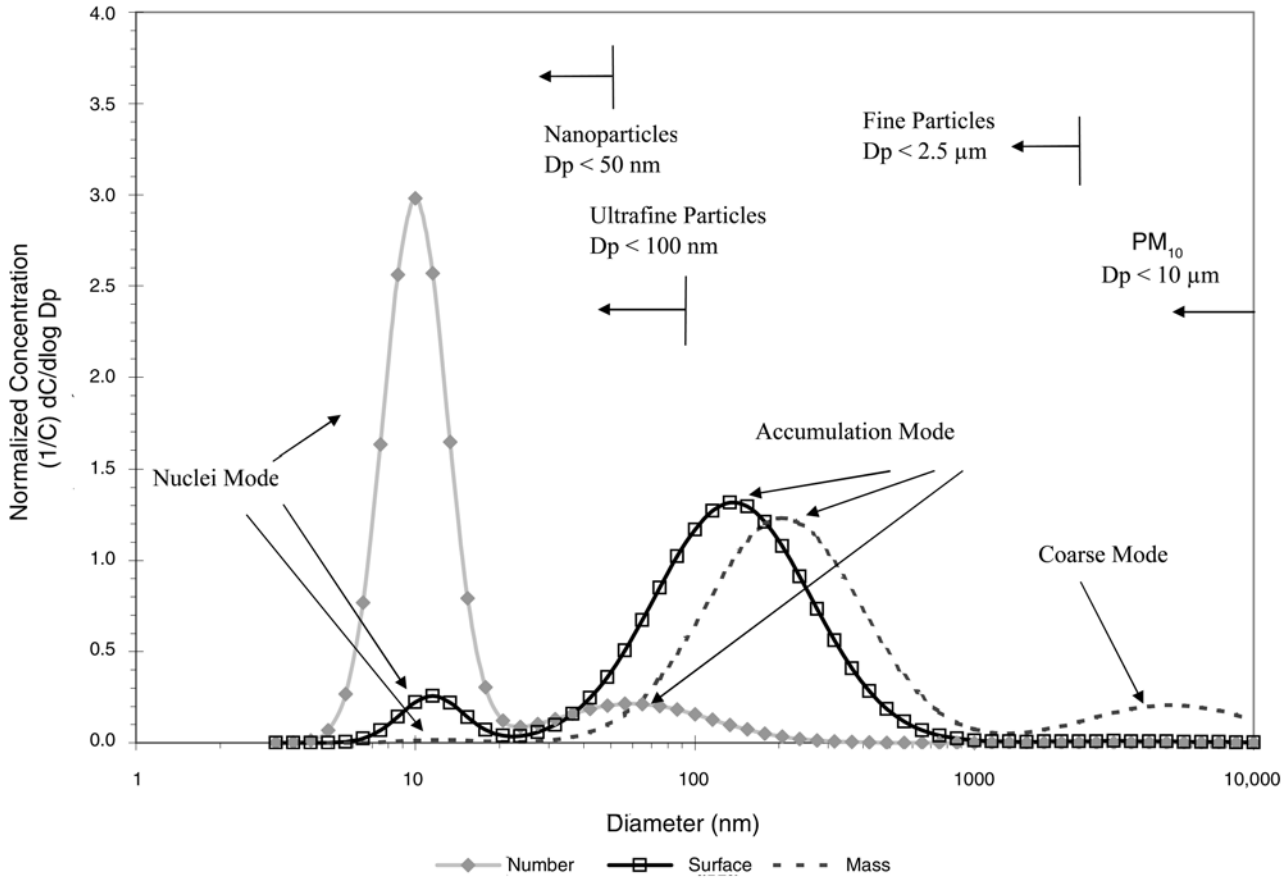

Figure 3.2. Normalized particle size distributions of typical roadway aerosol. Dp represents the particle diameter; (1/C)dC/dlog Dp represents the logarithmic particle-concentration-distribution function weighted by number, volume (surface), and mass. Here, C is the concentration (number, surface, or mass) in a particular size range and C is total concentration summed over all sizes. (Courtesy of David Kittelson and Win Watts 2009.)

numerous intercomparisons are available to help us understand the similarities and differences between methods for measuring EC (or BC or BS) (Edwards et al. 1984; Hansen and Rosen 1990; Chow et al. 1993, 2001, 2003; National Institute of Occupational Safety and Health 1999; Mader et al. 2001; Schmid et al. 2001; Watson and Chow 2002; Borak et al. 2003; Jeong et al. 2004; Park et al. 2006). Knowledge of the measurement methods used for specific studies is essential for understanding and comparing exposure studies involving the measurement of EC.

3.II.1 IN-VEHICLE AND ON-ROAD MEASUREMENTS

Data from U.S. travel surveys indicate that commuters spent 81 minutes per day in vehicles in 2001, on average, which was 10% higher than in 1995, and that children spent 48 minutes per day in vehicles (Hu and Reuscher 2004). A large-scale U.S. time–activity study found that the 95th percentile of time spent in vehicles and near vehicles was 270 and 425 minutes per day, respectively (Tsang and Klepeis 1996).

A number of studies have measured pollution concentrations inside or immediately outside of vehicles traveling on roadways (Chan et al. 1991; Ott et al. 1994; Lawryk et al. 1995; van Wijnen et al. 1995; Fromme et al. 1998; Rodes et al. 1998; Alm et al. 1999; Adams et al. 2001a; Chan and Liu 2001; Chan and Chung 2003; Lau and Chan 2003; Riediker et al. 2003; Behrentz et al. 2005; Kaur et al. 2005; Sabin et al. 2005; Westerdahl et al. 2005; Lewné et al. 2006; Saksena et al. 2006; Zhu et al. 2007; Fruin et al. 2008). The studies most frequently indicated that roadway concentrations were high compared with ambient concentrations measured at air-monitoring stations and were highly variable. In-vehicle concentrations were also higher than ambient concentrations for most but not all pollutants measured (Kaur et al. 2007). For example, average in-vehicle concentrations of $PM_{2.5}$ and CO were 2.5 and 6 times higher, respectively, than concentrations measured at nearby urban

Table 3.1. Comparison of Pollutant Concentrations in Vehicles with Ambient Air in Los Angeles[a]

Pollutant[b]	In-Vehicle Concentration Range	In-Vehicle Trip Average Concentration	Ambient Concentration Range
MTBE	20–90	31–60	10–26
Benzene	10–22	13–17	3–7
Toluene	23–58	30–51	10–40
Formaldehyde	0–24	7–20	7–21
$PM_{2.5}$	23–107	32–83	21–64
PM_{10}	23–111	36–89	54–103
CO (ppb)	0–1	0–1	0–4

[a] Data are derived from Rhodes et al. 1998.

[b] Units are (μg/m3) except where noted. MTBE indicates methyl tertiary butyl ether.

fixed sites (Chan et al. 1991; Adams et al. 2001a; Kaur et al. 2005). This suggests that individuals are likely to be exposed to the highest concentrations of traffic-related pollutants when traveling in or near vehicles, which is not surprising given the proximity of these microenvironments to the sources.

With the possible exception of some newer vehicles that have advanced filtration systems, the in-vehicle pollution studies have dispelled the notion that vehicles offer good protection from polluted air. Most of these studies suggest that air-exchange rates in vehicles are high compared with those in buildings, regardless of the ventilation-system settings and window positions and thus that highly polluted air from the roadway routinely infiltrates vehicles. Characterization of population exposures in or near vehicles is difficult because of variability caused by the types of vehicles, degrees of congestion, proximity to "high emitters" (vehicles, generally older, that emit unusually large volumes of pollutants), meteorologic conditions, and other factors.

Early studies focused on CO and nitrogen oxides (NO_x) because of health concerns and the ease with which these pollutants could be measured (Limasset et al. 1993; Ott et al. 1994; Shikiya et al. 1989). With the development of fast-response continuous instruments, the spectrum of pollutants measured in motor vehicles expanded dramatically. Rodes and colleagues (1998) conducted a study in Los Angeles and Sacramento, Calif., in which many more pollutants were measured inside a 1991 Chevrolet Caprice, a 1997 Ford Taurus, a 1997 Ford Explorer, and a school bus. Based on 29 daily trips, they found that, depending on location and weather, in-vehicle concentrations of more than a dozen pollutants, including formaldehyde, benzene, toluene, and CO, were consistently higher than those found within 6 m of the roadway and about two to ten times higher than those at a nearby ambient-air monitoring station (see Table 3.1 for the ranges of concentrations measured). Concentrations of some metals, such as lead and chromium, were similar to or lower than those in roadside or ambient air, and sulfur concentrations were somewhat higher, although the authors cautioned that too few samples of sulfur had been taken to draw any conclusions. The concentrations measured when driving in a Los Angeles freeway carpool lane tended to be lower in almost all instances than those for any of the rush-hour or off-peak freeway and arterial scenarios. However, for many of the pollutants even the carpool readings were three to four times higher than those of the ambient Los Angeles air.

Congested traffic conditions led to similarly high concentrations on both freeways and arterial roads in both cities, although congestion occurred less frequently in Sacramento. On Sacramento's rural roads, concentrations of in-vehicle pollutants tended to be much lower than those on the city's freeway and arterial roads but were still generally higher than those at the side of the road. The one significant exception in both Sacramento and Los Angeles was $PM_{2.5}$ concentrations inside vehicles, which were usually up to 40% lower than those at the side of the road or in ambient air, most likely because particulates were partially filtered out as they entered the vehicle. Overall, drivers in Los Angeles had a substantially higher burden of pollutants than those in Sacramento, probably because of the closer vehicle spacing in Los Angeles and higher pollutant concentrations in the city's ambient air.

Regardless of city, Rodes and colleagues found that type of vehicle and ventilation settings made little difference in in-cabin concentrations. They observed, however, that the quantity of exhaust emitted immediately in front of a vehicle was important. Exhaust from a diesel-powered bus or truck could double short-term PM concentrations inside a closely trailing vehicle; lower PM and BC concentrations were

observed when following buses powered by compressed natural gas rather than diesel fuel. Older and out-of-tune gasoline-powered vehicles also significantly increased pollutant concentrations in a closely trailing vehicle. Higher wind speeds were effective in reducing pollutant concentrations near roadways and inside trailing vehicles.

Most in-vehicle studies have reported a range of concentrations but did not attempt quantitative estimates of general population exposures in this microenvironment. Fruin and colleagues (2004) used data from Rodes and colleagues (1998) to assess in-vehicle exposures to BC as an indicator of diesel-exhaust particulate matter (DPM; also referred to as DEP in Chapter 5) exposures. They evaluated associations between real-time BC measures and traffic conditions and the effects of following certain vehicles from videotapes and notes in Los Angeles and Sacramento, Calif. In-vehicle BC concentrations were highest when diesel-powered vehicles were directly followed, particularly those with a low exhaust pipe. The lowest BC concentrations were observed when gasoline-fueled passenger cars were followed. To calculate representative exposures, in-vehicle BC concentrations were grouped by the type of vehicle followed, for each road type and degree of congestion. These groupings were then resampled stochastically, in proportion to the fraction of California vehicle miles traveled (VMT) under each of those conditions. The approximately 6% of time spent following diesel vehicles led to 23% of the in-vehicle BC exposure; the remaining exposure was caused by elevated concentrations of roadway BC. In-vehicle BC exposure estimates, adjusted for expected frequency of following certain types of vehicles, averaged 5.9 ± 18 μg/m^3 (high congestion) in Los Angeles and 3.1 ± 9.3 μg/m^3 (moderate congestion) in Sacramento. These correspond to DPM concentrations of 11 to 33 μg/m^3 in Los Angeles and 5.6 to 17 μg/m^3 in Sacramento depending on the aethalometer response to EC and the EC fraction of the DPM. The estimated statewide average for in-vehicle BC exposure was 4.1 ± 12 μg/m^3, corresponding to a DPM concentration of 7 to 23 μg/m^3. In-vehicle contributions to overall DPM exposures ranged from approximately 30% to 55% of total DPM exposure on a statewide population basis (depending on the BC-to-DPM conversion factor). Thus, although time spent in vehicles was only 1.5 hours per day on average, vehicles were likely to be an important microenvironment for DPM exposure.

Children's exposure to traffic-related pollutants while traveling in school buses is a concern. Sabin and colleagues (2005) collected real-time and integrated measurements of gaseous and PM pollutants inside five conventional diesel school buses, a diesel bus with a PM trap, and a bus powered by compressed natural gas to determine the range of children's exposures during school-bus commutes and the conditions leading to high exposures. Measurements were made during 24 morning and afternoon commutes on two Los Angeles Unified School District bus routes from South to West Los Angeles, with seven additional runs on a partly rural, partly suburban route, and three runs to test the effects of window position. For these commutes, the mean concentrations of pollutants from diesel vehicles ranged from 0.9 to 19 μg/m^3 for BC, 23 to 400 ng/m^3 for particle-bound polycyclic aromatic hydrocarbons (PB-PAHs), and 64 to 220 μg/m^3 for NO_2. Concentrations of benzene and formaldehyde ranged from 0.1 to 11 μg/m^3 and 0.3 to 5 μg/m^3, respectively. The highest real-time concentrations of BC, PB-PAHs, and NO_2 inside the buses were 52 μg/m^3, 2000 ng/m^3, and 370 μg/m^3, respectively. These pollutant concentrations were significantly higher inside conventional diesel buses compared with the bus powered by compressed natural gas, although formaldehyde concentrations were higher inside the latter bus. Mean concentrations of BC, PB-PAHs, benzene, and formaldehyde were higher when the windows were closed, compared with partially open, in part because of intrusion of the bus's own exhaust into the bus cabin, as demonstrated through the use of a tracer gas added to each bus's exhaust. These pollutant concentrations tended to be higher on urban routes compared with the partly rural, partly suburban route, and substantially higher (four to ten times) inside the bus cabins compared with ambient measurements.

Roadway air pollution continues to be a major problem in large cities, especially Asian cities. Emissions from vehicles are a leading contributor to deteriorating air quality in Asian cities. The extensive use of two-cycle two-wheel vehicles and diesel buses raises concern for in-vehicle and roadway exposures. Saksena and colleagues (2006) conducted a pilot study in Hanoi, Vietnam, of personal exposures to PM_{10} and CO while traveling on four major roads. They found that the mean 2-hour average PM_{10} concentration was 455 μg/m^3, with 580 μg/m^3 measured on motorbikes, 495 μg/m^3 while walking, 408 μg/m^3 in cars, and 262 μg/m^3 in buses. The mean 2-hour average CO concentration was 15.7 ppm, with 18.6 ppm measured on motorbikes, 8.5 ppm while walking, 18.5 ppm in cars, and 11.5 ppm in buses. Higher PM_{10} and CO concentrations were measured during rush hour than during non–rush-hour periods, but the differences were not all significant. In cars, air-conditioner use reduced PM_{10} concentrations by 62% but had no effect on CO. PM_{10} concentrations were lowest on the road with the least traffic, but this was not true for CO. In the vicinity of a fixed monitoring site, average in-car CO concentrations were 6 ppm compared with 1.5 ppm measured by a roof-top station. The study provided evidence of the extremely high concentrations of pollution experienced by commuters in Asian cities and suggests a need for further study.

Several researchers have made detailed aerosol measurements outside vehicles on roadways that included UFP counts and aerosol size distributions (Kittelson et al. 2001; Kittelson et al. 2004; Westerdahl et al. 2005; Fruin et al. 2008; Zhu et al. 2008). Kittelson and colleagues (2004) found that number concentrations for on-road aerosols ranged from 10,000 particles/cm^3 to 1,000,000 particles/cm^3 in measurements collected on residential streets and highways in various traffic conditions in Minnesota and that most of the particles were less than 50 nm in diameter (known as nanoparticles), as illustrated in Figure 3.2. The highest nanoparticle concentrations were associated with high-speed traffic (i.e., approximately 120 km/hr). Particle-number concentrations were lower and particle sizes were larger in heavy traffic with speeds of less than 32 km/hr.

Westerdahl and colleagues (2005) measured particle number, particle size, and other factors on Los Angeles freeways and residential streets. Pollutant concentrations varied widely by location, roadway type, and nature of traffic sources. Average particle-number concentrations ranged from 13,000 particles/cm^3 on residential streets in Pasadena, Calif., to 190,000 particles/cm^3 on an interstate highway with 25,000 diesel trucks per day. Short-term peak concentrations reached 800,000 particles/cm^3 on freeways. This was quite similar to peak concentrations measured on Minnesota freeways (Kittelson et al. 2001). Measurements on freeways with 3,500 and 10,000 diesel trucks per day averaged 47,000 particles/cm^3 and 130,000 particles/cm^3, respectively. The particle number size distribution showed a sharp UFP mode with a peak around 0.02 µm, similar to that shown in Figure 3.2 for Minnesota and also observed in Helsinki (Pirjola et al. 2004) and Zurich (Bukowiecki et al. 2002). The number concentrations on the highway were considerably higher than number concentrations measured in residential areas 10 to 20 m from a highway, but the size distributions were similar. Much lower number concentrations and larger particles were observed in residential areas located 500 to 700 m from a highway.

An analysis of the same data by Fruin and colleagues (2008) found that concentrations of UFP, BC, nitric oxide (NO), and PB-PAHs on freeways were generated primarily by diesel vehicles, despite the relatively low percentage (i.e., approximately 6%) of such vehicles on Los Angeles freeways. Concentrations of UFP on arterial roads appeared to be driven primarily by proximity to gasoline-fueled vehicles accelerating quickly. Concentrations on arterial roads were roughly one-third of those on freeways. By using a multiple regression model for the freeway measurements, the researchers were able to explain 60% to 70% of the variability in concentrations of UFP, BC, NO, and PB-PAHs using measures of diesel-truck traffic density and hour of day (as an indicator of wind speed). Diesel-truck traffic density was more important than time of day in explaining the concentrations. Freeway concentrations of these pollutants were also well correlated with readily available annual average daily truck counts, potentially allowing improved population exposure estimates for epidemiologic studies. However, the freeway concentration measurements were not significantly associated with total vehicle counts. Speed also showed only modest correlation, in contrast to dynamometer studies, in which high speeds have been shown to be associated with significantly higher vehicle emissions per mile. The result for speed was likely caused by the offsetting effects of the larger following distances and greater turbulent mixing that accompany high speeds. The researchers estimated that 33% to 45% of total UFP exposure for Los Angeles residents occurs during time spent traveling in vehicles, based on the roadway measurements and average driving time (i.e., approximately 90 minutes per day).

Measurements of aerosol size and number inside vehicles show that UFPs penetrate vehicles and affect occupant exposures. Zhu and colleagues (2007) reported in-cabin and outdoor measurements of particle-number concentrations and size distributions from three vehicles (model years 2002 to 2005) driven on Los Angeles freeways. Particle-number concentrations and size distributions were measured under various vehicle-ventilation settings. When the circulation fan was turned on, with substantial external air intake, outside changes in particle counts caused corresponding in-cabin changes approximately 30 to 60 seconds later, indicating a maximum air-exchange rate of about 60 to 120 exchanges per hour. Maximum in-cabin protection (i.e., approximately 85%) was obtained when both the fan was on and the recirculation vents were open. In-cabin and outdoor particle-size distributions in the range of 8 to 217 nm were observed to be mostly bimodal, with a primary peak occurring at 10 to 30 nm and a secondary peak at 50 to 70 nm. The vehicle's manufacturer-installed particle filter offered in-cabin protection of about 50% for particles in the range of 7 to 40 nm and of 20% to 30% for particles in the range of 40 to 200 nm. Zhu and colleagues' results for UFP concentrations in these late-model vehicles were much more sensitive to ventilation-system settings than the results Rodes and colleagues (1998) found for gases and larger particles in vehicles dating from the 1991 to 1997 model years. This difference in sensitivity was most likely due to improvements in vehicle air-filtration systems. Zhu and colleagues estimated that, for a one-hour daily-commute exposure, the

in-vehicle microenvironment contributes approximately 10% to 50% of people's daily exposure to UFP from traffic.

3.II.1.A Summary

Measurements of outdoor air quality on roadways indicate that concentrations of UFP, BC, PB-PAHs, NO, NO_2, CO, benzene, and formaldehyde are high compared with ambient concentrations measured at air-monitoring stations and are highly variable. Short-term UFP measurements on freeways in California and Minnesota indicate 800,000 to 1,000,000 particles/cm^3, which is an order of magnitude higher than results from fixed-site air-monitoring stations. Concentrations of traffic-related pollutants are much lower on rural roads than on urban roads and much lower on arterials than on freeways.

In-vehicle concentrations of most traffic-related gases and aerosols are higher than ambient concentrations and lower than roadway concentrations. Most vehicles have high air-exchange rates and low filtration efficiencies, resulting in in-cabin passenger-car concentrations that are 15% to 90% of the corresponding roadways concentrations. Measured concentrations of BC, PB-PAHs, benzene, and formaldehyde in diesel school buses are high, especially when the windows are closed, in part because of the intrusion of the bus's own exhaust into the bus cabin.

In the United States, adult commuters spend an average of 81 min per day in vehicles. Individuals are most likely to be exposed to the highest concentrations of traffic-related pollutants when traveling in or near vehicles and to receive a disproportionate (up to 50%) share of their daily exposure to traffic-related pollutants in this microenvironment.

3.II.2 DISTANCE-DECAY GRADIENTS IN POLLUTANT CONCENTRATIONS NEAR BUSY ROADWAYS

This section summarizes studies that have examined gradients in pollutant concentrations as a function of distance from roadways. Concentrations around roadways may represent direct influences from the road traffic and from background concentrations. The degree of gradient also seems to be a function of the reactivity of specific pollutants. Particles, such as UFP, $PM_{2.5}$, PM_{10}, and BS, have generally been the focus of the studies, but some gaseous pollutants have also been studied. Hitchins and colleagues (2000) reported a 50% decrease in $PM_{2.5}$ and UFP within 100 to 150 m from a road (Hitchins et al. 2000). A decay to background concentrations within as little as 50 m has been described for $PM_{2.5}$ mass concentration (Tiitta et al. 2002), although $PM_{2.5}$ tends to be more spatially homogeneous than UFP. Roorda-Knape and colleagues (1998) found that concentrations of BS, $PM_{2.5}$, NO_2, and benzene decreased to background concentrations within 100 to 150 m (Roorda-Knape et al. 1998). In an environment with greater volumes of traffic, Zhu and colleagues (2002) found that UFP, BC, and total PM counts decreased rapidly in the first 150 m and then leveled off. $PM_{2.5}$ was found to be elevated only modestly (i.e., in the range of 20%) near roadways. Recent updates to their work conducted during nighttime hours suggest that distance-decay gradients extend to at least 500 meters on the downwind side (Zhu et al. 2006). Some studies concurrently measured pollutants, such as NO_2 and volatile organic compounds (VOCs) (Roorda-Knape et al. 1998; Weisel et al. 2005) and CO (Zhu et al. 2002; Zhang et al. 2005), to assess pollutant mix.

Zhu and colleagues (2002) found that distance decay on the downwind side of a highway was similar for UFP, BC, and CO (i.e., a 60% to 80% decrease from roadside concentrations within 100 m). Gilbert and colleagues (2003) found distance-decay gradients in NO_2 around a busy highway in Montreal. They reported that pollutant concentrations were systematically higher downwind than upwind and decreased with increasing logarithm of the distance from the highway. They reported an R^2 association of 0.97 with distance and wind direction (i.e., downwind and up to 1400 m). The greatest decrease in NO_2 concentrations occurred within the first 200 m.

In general, distance-decay gradients have different characteristics on upwind and downwind sides of an expressway (Roorda-Knape et al. 1998; Zhu et al. 2002; Gilbert et al. 2003; McConnell et al. 2006b). On the upwind side, concentrations drop off to near background levels within 200 m and, in the case of particles, probably within 100 m or less. On the downwind side, concentrations do not generally reach background levels until 300 to 500 m. In some studies, this was extended to up to 1500 m for NO_2 (Gilbert et al. 2003; Jerrett 2007) and 800 m for UFP number counts (Reponen et al. 2003). The more gradual decline on the downwind side underscores the importance of obtaining meteorologic data.

Because NO_2 is widely used as a surrrogate of traffic pollution in epidemiologic studies, a recent study has attempted to characterize the distance-decay patterns for NO_2 and to correlate these with decay patterns in VOCs and various particle species (Beckerman et al. 2008). The study relied on measurements taken at two transects along Highway 401 in Toronto, which consistently ranks as one of the top three busiest highways in North America (annual average daily traffic flow was in the range of 365,000 to 395,000 vehicles per day at the two transects). Distance-decay gradients for NO_2 were found to be similar to those for VOCs and, surprisingly, to those for peak fine particles and UFP, although the latter had much sharper decay gradients

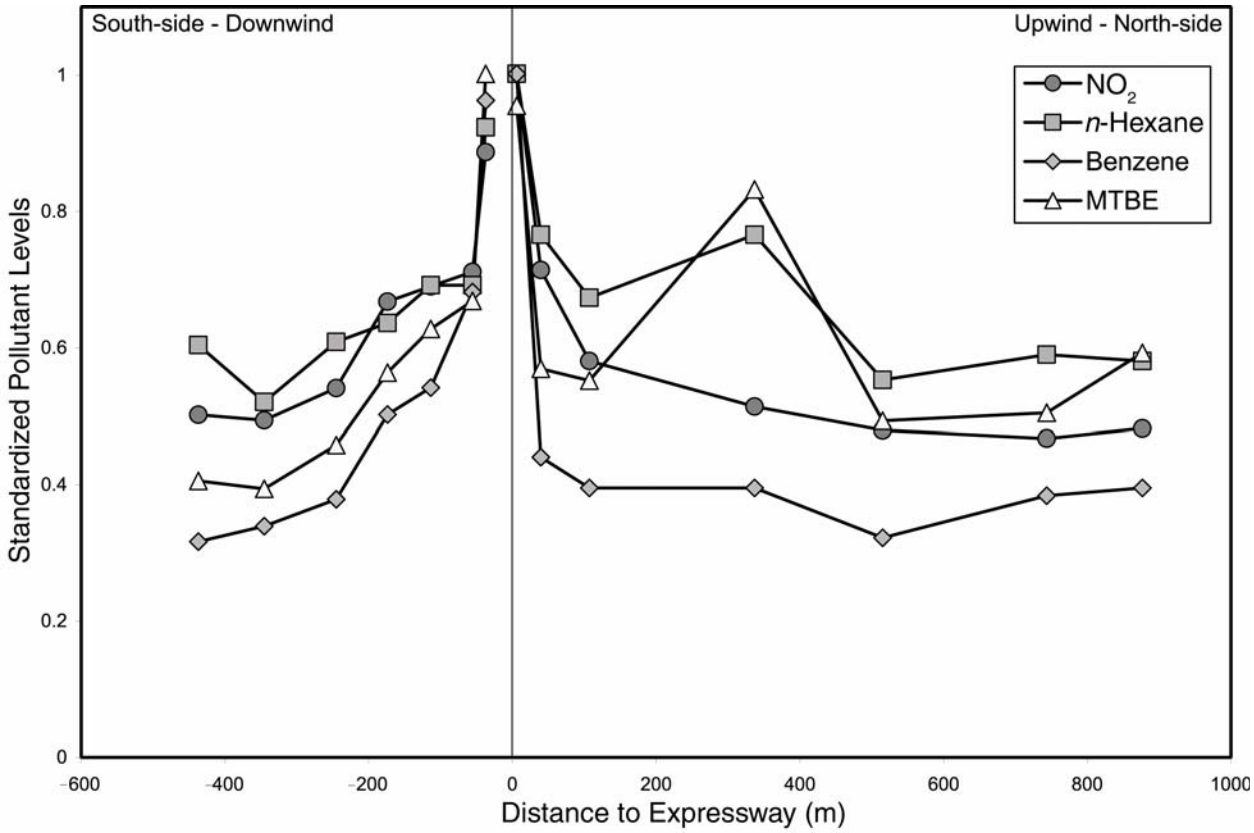

Figure 3.3. Distance-decay gradients of benzene, methyl *tert*-butyl ether (MTBE), and *n*-hexane at the Resources Road (MOE) site in Toronto compared with those observed with NO_2. All gradients decreased consistently with distance from the roadway and correlate with NO_2. The pollutants gradient concentrations (*y* axis) were normalized by dividing each pollutant by the largest value observed at a given study site. (Reprinted from Beckerman et al. 2008, with permission of Elsevier.)

than the gradients for NO_2 did (see Figure 3.3 and Figure 3.4).

Although the overall patterns of distance decay for most traffic pollutants were well correlated with those for NO_2, there were major differences between the upwind and downwind transects. Downwind concentrations were elevated between 250 and 400 m from the roadway compared with upwind distances of 200 m. In addition, VOC concentrations appeared to be influenced by local sources of traffic or topographic variation, which produced unexpectedly high concentrations at distances farther away from the highway.

These empirical results agree with a recent meta-analysis by Zhou and Levy (2007). The authors pooled estimates from more than 30 studies and characterized the distance decay from the road source for various combinations of reactive or nonreactive pollutants in areas of either high or low background pollution. Further simulations using dispersion models were employed to augment the empirical results. Overall, the distance-decay gradients demonstrated a heterogeneity that could be explained by background concentrations, pollutant characteristics, and local meteorologic conditions (such as wind speed) (see Figure 3.5 for a summary). Based on dispersion simulations for EC, the distance-decay gradient was in the range of 100 to 400 m from the source. For UFP counts, the gradient was 100 to 300 m; NO_2 had gradients of 200 to 500 m. Zhou and Levy concluded that these findings demonstrated the need for high-resolution monitoring near the source. They also cautioned about making comparisons across studies without specifying a pollutant, the conditions under which the data were collected, and the underlying definitions of spatial characteristics.

3.II.2.A Population Exposure Based on Spatial Gradients

Gradient studies contribute to an understanding of the population potentially affected by exposure to elevated concentrations of traffic pollution. For illustrative purposes, the highway and major road networks of Toronto and Los Angeles were subdivided using various combinations of

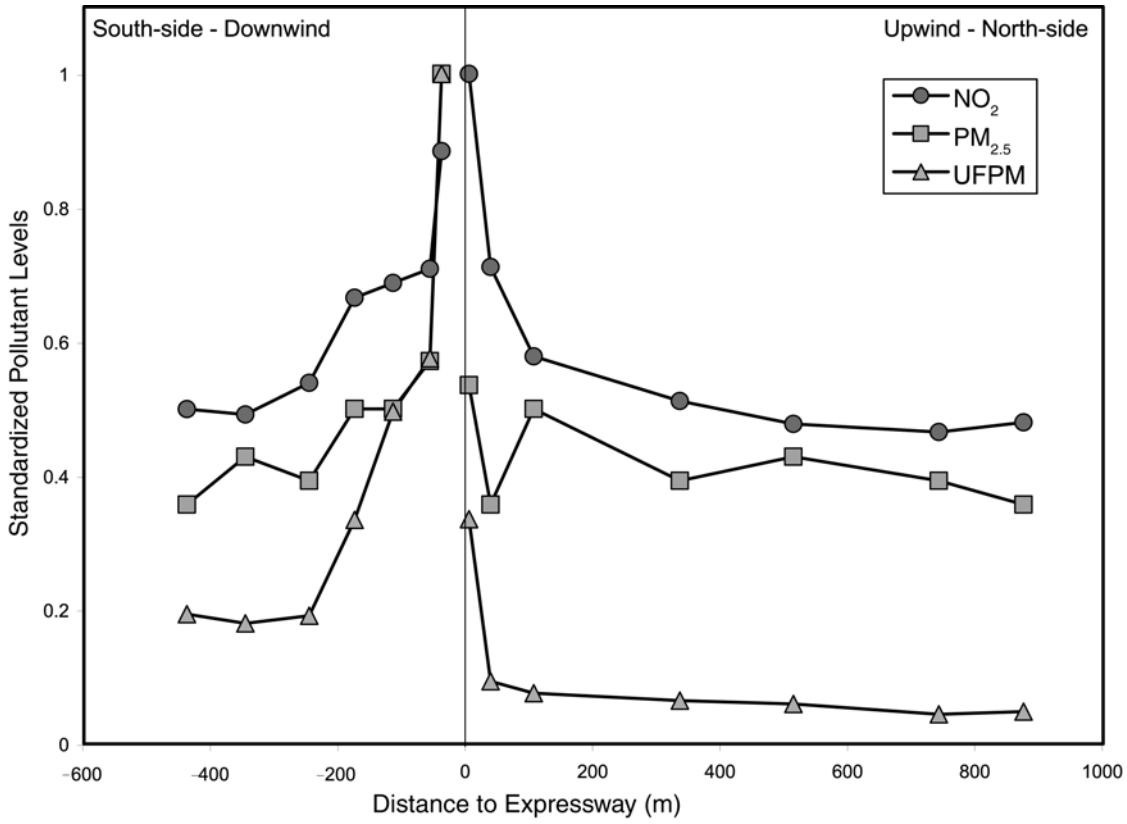

Figure 3.4. Distance-decay gradients of PM at the Bayview site in Toronto compared with those observed for NO_2. Gradients of $PM_{2.5}$ and UFPM (ultrafine particulate matter) were similar to that of NO_2. The pollutants' gradient concentrations (*y* axis) were normalized by dividing each pollutant by the largest value observed at a given study site. (Reprinted from Beckerman et al. 2008, with permission of Elsevier.)

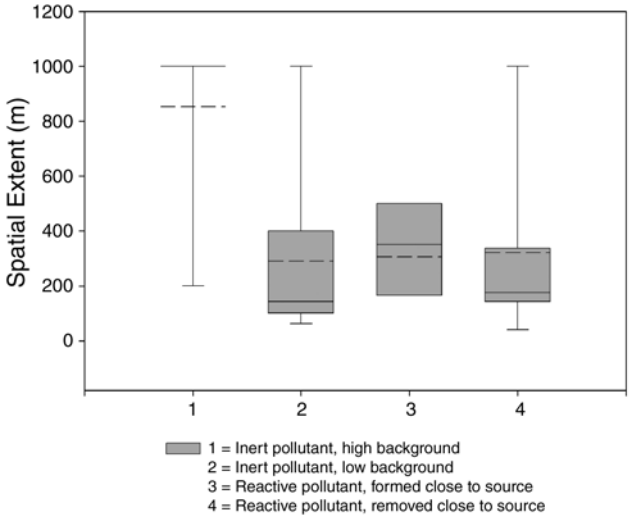

Figure 3.5. Spatial-extent estimates from studies in meta-analysis, stratified by type of pollutant. The dashed lines represents the mean, the solid lines the median, the shaded boxes the 25th–75th percentile range, and the whiskers the 5th–95th percentile range. Pollutants analyzed were categorized based on their chemical properties as follows: (1) PM mass without background removed; (2) CO, benzene, EC/BS, PM mass with background removed; (3) NO_2; and (4) NO and UFP. (Reprinted from Zhou and Levy 2007.)

distances to characterize the potential population exposures (Michael Jerrett, personal communication, May, 2008). Toronto was selected to represent a densely populated city in North America with a comprehensive and well-used public-transit system. Los Angeles was selected as a less densely populated city with a high degree of automobile dependence and an incomplete public-transit system with low ridership.

Because most distance-decay studies were conducted around major highways, a 500-meter buffer might be too large for major roadways, because they probably have a smaller area of influence than the highways do. Evidence from LUR modeling indicates that where major roads were used as a predictor, there was a significant elevation in NO_2 for major road lengths of 50 m in Toronto (Jerrett et al. 2007) and 100 m in Montreal (Gilbert et al. 2005). Based on these distances, population estimates were adjusted to include populations within 500 m of a highway and within 50 or 100 m of a major road. The estimates were intended to represent conditions without significant influence from buildings and other topographic features that might tend to concentrate pollution (such as street canyons).

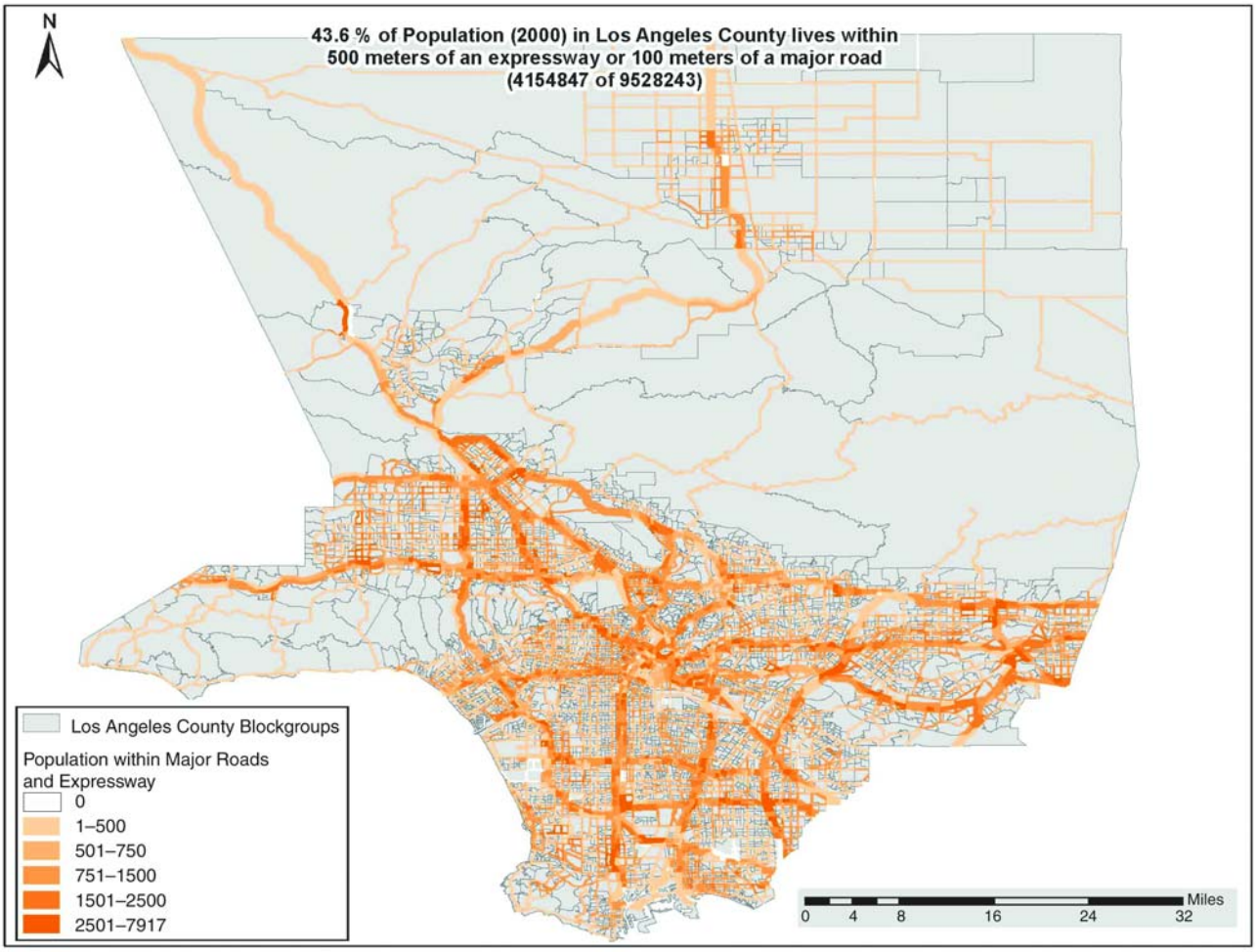

Figure 3.6. Population in Los Angeles County living near an expressway or major road. In 2000, 4,154,847 of 9,528,243 people (or 43.6%) of the population of Los Angeles County lived within 500 m of an expressway or 100 m of a major road. (Courtesy of Michael Jerrett and Bernardo Beckerman.)

Maps illustrating these combinations are shown in Figure 3.6 and Figure 3.7. About 45.2% of the total population of Toronto and 43.6% of Los Angeles live within 500 m of a highway and 100 m of a major road. If the 50-meter cut-off is used for major roads, the percentages drop to about 32.7% of the total population in Toronto and 32.6% in Los Angeles, two remarkably similar percentages given the differences in the cities' urban structures.

Estimates of the percentage of the population exposed to pollution from traffic range from 30% to about 45%, depending on the distance chosen to represent near-source effects. Traffic-related pollution, in short, affects a large percentage of the urban population.

3.II.2.B Summary

Gradient studies indicate exposure zones for traffic-related air pollution in the range of 50 to approximately 1500 m from roads. Meta-analyses suggest a range of up to 300 to 500 m from highways and major roads depending on background pollutant concentrations and meteorologic factors. Meteorology plays an important role in determining the size and diurnal and seasonal stability of impact zones. An examination of various factors in two large North American cities suggests that between 30% and 45% of the total urban population lies within such zones.

3.II.3 URBAN MEASUREMENTS OF TRAFFIC-EXPOSURE SURROGATES

This section summarizes the U.S. EPA's estimates of emissions rates and air-quality-monitoring data and evaluates the peer-reviewed studies published since 1998 that have reported measures of traffic-exposure surrogates and their use in epidemiologic studies of traffic exposure and health outcomes. Current emissions and changes in emissions over time for selected traffic-exposure surrogates

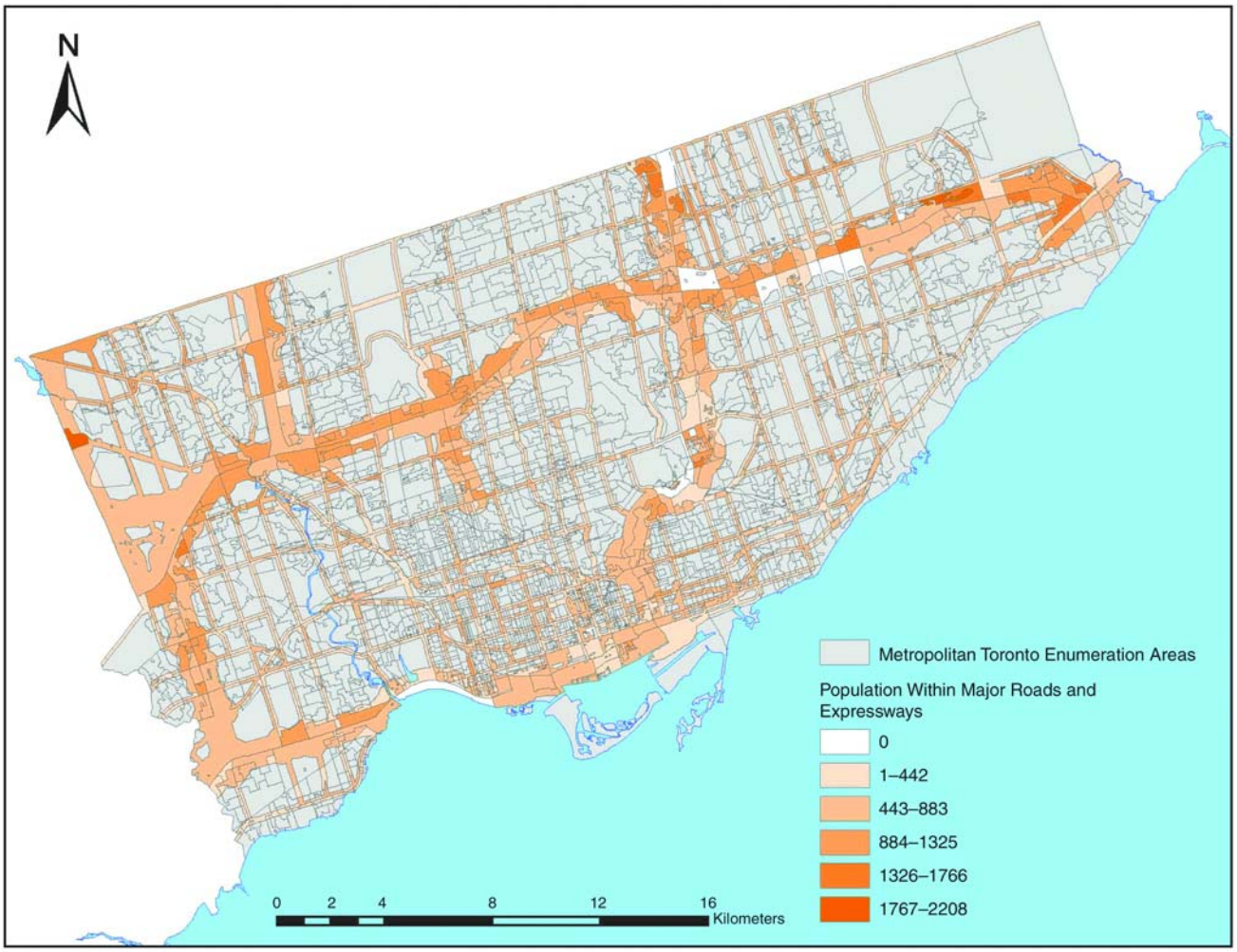

Figure 3.7. Population in Metropolitan Toronto living near an expressway or major road. In 1996, 1,078,635 of 2,385,420 people (or 45.2%) of the population in Metropolitan Toronto lived within 500 m of an expressway or within 100 m of a major road. (Courtesy of Michael Jerrett and Bernardo Beckerman.)

were extracted from the U.S. EPA's National Emissions Inventory (NEI) Air Pollutant Emissions Trend Data* for data up to 2007 (U.S. EPA 2008d). Emissions from mobile sources are reported separately for on- and off-road vehicles. The NEI develops its national estimates of emissions by source category from data gathered on a per-county basis. Thus, it is not possible, using the NEI data, to estimate the percentage contribution of the traffic-surrogate pollutants on urban or local scales, where the contribution might be greater than the national estimates. Vehicle numbers and VMT are also most likely higher in urban areas (see Section 2.V in Chapter 2).

Data from the U.S. EPA's Air Trends database (U.S. EPA 2008c) were used to assess changes in ambient concentrations of traffic-exposure surrogates measured at U.S. EPA central monitoring sites. Central sites capture regional changes over time but are not located so as to capture local spatial gradients. Many of the studies reviewed measured several highly correlated surrogates.

In theory, a surrogate for traffic emissions should (1) have traffic as the principal source of atmospheric emissions, (2) vary with other constituents of motor-vehicle exhaust over time, (3) be measurable at low concentrations using reasonably inexpensive and accurate methods, and (4) not have independent adverse health effects associated with it at concentrations encountered in various environments. In addition, the ultimate goal in most epidemiologic studies is to relate individual exposures to some health-related out-

* The U.S. EPA changed the name "Air Pollutant Emissions Trend Data" to "National Emissions Inventory (NEI) Air Pollutant Emissions Trend Data" on August 8, 2005. In this review we will refer to the data as NEI Air Pollutant Emissions Trend Data, or NEI data.

come, so a surrogate measure should reasonably approximate personal exposure to traffic emissions.

In practice, none of the most commonly used traffic pollutants considered here as surrogates for traffic emissions (namely CO, NO_2, PM mass and number, BC, and benzene) meet all of these criteria for an ideal surrogate for traffic-related air pollution. Traffic is a major source of CO, NO_x, benzene, UFP, and EC, but not the only source; and although traffic is an important source of PM mass (PM_{10} and $PM_{2.5}$), it is not a major source of primary PM emissions. All of the surrogates have important indoor sources not related to traffic. Little is known about the ratios of these surrogates to the complex pollutant mixtures emitted by traffic or how these ratios have varied over time. In addition, little is known about the ratio of the surrogates to the secondary air pollutants associated with traffic. Each surrogate has health effects associated with exposure to it (this topic will be discussed later, in Chapter 5). There is a rich history of outdoor monitoring data for CO, NO_2, PM mass, and benzene but only limited data for ambient UFP and EC. Nevertheless, despite the lack of an ideal air-pollutant surrogate for traffic, the surrogates discussed here have proven to have utility in both exposure studies and epidemiologic studies.

There have been hundreds of studies that examined factors affecting atmospheric concentrations of traffic-related air pollutants. The studies have varied greatly in pollutant-measurement methods, sampling times, numbers of measurements, distances from traffic, traffic characteristics (such vehicle mix, vehicle use, and traffic volume), study location, microenvironments, sampling seasons, and meteorologic conditions. Given this variability, it is difficult to develop criteria to compare results across studies. In this chapter, we provide summary figures for the primary surrogates (CO, NO_2, $PM_{2.5}$, and EC) measured in studies of exposure to traffic-related pollution. The figures present the mean concentrations associated with traffic measured in each study by location (in-vehicle, roadside, urban, suburban, rural, in homes, in schools, and personal exposure) averaged over different sampling times. Shorter times (less than 2 or 24 hr) may be associated with peak concentrations and exposures, and longer averaged times (such as 24 hours or 2 weeks) may better reflect long-term exposures. These figures represent the range of concentrations associated with traffic in various microenvironments across a variety of studies. They provide a context for the range of real-world concentration conditions, in which there can be substantial variation in vehicle types, vehicle ages, operating and maintenance conditions, exhaust treatments, type and quality of fuels, wear of parts, and engine lubricants as well as in fleet composition, traffic characteristics, meteorologic conditions, road dust, and topography. The sources of the data used in the figures can be found in the tables in Appendix A in this chapter. Epidemiologic studies on the health effects of exposure to the surrogates considered here include those that used either surrogate pollutants or models that are linked to traffic. Appendix B (available on the HEI Web site) describes some of the studies referred to in this chapter as examples of the approaches used (they are also considered in Chapter 4).

3.II.3.A Carbon Monoxide

Carbon Monoxide in Ambient Air as a Traffic Surrogate

CO emissions from all sources today are at approximately 43% of concentrations measured in 1970, while emissions from on-road (also referred to as "highway" by the U.S. EPA) vehicles have decreased to 25% of the 1970 concentrations (U.S. EPA 2008d), owing to vehicle modifications designed to reduce emissions and in spite of increases in the number of vehicles on the road and VMT (see *www.transtats.bts.gov* and also Section III of this chapter). Over the same period, off-road emissions have increased by 65%, and emissions from all other sources have decreased by only 5%. The result has been a decrease in mean ambient concentrations of CO of more than 76% from 1980 to 2007, with a median annual second maximum 8-hour average concentration in 2007 of less than 3 ppm (U.S. EPA 2008c). The low ambient CO concentrations currently encountered have resulted in measurement challenges. Very low CO concentrations are associated with instrument problems related to zero drift and poor sensitivity (U.S. EPA 2009). Despite these decreases in ambient concentrations, on-road vehicles continue to be the principal anthropogenic source of CO, accounting for approximately 47% of total CO emissions (and 21% of off-road CO emissions) in the United States in 2007 (Figure 3.8).

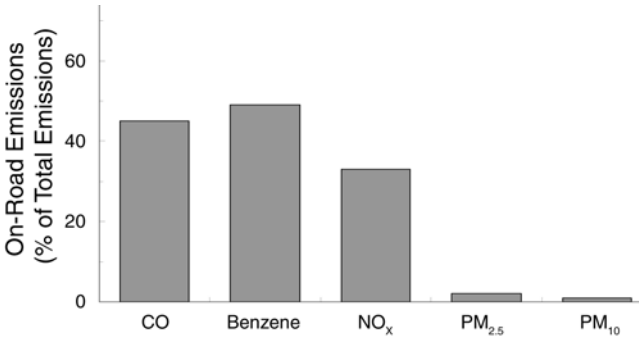

Figure 3.8. Percent contribution of on-road emissions to emissions from all sources in 2007. Note: the emissions estimates for $PM_{2.5}$ and PM_{10} are for primary emissions only and do not include secondary aerosol formation. Data from 2005 NEI data projected to 2007 (U.S. Environmental Protection Agency 2008d).

The dominant contribution of motor vehicles to ambient CO would suggest it might be a reasonable surrogate for traffic-related exposure. Traffic-related CO concentrations are highest in vehicles and in traffic (Chan et al. 1999; U.S. Environmental Protection Agency 2000; Riediker et al. 2004; Holmes et al. 2005; Namdeo and Bell 2005) and fall off rapidly away from roads (Chan et al. 1999; Zhu et al. 2002; Namdeo and Bell 2005), suggesting a strong spatial gradient. Riediker and colleagues (2004), for example, found that the CO concentrations in patrol cars during 25 work shifts averaged 2.6 ppm (with a range of 0.7 to 5.9 ppm), while roadside concentrations averaged 1.1 ppm (with a range of 0.4 to 1.7 ppm) and concentrations at an ambient site averaged 0.8 ppm (with a range of 0.3 to 1.5 ppm). The rapid decay of CO concentrations with distance from a roadway, as discussed earlier, was clearly demonstrated by Zhu and colleagues (2002), who found that concentrations near a major road in Los Angeles averaged 2.3 ppm (with a range of 1.9 to 2.6 ppm) at a distance of 17 m downwind of the road and 0.5 ppm (with a range of 0.2 to 0.7 ppm) at a distance of 90 m, a decrease of almost 80% over 73 m. The most recent CO Criteria Document (U.S. EPA 2000) concluded that the spatial variability of CO in several air sheds was highly heterogeneous. The document also noted that "fixed-site monitors…tend to overestimate 8-hour exposure values for people living in areas of lower traffic and underestimate the exposure of people living in areas of higher traffic." In addition, the document provided an extensive review of data on CO concentrations in a variety of microenvironments affected by motor-vehicle emissions and indoor CO sources (such as fireplaces and gas stoves). Concentrations associated with indoor sources, particularly in garages and homes with unvented combustion sources, can be an order of a magnitude higher than those found outdoors (U.S. EPA 2000).

Carbon Monoxide as a Traffic Surrogate in Epidemiologic Studies Appendix Table B.1 (available on the HEI Web site) summarizes some of the epidemiologic studies of traffic-related pollution that used CO as a surrogate for traffic exposure. Because they are readily available, data on CO from central-site monitors have been used in some studies as a surrogate for traffic exposure. Other studies have used data from fixed sites in close proximity to the homes of the subjects. A few studies have factored out the background contribution to CO concentrations in an effort to isolate the traffic-related component. Other studies have limited the study population to subjects living within a certain arbitrary distance of the central-site monitor in order to control for spatial variability. Depending on health outcome, daily values were sometimes averaged over an entire year, which reduced day-to-day variability; this might not have been unreasonable, because traffic patterns tend to be fairly stable across a year.

Other measures of traffic-related CO exposure that have been used in health studies include mobile monitoring, biomarkers of exposure, and modeled exposures (see Table B.1, Appendix B). For example, in a study in Germany (Hirsch et al. 1999), monitoring stations were placed on mobile caravans in each one-kilometer square of a 182-square grid in the city of Dresden every two weeks for one year. School and home addresses of study subjects were assigned the values from the nearest four grid squares, and annual mean and peak exposures were calculated. In order to account for time variability, the monitoring included an equal distribution of times and weekdays in each square. This method might provide more accurate measures of exposure, but is not practical for most epidemiologic studies.

Carboxyhemoglobin status is a specific biomarker for CO exposure and might reflect an "effective dose" of exposure by accounting for individual differences in metabolism and clearance. A study in Ecuador measured carboxy-hemoglobin status in subjects (Estrella et al. 2005). Although carboxyhemoglobin status might be a reasonable biomarker in subjects with extremely high exposures, such as in the city of Quito, where 82% of air pollution is from traffic, its usefulness as a biomarker might be limited in subjects studied where concentrations and exposures are much lower, as in the United States. In addition, important non-traffic sources of CO (such as active smoking, passive smoke, and indoor combustion sources) also affect carboxy-hemoglobin status.

Few population-based studies have modeled personal exposure to CO. One Swedish study used a dispersion model to estimate CO concentrations at individual residences over a 30-year period (Rosenlund et al. 2006). An emission database from various sources in Sweden provided information that allowed the researchers to calculate annual mean concentrations of traffic-related CO as well as other pollutants (NO_x, NO_2, PM_{10}, and $PM_{2.5}$). Spatial-distribution resolutions differed for inner-city (25×25 m), urban (100×100 m), and regional countryside (500×500 m) locations. Models were calibrated to minimize deviance from actual measured concentrations when available. A street-canyon contribution was also estimated for the most traffic-dense areas of the city center. Input parameters are crucial to a successful model, and variations in the parameters considered, the spatial resolutions used, and the availability and quality of emission data can lead to differences in estimated concentrations and study findings.

Summary The contribution of vehicle emissions to ambient CO and the spatial variability in ambient concentrations suggest CO as an appropriate surrogate for traffic

exposure. The highest ambient exposures are likely to occur in traffic or close to traffic. However, the rapid decrease in ambient concentrations of CO away from traffic to very low concentrations, the challenges related to the measurement of CO at low atmospheric concentrations, the increasing relative contributions in emissions from other sources (off-highway contributions, for example, have increased from 5.5% in 1970 to 21% in 2007, while other sources have increased from 14% to 31% over the same period), the limited information on the ratio of CO to other emission components, and the need to control for other microenvironmental CO exposures (such as parking garages and homes with gas appliances) limit the value of CO as a surrogate for traffic-related pollution exposure. Unlike other traffic-related pollutants, CO is not easily measured by passive samplers, which limits the multi-location monitoring needed to characterize spatial variability.

3.II.3.B Nitrogen Dioxide

Ambient Nitrogen Dioxide as a Traffic Surrogate

On-road vehicles accounted for 33% of NO_x (NO and NO_2 and other nitrogen compounds) emissions in the United States in 2007 (Figure 3.8) (off-road vehicles contributed another 24%) and 44% of NO_x emissions in 1970. NO_x emissions from all sources were at 63% of 1970 emissions levels (U.S. EPA 2008d). NO_x emissions in traffic are dominated by NO ($\geq$ 90%) (U.S. EPA 2008a), which is converted to NO_2 and decays exponentially with distance from traffic (as discussed earlier in Section 3.II.2.A and, for example, in Singer et al. 2004). Once emitted from a source, ambient concentrations of NO, NO_2, and other inorganic and organic nitrogen species vary with distance and time as a function of mixing, intensity of sunlight, and ozone concentration.

Measures of ambient concentrations of NO_2 in the United States are available because NO_2 is listed as one of the six criteria pollutants, i.e., pollutants whose maximum ambient concentrations are set by the U.S. EPA through the National Ambient Air Quality Standards. The average national NO_2 ambient concentration in 2007 decreased 43% compared with concentrations in 1980, when the monitoring of NO_2 became widespread (U.S. EPA 2008a). As with CO, the centrally located U.S. EPA monitoring network captures temporal changes in ambient NO_2 at the regional level, to which traffic and other sources contribute. The network cannot capture the spatial variability of NO_2 associated with traffic emissions near or at various distances from highways.

The availability of inexpensive and light passive monitors for NO_2 (see, for example, Palmes et al. 1976) that can be carried by subjects enrolled in a study has resulted in a rich database of measures of ambient, indoor, and personal concentrations of NO_2. More recently, a passive monitor that allows the measurement of both NO and NO_2 has been developed (Ogawa & Company USA 2008), but data on NO concentrations are limited. Exposure to ambient and indoor concentrations of NO_2 and personal NO_2 exposures have been associated with a range of health effects (see Chapter 4) and are the target of health-based standards. The major contribution of highway vehicles to urban concentrations of NO_2 has focused attention on NO_2 as a surrogate for traffic emissions (see, for example, Rijnders et al. 2001; Lewné et al. 2004; and U.S. EPA 2008c).

Over the past several decades, many studies have reported NO_2 concentrations in ambient air, in a variety of microenvironments (such as residences and parking garages), and as personal exposures. In addition, there have been many epidemiologic studies investigating the association between NO_2 and a variety of acute and chronic health outcomes. The recently released draft of the *Integrated Science Assessment for Oxides of Nitrogen* (U.S. EPA 2008b) summarizes this literature. In this section, we consider only NO_2 measurements used as a surrogate for traffic emissions. Traffic-based models used to predict ambient NO_2 are considered below, in Section IV.

Many studies that relate NO_2 measurements to traffic emissions in various microenvironments (see Figure 3.9, and Table A.1 in Appendix A at the end of this chapter) have been conducted outside the United States, most of them in Europe. These studies have found considerable

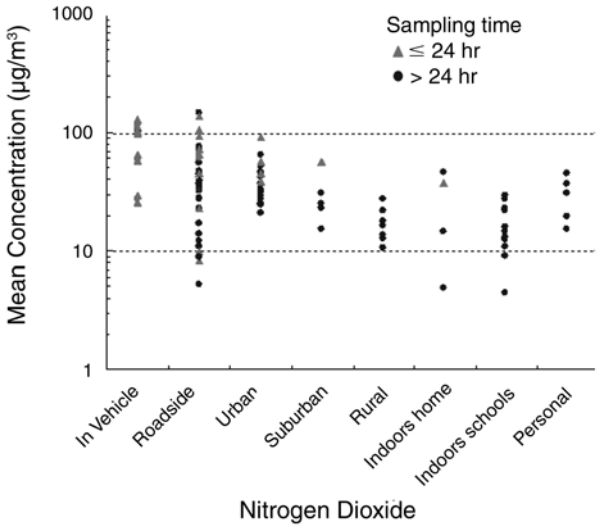

Figure 3.9. Mean NO_2 concentrations measured in various traffic-pollution studies focusing on location. Data used are primarily from studies published since 1998 linking NO_2 to traffic emissions. Data represent averaging times from minutes to more than a year. Passive and active monitors were used in the study. Sampling times are ≤ 24 hr (triangle) or > 24 hr (circle). See Appendix A, Table A.1, for references from which the data were extracted as well as the data used in this figure. (Courtesy of Brian Leaderer and Elizabeth Triche.)

variability in average concentrations by location (in-vehicle, roadside, etc.). Average concentrations tended to be higher in vehicles (ranging from 26 to 131 μg/m^3). Roadside mean concentrations varied considerably from study to study (from 5.3 to 150 μg/m^3). Distance to roadways, vehicle factors (such as the mix of vehicle types, ages, and fuels), and vehicle-use conditions (such as driving conditions, topography, and meteorology) are all factors that might account for the observed variability in roadside NO_2 concentrations. Mean concentrations in urban areas near roadways but not directly affected by roadways showed less variability than roadside concentrations (ranging from 21 to 93 μg/m^3). Urban concentrations tended to be at the upper end of the range of those measured at roadsides, reflecting a direct impact from traffic as well as other sources. Concentrations measured in suburban and rural locations tended to be lower than those in urban locations (with less traffic), which is consistent with the decay gradient of NO_2 concentrations with distance from roadways (as discussed earlier, in Section 3.II.2). As part of the Traffic-Related Air Pollution and Childhood Asthma study conducted in the Netherlands, Germany, and Sweden, the contribution of local traffic to urban NO_2 was estimated at 26% to 27% for Sweden (8 μg/m^3) and the Netherlands (10 μg/m^3) and 9% for Munich (3 μg/m^3) (Lewné et al. 2004). These increases from local traffic were over and above the traffic contribution to urban and regional concentrations.

A limited number of studies have assessed the contribution of outdoor NO_2 (where traffic was not identified as the major potential source) to indoor concentrations in spaces with and without indoor sources (U.S. EPA 2008b). These studies suggested that indoor NO_2 concentrations in homes without indoor sources are roughly 50% of outdoor NO_2 concentrations. In homes with indoor sources, indoor concentrations can be considerably higher than outdoor concentrations. Three studies conducted in the Netherlands reported NO_2 concentrations measured in schools located near highways and outdoors (Roorda-Knape et al. 1998; Janssen et al. 2001; Rijnders et al. 2001). Janssen and colleagues reported that the concentrations in the schools were on average 50% of outdoor concentrations and increased with increasing traffic density. Rijnders and colleagues found that, in all seasons, personal and home outdoor NO_2 concentrations decreased with increasing distance of the home from a highway. The study also found higher concentrations associated with urbanization. Roorda-Knape found that NO_2 concentrations in the classrooms were significantly correlated with car and total traffic intensity and distance of the school from a highway. Smargiassi and colleagues (2005) explored the variability of NO_2 (and other pollutants) at four residential sites at various distances from major roads in Montreal. The researchers observed a decay gradient across sites that depended on traffic volume. Statistically significant differences were observed between background concentrations and concentrations at the traffic sites.

Nitrogen Dioxide as a Traffic Surrogate in Epidemiologic Studies NO_2 is the most common surrogate for traffic-related exposure used in health studies (see Table B.1 in Appendix B, available on the HEI Web site, for examples). As compared with measurement of other pollutants, direct measurement of NO_2 is relatively easy and can be accomplished using inexpensive passive monitors at locations of interest (such as homes, schools, and workplaces). Personal monitoring of NO_2 has been limited by subject compliance. Only a small number of studies have related integrated measures of exposure at home to health outcomes (Gauderman et al. 2005; Sunyer et al. 2006; Jerrett et al. 2008). A few studies used directly measured concentrations together with modeling to estimate personal exposure to NO_2. Krämer and colleagues (2000) assessed traffic-related exposure using a combination of three methods: passive monitoring of 158 sampling points in urban and suburban areas with 150-to-200-meter resolution to interpolate outdoor NO_2 measurements at subjects' homes; personal monitoring (using integrated measurement over a one-week period); and a microenviron-mental model that passively measured concentrations indoors and outdoors at home, at school, and by the main road. The researchers then used time–activity patterns to estimate individual exposure to NO_2. Another study used personal and indoor passive samplers for 48 hours and then applied an air-dispersion model of traffic exhaust to factor out the regional contribution (Zmirou et al. 2002).

Some studies have measured NO_2 using mobile monitors. Sekine and colleagues (2004), for example, measured NO_2 and PM_{10} at zero m and 20 m from roads with varying amounts of traffic. Subjects' homes were classified as having low, medium, or high exposure. This categorical exposure index was compared with health outcomes. Another study placed continuous-monitoring stations on mobile caravans at four corners of one-kilometer squares in a 182-square grid to measure NO_2 along with CO and ozone and then assigned the values at the four grid squares nearest to homes and schools (Hirsch et al. 1999). This approach is not practical for large epidemiologic studies covering wide areas.

Some studies used data from central sites or from monitors placed at sites with varying traffic densities throughout an area to model individual exposure to NO_2. Some of these modeled the relationship between data from sites

throughout the city together with traffic variables to estimate exposure to NO_2 at home addresses (Brauer et al. 2002; Brauer et al. 2007). The variables included the number of roads, traffic density within buffers, the distances to roads, traffic intensity, and other relevant factors (such as population density, land use, and meteorologic data) at the home addresses. Other studies assigned values from previous traffic studies to classify "exposed" and "unexposed" subjects (Hoek et al. 2001; Hoek et al. 2002; Beelen et al. 2008). In these studies, local, urban, and regional background source concentrations were modeled separately from fixed-site monitors and inverse distance weighting was applied. In another study, fixed-site concentrations were modeled to estimate concentrations at the homes of subjects using a geographic information system that included traffic counts and traffic characteristics at various distances from the homes (Nicolai et al. 2003).

Some studies also used data from central monitoring stations in the study area to estimate exposure (e.g., Gehring et al. 2006). Depending on the health outcome, a potential advantage of central-site data is that they are usually available on a daily basis and allow for time-series analyses. However, the inability to account for small-scale spatial variability can lead to significant misclassification because central-site monitors are not located to capture spatial variability. In an effort to address this, some studies have limited the study population to those living within a certain arbitrary distance of the monitor, but doing so might not capture the traffic-related exposure.

Summary NO_2, like CO, is a potential surrogate for vehicle emissions of NO_x. NO_x emissions from vehicles are dominated by NO, which is converted to NO_2. Limited information is available on ambient concentrations of NO. The designation of NO_2 as a criteria air pollutant has resulted in the development of an extensive database on ambient and indoor NO_2 concentrations. Outdoor concentrations measured at central monitoring sites provide data on temporal changes over large geographic areas but cannot provide the spatial resolution needed to assess traffic-related exposures. Indoor sources related to combustion represent an important contribution to personal exposure. Inexpensive passive monitors are available to assess NO_2 and can provide fine spatial resolution of ambient concentrations in traffic-related pollution studies. The use of measured ambient NO_2 concentrations as a surrogate for traffic emissions, either in exposure studies or as a measure of exposure in epidemiologic studies, might be limited because on-road vehicles account for only 33% of NO_x emissions. Using ambient NO_2 concentrations in combination with indicators of traffic or traffic models (such as distances to roads and traffic volume; see Section 3.IV) has utility as an important surrogate for traffic emissions in urban areas, particularly when used on the local scale.

3.II.3.C Particulate Matter

Particulate air pollution is a complex mix of particles of varying size and chemical composition. Ambient concentrations arise from sources including motor vehicles and as by-products of reactions that form secondary particles. PM_{10}, $PM_{2.5}$, and UFP have been explored as surrogates for traffic emissions. Lead was a widely used surrogate for ambient PM related to motor vehicles but has been of limited use since its removal from gasoline in the United States. More recently elemental carbon has been explored as a surrogate for PM related to motor-vehicle emissions.

PM_{10}

PM_{10} in Ambient Air as a Traffic Surrogate Emissions of PM_{10} (Figure 3.8) from on-road vehicles accounted for about 1.0% of total PM_{10} emissions in the United States in 2007 (off-highway emissions accounted for another 1.8%) and have decreased by 65% since 1990 (U.S. EPA 2008d). A summary of source-receptor-modeling studies (see Table 3-10 in Air Quality Criteria for Particulate Matter, Vol. II [U.S. EPA 2004]) conducted from the late 1980s to early 1990s suggests that primary motor-vehicle emissions contributed 10% of ambient PM_{10} concentrations, with considerable variability (from less than 1% to over 40%). Concentrations of PM_{10} associated with motor-vehicle traffic have been assessed in several studies. Lewné and colleagues (2006) reported average concentrations of 26 $\mu g/m^3$, 44 $\mu g/m^3$, and 57 $\mu g/m^3$ in taxis, buses, and trucks, respectively, in Stockholm. Eleven studies (Janssen et al. 1997; Roorda-Knape et al. 1998; Lam et al. 1999; Fischer et al. 2000; Funasaka et al. 2000; Harrison et al. 2003; Harrison et al. 2004a; Harrison et al. 2004b; Namdeo and Bell 2005; Lin et al. 2007; Marconi et al. 2007) reported average PM_{10} roadside concentrations ranging from 18.8 $\mu g/m^3$ in London (Harrison et al. 2003), to a high of 192 $\mu g/m^3$ in Taiwan (Lin et al. 2007), although average concentrations in the majority of studies were generally below 50 $\mu g/m^3$. Traffic volume in these studies ranged from low-intensity traffic volume (< 8900/day, see Janssen et al. 1997, for example) to more than 130,000 vehicles per day (Namdeo and Bell 2005). Harrison and colleagues (2004b) compared mean roadside measurements with corresponding mean urban concentrations in London and found roadside concentrations to be 11.5 $\mu g/m^3$ higher than urban concentrations (mean 34.7 $\mu g/m^3$ versus 23.2 $\mu g/m^3$). In this study, vehicle volume ranged from 27,300 vehicles per day to more than 104,400 vehicles per day. Namdeo and Bell found average yearly roadside, urban, and rural PM_{10} concentrations of

29.2, 19.6, and 14.0 μg/m^3, respectively, in London (Namdeo and Bell 2005). Funasaka and colleagues (2000) measured indoor and outdoor average PM_{10} concentrations for homes with no smokers within 5 to 150 m of roads (traffic volume 54,000 to 58,000 vehicles/day) in Osaka City. The concentrations of PM_{10} at the two sites closest to roads were 55 μg/m^3 and 41 μg/m^3; those at three sites farther from the road ranged from 35 to 41 μg/m^3. Correlations in this study between outdoor and indoor PM_{10} were poor (r = 0.44). Roorda-Knape and colleagues (1998) reported an average concentration of 91.6 μg/m^3 for PM_{10} in 11 schools located near highways. The authors pointed out, however, that indoor concentrations of PM_{10} were largely controlled by indoor activities of the occupants rather than by traffic.

The contribution of motor-vehicle emissions to roadside, urban, or indoor concentrations is difficult to assess from the published literature because of different study conditions, including differences in traffic volume, vehicle mix, vehicle-use conditions, location of measurements (variable distances from roadways), topography, and meteorology. An additional challenge in using PM_{10} or other PM indicators as a surrogate is controlling for background concentrations and indoor sources. Annual concentrations from the U.S. EPA Air Trends database (U.S. Environmental Protection Agency 2008a) show a 29% decrease in ambient PM_{10} concentration between 1990 (when monitoring started) and 2007, but the database cannot provide data on the spatial variability related to traffic.

PM_{10} as a Traffic Surrogate in Epidemiologic Studies As with exposure estimates for CO, estimates of traffic-related PM_{10} exposures used in epidemiologic health studies have in some cases relied on central-site data (see Appendix B available on the HEI Web site). Attempts to reduce misclassification of exposure have been limited to restricting the study population to subjects within a certain distance of the fixed monitor. One of the studies described in Appendix B estimated individual exposures based on emission-inventory data and a dispersion model (Rosenlund et al. 2006). A study by Sekine and colleagues (2004), however, measured NO_2 and PM_{10} at zero m and 20 m from roads with varying amounts of traffic. These data were used to classify the residences of the subjects into three groups (low, medium, and high exposure). Health outcomes were compared between the three. None of the studies used personal monitoring of PM_{10}.

$PM_{2.5}$

$PM_{2.5}$ in Ambient Air as a Traffic Surrogate Approximately 90% or more of PM associated with motor vehicles is in the $PM_{2.5}$ size range. Similar to PM_{10} emissions, $PM_{2.5}$ emissions from on-road vehicles constituted a small percentage of total emissions in 2007 (2.1%; see Figure 3.8); off-road emission added another 5.6% (U.S. EPA 2008d). $PM_{2.5}$ emissions from on-road vehicles have decreased 65% between 1990 and 2007. A summary of source-receptor-modeling studies (see Table 3-9 in Air Quality Criteria for Particulate Matter, Vol. II [U.S. EPA 2004]) conducted from the early 1980s to the late 1990s suggests that motor-vehicle emissions (primary and secondary) ranged from less than 1% to more than 40% of ambient $PM_{2.5}$ concentrations. A recent paper (Watson et al. 2008) reviews the results of receptor models applied to ambient $PM_{2.5}$ collected at seven U.S. EPA supersites. The results indicated that approximately 15% (with a range of 4% to 25%) of $PM_{2.5}$ is attributable to motor-vehicle emissions.

Annual concentrations measured by the U.S. EPA's nationwide monitoring network showed that from 2000 (when monitoring began) to 2007 $PM_{2.5}$ concentrations decreased by approximately 12% (U.S. EPA 2008a). $PM_{2.5}$ tends to be well mixed within a region, and a pronounced concentration gradient is unlikely. This is not surprising, because (1) primary emissions from motor vehicles contribute only a small percentage of the total $PM_{2.5}$, (2) secondary $PM_{2.5}$, which is derived from gas-phase emissions that react in the atmosphere to form new particles (see Chapter 2, section 2.X.1), is a major contributor, and (3) central- or fixed-site monitoring networks are typically placed to assess concentrations on an urban scale rather than a local scale. As with PM_{10}, untangling the contribution of the regional or urban background concentrations of $PM_{2.5}$ from the local contribution is a challenge.

Figure 3.10 summarizes data from recent studies focusing on measuring $PM_{2.5}$ in various microenvironments. Similar to the NO_2 studies, many of these studies have been conducted outside the United States. The range of mean $PM_{2.5}$ concentrations in vehicles (generally 20 to 42 μg/m^3) was similar to that measured at roadside locations, but showed more variability. One study conducted in Hong Kong (Lam et al. 1999) and another in Taiwan (Lin et al. 2007) reported that average roadside $PM_{2.5}$ concentrations were greater than 100 μg/m^3 and that the maximum concentration was 200 μg/m^3. In urban areas, the range of average concentrations (11.2 to 35 μg/m^3) appeared to be somewhat lower and showed more variability than the range of concentrations measured at roadsides. As discussed earlier, $PM_{2.5}$ does not exhibit the sharp distance-decay gradient evident for CO, NO_2, or UFP. Average $PM_{2.5}$ concentrations in homes affected by traffic ranged from 14.4 to 59.0 μg/m^3, which is the same range as concentrations measured at roadside or urban settings. In the few studies reporting $PM_{2.5}$ average concentrations in rural areas, concentrations were

lower than, but in the same range as, those measured in urban areas. One study (Fromme et al. 2005) measured indoor $PM_{2.5}$ concentrations in 73 schools in Berlin and reported an average concentration of 53.8 μg/m^3. The schools were in an urban setting near roads, but neither the distance to roadways nor the volume of traffic on the nearest roads was provided. It is likely that indoor activity at the schools affected the measured $PM_{2.5}$ concentrations. Janssen and colleagues (2001) measured $PM_{2.5}$ both inside and outside 24 schools in the Netherlands. In this study, the $PM_{2.5}$ concentrations in both settings increased with increasing truck-traffic density and decreased with distance from roadways.

$PM_{2.5}$ as a Traffic Surrogate in Epidemiologic Studies
As for the other pollutants, some epidemiologic studies used $PM_{2.5}$ measurements from central- or fixed-sites monitors. As noted above for PM_{10}, attempts to reduce misclassification of exposure caused by spatial variability were limited to restricting the population to those subjects living within a certain distance of the monitoring site.

Several studies modeled $PM_{2.5}$ exposure based on 40 monitors placed throughout Munich (Brauer et al. 2002; Gehring et al. 2002; Brauer et al. 2006; Morgenstern et al. 2007). Measured concentrations at the monitoring sites together with traffic variables were used to estimate individual exposure at the subjects' home addresses. This is an attractive method when extensive monitoring of an area is possible, but it could produce inaccurate estimates if the number of monitors is small in relation to the size of the study region.

Zmirou and colleagues (2002) calculated "lifelong" cumulative exposure to traffic pollutants using traffic-density variables at home and school addresses of the subjects (children 4 to 14 years of age), along with current personal and indoor measurements of $PM_{2.5}$ and NO_2. Because of the weight of the personal monitors, only children 8 and older were asked to participate in the study. Respondent burden and the difficulty of ensuring compliance limit the usefulness of this approach in large epidemiologic studies.

Adar and colleagues (2007) used mobile monitoring carts with continuous samplers on buses during trips to and from downtown, during activities in the downtown area, and in the subjects' residences. This method is not practical for large-scale epidemiologic studies.

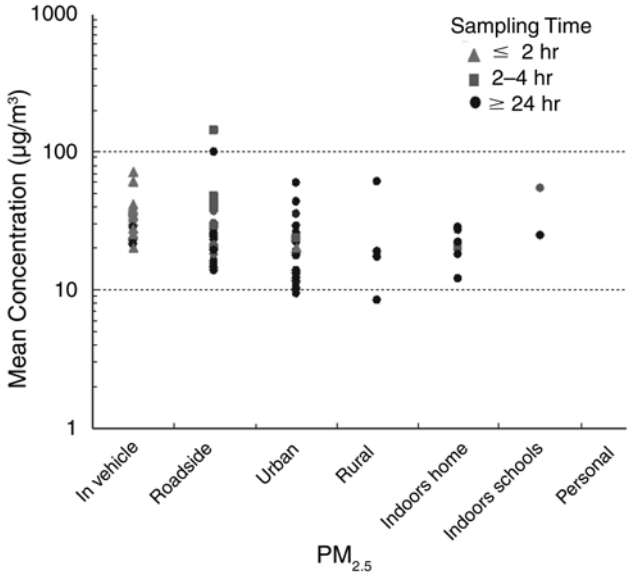

Figure 3.10. Mean $PM_{2.5}$ concentrations measured in traffic-pollution studies focusing on the location. Data used are primarily from studies published since 1998 linking $PM_{2.5}$ to traffic emissions. Sampling methods included both gravimetric and TEOM sampling. Data represent sampling times of ≤ 2 hours, 2 to 4 hours, or ≥ 24 hours. Average times were from minutes to more than a year. See Appendix A, Table A.2, for references from which the data were extracted as well as the data used in this figure. (Courtesy of Brian Leaderer and Elizabeth Triche.)

UFP

UFP in Ambient Air as a Traffic Surrogate UFP is high in number concentration and low in mass. It is generated from fresh sources of combustion and from nucleation events in the atmosphere during specific meteorologic and air-quality conditions. Extensive particle-size measurements performed during special studies as part of the U.S. EPA PM Supersite program (Solomon and Hopke 2008) identified significant sources of UFP from fuel combustion, including near-roadside vehicle-exhaust plumes, wood smoke, and industrial sources, as well as from new-particle-production (nucleation) events from chemical reactions associated with the production of sulfate, nitrate, and organic PM. The atmospheric lifetimes of UFP are short, and UFP concentrations decrease rapidly with distance from the source (Zhu et al. 2006 and Figure 3.4).

There are no emissions inventories or national monitoring networks for UFP, but special field-study programs continue to measure UFP concentration gradients in the vicinity of roadway traffic (see Singh et al. 2006). Two studies reported in-vehicle concentrations of UFP (Weijers et al. 2004; Kaur et al. 2005) ranging from 50×10^3 to 88×10^3 particles/cm^3 with a maximum of 650×10^3 particles/cm^3 (Weijers et al. 2004). Average roadside concentrations reported in six studies (Harrison et al. 2003; Reponen et al. 2003; Harrison and Jones 2005; Holmes et al. 2005; Zhu et al. 2006; Marconi et al. 2007) ranged from 32×10^3 to 115×10^3 particles/cm^3. Holmes and colleagues (2005) reported UFP concentrations in Brisbane, Australia, ranging from 19.7×10^3 to 32.5×10^3 particles/cm^3, with a maximum concentration

of 91 $\times$ 10^3 particles/cm^3 at ten roadside locations. Harrison and Jones (2005) measured particle-number concentrations over a number of years at urban, background, and curbside locations. Mean monthly particle-number concentrations at curbsides averaged 118 $\times$ 10^3 particles/cm^3. Average monthly concentrations at five urban centers ranged from 30 $\times$ 10^3 to 60 $\times$ 10^3 particles/cm^3 range, and at two urban background sites the concentrations were below 30 $\times$ 10^3 particles/cm^3. The authors also summarized the particle-number concentrations reported by a number of other studies.

UFP as a Traffic Surrogate in Epidemiologic Studies The use of UFP as a surrogate for traffic exposure in health studies is limited (Vinzents et al. 2005; McCreanor et al. 2007). McCreanor and colleagues measured the exposure to UFP (as well as several other traffic-related pollutants) of subjects walking along a busy street or in a park in London. The median particle-number concentration measured along the road was 63 $\times$ 10^3 particles/cm^3 and 18 $\times$ 10^3 particles/cm^3 in the park. Vinzents and colleagues studied oxidative damage in 15 participants who were asked to carry monitors in backpacks while bicycling five days in rush-hour traffic and one day in a chamber. The exposure to UFP while bicycling in traffic was directly correlated with the concentrations of NO_2 and CO measured at both the background and street monitoring stations. The usefulness of this approach in large-scale epidemiologic studies is limited because of the cost of the monitors and the burden for the subjects.

Particulate Matter Summary The use of PM as a surrogate for traffic emissions, in the absence of the determination of particle constituents that are specific to traffic emissions, is limited for several reasons. First, traffic is one of the many sources of primary and secondary $PM_{2.5}$. Second, $PM_{2.5}$ concentrations in an urban area are typically well mixed within a region, making it difficult to assess the contribution of motor vehicles at the local (i.e., within 500 m of traffic) or residential scale. Third, there are multiple sources of PM in indoor environments, which presents a challenge in apportioning the contribution to personal exposure of PM from motor vehicles. The current U.S. central-site air-quality monitoring network for PM_{10} and $PM_{2.5}$ is of limited use in assessing the contribution of traffic to ambient concentrations for use in either exposure or epidemiologic studies because it cannot provide spatial resolution. The use of UFP as a surrogate is limited because, while concentrations are high in or near traffic, they drop off dramatically with distance and mix with background concentrations. In addition, there are limited data on atmospheric concentrations of UFP. Atmospheric PM is highly variable in particle size, chemical composition, and the reactive nature of the aerosol, all of which present challenges in linking ambient concentrations to motor vehicles. Personal monitors are available to assess personal exposures to PM_{10} and $PM_{2.5}$, and hand-held continuous monitors are available for UFP; however, they are a considerable burden for the subjects and are expensive.

Elemental (or Black) Carbon

Elemental Carbon in Ambient Air as a Traffic Surrogate

Carbonaceous components of particles, organic carbon (OC), and elemental carbon (EC) account for 35% to 50% of ambient $PM_{2.5}$ (Watson et al. 1994b; Watson et al. 2001). OC is formed in the atmosphere as a secondary by-product of the oxidation of hydrocarbons emitted by primary sources, including combustion of fossil fuels, wood (e.g., wildfires), and vegetation. Motor vehicles account for approximately 30% to 50% of ambient carbonaceous particles (Chow and Watson 2002; Watson et al. 2008). EC (also known as black carbon [BC], light-absorbing carbon, or soot in some analyses) is a component of atmospheric particulates that originate predominantly from the incomplete combustion of fossil fuels. Sources of EC include coal and fuel-oil-fired plants, biomass combustion, and motor vehicles. EC is a significant component of particulate mass from diesel exhaust, accounting for more than 70% of the emitted mass (Schauer and Cass 2000; Zheng et al. 2002; Schauer 2003; Fujita et al. 2007), and has been used as a surrogate for diesel emissions in studies of urban environments (e.g., Kinney et al. 2000; Fromme et al. 2005; Van Roosbroeck et al. 2006). Fractions of OC and EC have been associated with gasoline and diesel exhaust (Watson et al. 1994a; Chow et al. 2004; Chow et al. 2007; Fujita et al. 2007; Mauderly and Chow 2008). Important sources of OC are found indoors (e.g., smoking and cooking), leading to higher concentrations indoors than outdoors (Ho et al. 2004; Na and Cocker 2005; Polidori et al. 2006). EC concentrations are typically higher outdoors than indoors, suggesting that there are few major indoor sources.

Considering EC as a marker for diesel PM, Schauer (2003) cautioned that all sources of EC need to be accounted for, and Reponen and colleagues (2003) suggested that "no single element or component of diesel exhaust can be used as a surrogate … but more comprehensive signature analysis is needed." There is no emissions database or ambient monitor system for EC. Twenty-four-hour average concentrations for EC are available for regional and urban monitoring sites through the U.S. Interagency Monitoring of Protected Visual Environments network (IMPROVE at *http://vista.cira.colostate.edu/ IMPROVE/*) and U.S. EPA Chemical Speciation Network (*www.epa.gov/ttamti1/speciepg.html*), but unlike CO, NO_2, PM_{10}, and

$PM_{2.5}$, there is no national monitoring network to provide historical trends for elemental carbon. Data on the concentrations and sources of carbonaceous aerosol are limited.

EC is measured from PM collected on quartz-fiber filters by thermal-optical reflectance or transmission. Several surrogate measures of EC have been and are currently used: light reflectance and absorption measurement of PM collected on Teflon filters; an automated, time-resolution tape system using particle light absorbance; and a continuous system using a photoacoustic technique. Several studies have found a reasonable agreement between the thermal-optical methods and the more broadly and more easily used nondestructive base reflectance and photoacoustic methods (e.g., Cyrys et al. 2003). Monitors such as aethalometers are available to measure EC continuously, but inexpensive passive monitors to measure it are not currently available.

Figure 3.11 (based on information from Table A.3 in Appendix A at the end of this chapter) summarizes recent studies that measured EC associated with various microenvironments. The studies used a variety of measures (such as reflectance and light absorbance) for estimating EC. Average concentrations, regardless of location, showed considerable variability.

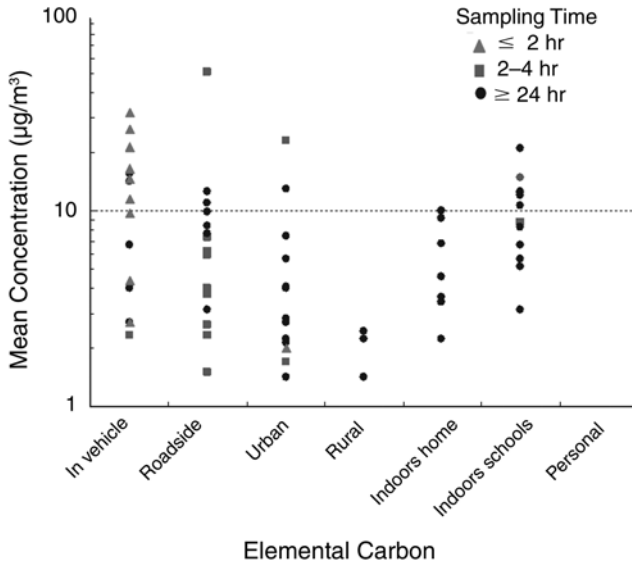

Figure 3.11. Mean EC concentrations measured in traffic-pollution studies focusing on location. Data used are primarily from studies published since 1998 linking EC to traffic emissions. Particle mass samples were typically collected on filters and analyzed by a number of methods (e.g., light absorbance, light reflectance/transmission, photoacoustic, or thermal optic). Independent of the sampling and analysis method, all data are presented as EC. Data represent sampling times of ≤ 2 hours, 2 to 4 hours, or ≥ 24 hours, with data averaging times ranging from minutes to more than a year. See Appendix A, Table A.3, for references from which the data were extracted as well as the data used in this figure. (Courtesy of Brian Leaderer and Elizabeth Triche.)

In-vehicle concentrations of EC ranged from 2.3 μg/m³ in police cars during work shifts in North Carolina (Riediker et al. 2003) to 31.5 μg/m³ in London traffic (Adams et al. 2002). In-vehicle averages over 10 μg/m³ were found in a study conducted in London (Adams et al. 2002). A study conducted in Los Angles and Sacramento (Fruin et al. 2004) found that mean EC concentrations in vehicles following non-diesel vehicles ranged from 2.2 to 4.1 μg/m³; mean concentrations in vehicles following diesel vehicles ranged from 4.7 to 92.0 μg/m³. The type and number of diesel vehicles on the roads played a significant role in the variability observed.

Roadside concentrations were between 2.0 and 10 μg/m³ and were similar to urban and in-vehicle concentrations, if the London data are not considered. The few studies reporting rural concentrations found them to be much lower than urban concentrations. Concentrations measured in homes typically ranged from 1 to 10 μg/m³ but were generally below 6 μg/m³ and appeared to be similar to those measured at roadside and in urban locations. EC concentrations measured in 73 nursery schools in Berlin (Fromme et al. 2005) and 11 schools near highways in the Netherlands (Roorda-Knape et al. 1998) appeared to be higher than in-home locations and were consistent with roadside concentrations. Janssen and colleagues (2001) measured EC (soot) inside and outside 24 schools in the Netherlands. In this study, EC concentrations in both settings increased with increasing truck-traffic density and decreased with distance from roadways.

Elemental Carbon as a Traffic Surrogate in Epidemiologic Studies A number of health-related studies have used EC measures as a surrogate for traffic exposures (see Appendix B, available on the HEI Web site). Studies measuring daily exposures used data from fixed monitoring sites and subjects who lived within a certain distance of the fixed sites (e.g., Gold et al. 2005). Adar and colleagues measured BC along with other particle metrics on mobile monitoring carts with continuous samplers on buses during trips to and from downtown, during activities in the downtown area, and in subjects' living facilities for 48 hours (Adar et al. 2007). This approach is not practical for large epidemiologic studies.

Several studies modeled average exposures to EC over longer periods of time. Four studies (Brauer et al. 2002; Gehring et al. 2002; Brauer et al. 2006; Morgenstern et al. 2007) used data collected at 40 monitoring sites throughout a city to model the relationship between measured concentrations of EC and traffic and related variables and then used the models to estimate individual annual average exposures. Nicolai and colleagues (2003) estimated

concentrations of soot (i.e., EC), NO_2, and benzene at subjects' home addresses based on a model that incorporated annual average measurements using traffic counts from 18 heavy-traffic sites and 16 light-to-medium traffic sites within zero to 50 m of the residence (Nicolai et al. 2003). Another study (Hoek et al. 2002) estimated urban and regional background concentrations of BS (i.e., EC) by inverse distance weighting of concentrations at central sites. Small-scale variability was estimated by applying values from two Dutch traffic studies to exposed (within 100 m of highway or 50 m of major roads) and unexposed subjects (greater the 100 m from a highway or 50 m from a major road). Similarly, Beelen (2008) modeled exposure to BS based on regional background, urban background, and local source concentrations (estimated separately) from fixed monitoring sites and applying inverse distance weighting to obtain the distance from home addresses to major roads (using data from a 20-year period).

Summary EC and important constituents of PM hold some promise as traffic-exposure surrogates. EC has been used in several studies as a surrogate for diesel exposures, but its utility is limited by the ability to control for other nonmobile sources (such as wood smoke) or for gasoline-fueled motor vehicles. Because EC is not a criteria pollutant, few historical data are available on ambient trends, and there is no national EC emissions database. EC can be measured easily by nondestructive methods in PM collected on filters and by continuous monitors, but standard calibration methods need to be established. Available data suggest that EC is highly variable in ambient air and is related to diesel PM, but the contribution of diesel exhaust needs to be evaluated against the background of emissions from gasoline-fueled vehicles and other anthropogenic sources. Studies that have combined EC measurements with traffic-related variables (e.g., proximity to traffic or traffic volume and type) hold promise in assessing exposures to emissions from diesel and gasoline-fueled vehicles in epidemiologic studies.

3.II.3.D Benzene

Benzene in Ambient Air as a Traffic Surrogate The emissions of VOCs from on-road vehicles in 2007 were 21% of those measured in 1970 and accounted for 20% of total VOC emissions in 2007 (U.S. EPA 2008d). Benzene is one of many VOCs emitted by motor vehicles and one of 21 air pollutants designated as a mobile-source air toxic from a list of 188 identified by the U.S. EPA (*http://epa.gov/otaq/toxics.htm*). The principal source of atmospheric emissions of benzene is on-road mobile sources, which account for 49% of total benzene emissions (Figure 3.8). Off-road emissions account for an additional 19%. Between 1996 and 2000, benzene emissions from on-road mobile sources decreased by 12% (U.S. EPA 2006). Mean ambient concentrations of benzene measured at urban sites in the United States have decreased by 47% between 1994 and 2000 and have decreased by 45% over a comparable time period at urban sites in Canada (HEI Air Toxics Review Panel 2007). A recent HEI report on mobile-source air toxics reviewed the sources, exposures, and health effects associated with exposure to benzene. The report noted that there is much information available on environmental concentrations of benzene and its associated health effects. The data on the concentrations of benzene in various microenvironments reported in the published literature can be found in Table 4 of that report (HEI Air Toxics Review Panel 2007). Average concentrations tend to be higher in vehicles and at urban roadsides (1 to 22 $\mu g/m^3$) and lower in urban areas (< 1 to 3.9 $\mu g/m^3$). Rural areas have the lowest concentrations, with modeled and ambient concentrations below 1 $\mu g/m^3$. The decrease in concentrations from roadside to urban to rural areas is consistent with that shown for benzene in Figure 3.3 and discussed in Section 3.II.2. It is also consistent with on-road emissions in rural areas being lower than those in urban areas. Indoor concentrations were in the same range as outdoor concentrations in urban areas; indoor concentration might be affected by indoor sources (such as tobacco combustion), which are important contributors to concentrations indoors and to personal exposures.

Benzene as a Traffic Surrogate in Epidemiologic Studies Benzene has been used as a surrogate for traffic-related pollution in health-related studies. Two studies in Drammen, Norway, used central-site data (Hagen et al. 2000; Oftedal et al. 2003). A third study predicted benzene concentrations using emissions models from 18 heavy and 16 light-to-medium traffic areas (Nicolai et al. 2003).

Summary Central monitoring sites have provided regional data on variations in benzene concentration over time since the early 1990s; however, they do not capture information about the spatial gradients of benzene concentrations (Figure 3.3). Although motor vehicles are a major source of benzene, data from recent studies and from the U.S. EPA sites have suggested that, with the possible exception of in-vehicle or roadside benzene measurements, benzene might not be a suitable surrogate for traffic-related emissions. Other sources, both indoors and out, make it difficult to untangle the contribution of motor vehicles. In addition, there are few epidemiologic studies that have used benzene as a surrogate for traffic exposure.

3.II.3.E Measures of Traffic

Several epidemiologic studies have assessed exposure to traffic-related pollution using measures of traffic itself

as a surrogate. Traffic measures include vehicle mix (i.e., diesel and gasoline-fueled vehicle volumes), traffic density or volume (for example, the daily number of vehicles), traffic density within buffers (from 50 to 5000 m), distance to roadways, street segments, and self-reported traffic exposures. To improve the specificity of exposure measurements, some of the studies have combined the traffic measures with measures from central monitoring sites or from targeted monitoring campaigns of one or more pollutants (such as NO_2, PM_{10}, or EC) that serve as a surrogate for traffic. More recently, several studies have added a geographic information system (GIS) to account for variables such as population density, topography, density of buildings, land use, and distance from roads. A series of studies conducted in Europe (Brauer et al. 2002; Gehring et al. 2002; Nicolai et al. 2003; Brauer et al. 2006; Morgenstern et al. 2007) used pollutant measurements recorded at 40 sites in the Netherlands and Munich in combination with GIS variables and traffic variables measured around each monitoring site to develop a model to estimate concentrations of traffic-surrogate pollutants near residences. Other studies used central-site monitoring data in combination with self-reported traffic intensity (Sunyer et al. 2006), traffic density (Zmirou et al. 2004; Lipfert et al. 2006), proximity to major roads (Schikowski et al. 2005; Gehring et al. 2006; Hoffmann et al. 2007), and dispersion modeling and distance to the nearest highways or highway segments within buffers (Bayer-Oglesby et al. 2006). Several studies used various combinations of pollutants, typically NO_2, recorded in several locations (e.g., central sites, personal, residential indoor and outdoor, and in schools) in combination with various traffic or GIS variables (Krämer et al. 2000; Hoek et al. 2001, 2002; Yang et al. 2002; Zmirou et al. 2002 Gauderman et al. 2005). Gauderman and colleagues, for example, used NO_2 measurements (from Palmes tubes) made outside of respondents' residences in combination with the distance to the nearest freeway, the average number of vehicles per day traveling within 150 m of the home, and model-based estimates of traffic-related NO_2 (derived from dispersion models) to characterize exposures.

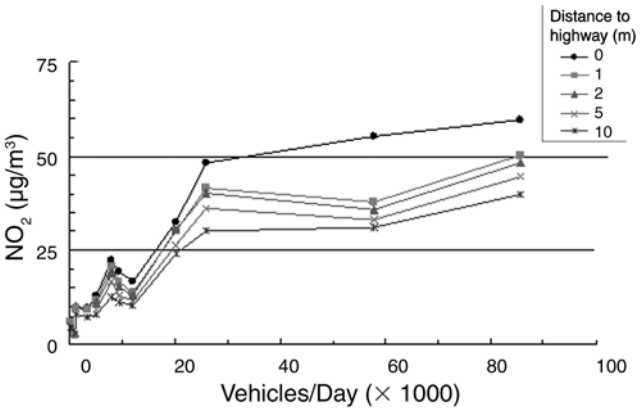

Figure 3.12. NO_2 concentrations by distance to roadway (0 to 10 m) as a function of total traffic density. (Courtesy of Brian Leaderer. Data from Cape et al. 2004.)

Models of pollution that incorporate traffic metrics, GIS technology, and measured pollutants might permit better spatial representation of the local impact of traffic against a background of regional and urban concentrations. The variables used in published models vary considerably, which makes comparisons and evaluations of the models difficult. Given the current effort to incorporate such models into epidemiologic studies, an effort to validate models is needed. Traffic exposure models are discussed in detail in Section 3.IV.

3.II.3.F Pollutant Concentration and Traffic Density

Several studies (e.g., Raaschou-Nielsen et al. 1997; Fischer et al. 2000; Adams et al. 2001b; Alili et al. 2001; Rijnders et al. 2001; Lena et al. 2002; Cape et al. 2004; Harrison et al. 2004b; Weijers et al. 2004; Fromme et al. 2005; Smargiassi et al. 2005; Westerdahl et al. 2005; da Silva et al. 2006) have determined the relationship between reported concentrations of individual air pollutants near roadways and traffic density and, in some cases, types and conditions of vehicles (cars, trucks, age of vehicles, etc.). The main findings are summarized below.

The associations between pollutant concentrations and traffic density have been shown to vary with the pollutant measured and the features of the sampling sites. For example, concentrations of NO_2 (and NO_x) and EC (measured as the absorbance of $PM_{2.5}$) have been found to be higher at sites near roads with high traffic density (Fischer et al. 2000; Alili et al. 2001; Janssen et al. 2001, Rijnders et al. 2001; Roemer and van Wijnen 2001; Lena et al. 2002; Cape et al. 2004; Smargiassi et al. 2005; da Silva et al. 2006) and high concentrations of UFP (Weijers et al. 2004). For PM_{10} and $PM_{2.5}$, the differences between sites were less pronounced (Fischer et al. 2000; Roemer and van Wijnen 2001; Lena et al. 2002; Westerdhal et al. 2005). Harrison and colleagues (2004a) found that the topography around the sites of roads (for example, whether roads are surrounded by open land or buildings) had an effect on PM concentrations.

Cape and colleagues (2004) recorded bimonthly NO_2 concentrations (with Palmes tubes) over a one-year period at five distances (at road's edge and at 1 m, 2 m, 5 m, and 10 m from the road's edge) from roads across Scotland. Measurements were made on 14 different roads with a wide range of traffic densities and types of vehicles. Figure 3.12, plotted from data presented in the paper (see Table 3 in Cape et al. 2004), shows the relationship between total traffic density

and distance from the roadway. NO_2 concentrations tended to be higher closer to roadways and on roads with higher traffic density. Concentrations diminished away from the roadways.

A few studies investigated the association between pollutant concentrations, traffic density, and vehicle types (cars and trucks) (e.g., Lena et al. 2002; Janssen et al. 2001).

Lena and colleagues (2002) measured the concentrations of $PM_{2.5}$ and EC at seven intersections in the South Bronx (in New York City) in high-density residential and commercial areas. They classified traffic into passenger cars, small trucks, and large trucks (diesel vehicles). They found that site-to-site variations were more pronounced for EC than for $PM_{2.5}$. Site-specific EC concentrations were more highly correlated with site-specific counts of large trucks ($r = 0.92$) than with passenger cars ($r = 0.72$) or small trucks ($r = 0.75$). The correlations for site-specific $PM_{2.5}$ concentrations and the three types of vehicles were lower ($r = 0.62$, $r = 0.58$, and $r = 0.72$, respectively).

Janssen and colleagues (2001) recorded weekly samples of NO_2, $PM_{2.5}$, and BC over a 16-week period inside and outside 24 schools in the Netherlands. The schools were located within 400 m of motorways. The distance from schools to the motorways ranged from 32 to 377 m (mean of 206 m). Total vehicle density ranged from 39,737 to 169,637 vehicles on a weekday (mean of 102,690). Truck density ranged from 5,190 to 22,326 vehicles (mean of 13,146) and car density ranged from 30,399 to 155,656 vehicles (mean of 89,544) on a weekday. Concentrations of $PM_{2.5}$ and BC outside the schools were found to increase with increasing truck-traffic density and decrease with distance from motorways. NO_2 and BC concentrations at the schools were associated with the percentage of time that the school locations were downwind of the motorways.

Taken together, the studies suggest that there is an association between concentrations of the air pollutants used as traffic-surrogates near roadways and variations in total traffic density and the mix of vehicles (cars and trucks). However, there is no consistent relationship across studies. Each study is most likely unique to the area it was conducted in and is probably not easily transferable to other geographic areas. It is very difficult to extend the findings of individual studies to draw more universal conclusions because the studies employed different measures of traffic density and mix of vehicle types, did not account for vehicle use and traffic characteristics, measured different pollutants, monitored pollutants at variable distances from the roads, were conducted under variable meteorologic conditions and different terrains, did not generally account for background pollutant concentrations, and employed variable sampling periods and averaging times.

3.II.3.G Summary

Emissions of air pollutants from on-road motor vehicles comprise numerous organic and inorganic compounds in both particle and gas phases. Many of these compounds undergo both physical and chemical transformations after being emitted. The type and quantity of emissions are a function of several variables (such as the mix of light- and heavy-duty vehicles, vehicle speeds, and vehicle density), meteorologic conditions, topography, and land use. Individual exposure is influenced by the rate at which these transformations take place, other ambient and microenvironment sources, and individual time–activity patterns. While focusing on the contribution of traffic to air pollution at the local scale, it is important to consider the contribution of other sources to background concentrations.

None of the surrogates considered meet all the criteria for an ideal surrogate of traffic. Emissions from both light- and heavy-duty vehicles have varied greatly over time, as have emissions of surrogates. Data are not available to assess the ratio of the surrogates to total emissions over time. On-road vehicle emissions of CO, benzene, and NO_x (the reaction by-product NO_2 is considered here) are all major contributors to emissions from all sources, accounting for 40% or more of total atmospheric emissions. All three compounds have significant ambient and microenvironmental sources, making it difficult to disentangle the contribution of motor vehicles. Primary on-road vehicle emissions of PM ($PM_{2.5}$ or PM_{10}) represent a small contribution to emissions from all sources (around 3%). When considering secondary aerosol formation, motor vehicles can account for 15% or more of ambient PM concentrations. Similar to CO, NO_2, and benzene, there are multiple sources of PM outdoors and indoors, making the assessment of the contribution of traffic difficult. UFP measurements performed during the U.S. EPA PM Supersite program identified significant UFP concentrations from combustion sources, including near-roadside exhaust plumes, wood smoke, and industrial sources, as well as new-particle-production (nucleation) events from chemical reactions associated with sulfate, nitrate, and organic secondary-reaction products. UFP concentrations are very high in vehicle-exhaust plumes but decrease rapidly with distance from the source, which poses a significant challenge to researchers characterizing the spatial and temporal concentration gradients of UFP from roadway traffic. In recent years, EC has been used as a surrogate, primarily for diesel exhaust. Further study is needed to account for

the contribution of EC from non-mobile sources and from gasoline-fueled motor vehicles. Standardization and calibration of nondestructive sampling methods are also needed. The current IMPROVE and STN networks measure 24-hour average EC concentrations for predominantly regional and urban monitoring sites, respectively. Typically the IMPROVE network samples once every 6 days, and the STN network samples once every 3 days. As with other pollutants studied, traffic-oriented measurement sites for EC are very few in number. Inexpensive passive monitors exist at this time only for NO_2.

Central monitoring sites cannot by themselves capture the spatial variability of traffic-related pollutants, because they were designed to collect data on pollutant concentrations on an urban or a regional scale rather than the local scale — the scale at which traffic-related air-pollution concentrations are highest and most variable. As a result, measurements from central monitoring sites are not sufficient for use in exposure assessment or for epidemiologic studies. However, traffic-specific monitoring sites are limited. Ambient monitoring is needed, either alone or in combination with various modeling techniques, to capture gradients of traffic-related exposure at the local scale.

A few studies link traffic density to concentrations of surrogates near roadways or at homes. These studies have suggested that there is an association between variations in total traffic and composition of traffic (i.e., the mix of cars and trucks) and the concentrations of traffic-surrogate air pollutants near roadways. Each study, however, is most likely unique to the area it was conducted in and probably not easily transferable to other geographic areas, because the studies employed different measures of traffic density or vehicle volume; differed in traffic composition, specific vehicle conditions and characteristics; collected data at varying distances from roadways under varying meteorologic conditions in different geographical areas; frequently did not account for background concentrations; and employed variable sampling periods and averaging times.

Incorporating one or more traffic measures and employing GIS technology along with measurements of the concentrations of traffic-surrogate pollutants is an approach that would allow better spatial representation of the local effect of traffic in the context of regional and urban pollution concentrations. Such an approach is increasingly being used in epidemiologic studies of traffic-related air pollution. Used with other modeling techniques (discussed in Section 3.IV), it might prove to be the most appropriate cost-effective approach to measure traffic exposure in epidemiologic studies.

3.III. CONSIDERATIONS IN ASSESSING EXPOSURE OF THE GENERAL POPULATION

This section addresses several aspects of assessing exposure to traffic-related air pollution that are relevant to the conduct and interpretation of epidemiologic studies. These include exposure misclassification, the limitations of existing monitoring networks, patterns of land use, and the social distribution of exposure.

3.III.1 EXPOSURE MISCLASSIFICATION

Exposure misclassification in health studies results from the discrepancy between assessed exposure and an individual's true exposure (see Wilson and Suk 2005 for a more detailed review of the complexities of time and space issues in exposure assessment). The effects of exposure misclassification vary by averaging period and study design. Time-series, case-crossover, and panel studies are best suited for investigating short-term acute effects of exposure to traffic-related pollution; cohort studies are used to investigate longer-term effects.

Spatial variability in traffic-related exposure is one source of exposure misclassification. As noted earlier, traffic pollution has a strong spatial gradient and the contribution from traffic is superimposed on background concentrations. When using an individual pollutant as a surrogate for traffic exposure, it is important to be able to factor out the background concentrations from non-traffic sources.

Bias from pollutant-exposure misclassification in daily time-series studies has been considered to be small when correlations between sites are high. However, ignoring spatial variability in pollutants, particularly traffic-related local components, can lead to the biasing of effect estimates toward the null. Concentrations from central monitoring sites that are assigned to individuals across a region have been found to adequately represent average exposure to a given pollutant in daily time-series studies. However, given that the local traffic contribution to overall concentrations measured at a central site might be large or small relative to the contribution from other sources, daily variability might or might not reflect variability in traffic exposure. In addition, if absolute concentrations are considerably lower in areas more distant from the monitors and traffic, results could be biased if there were a health-effect threshold. The need to expand monitoring capacity to improve exposure assessment in epidemiologic studies is discussed below.

Exposure conditions also vary across time. Variations in pollutant concentrations over shorter time periods (such as hourly or daily) tend to be much greater than concentrations averaged over longer time periods (such as annual average or cumulative lifetime average). This issue is particularly relevant for cohort studies enrolling individuals from different communities over time. It is important to compare short-term exposures over identical time periods and to compare long-term exposures over identical or very similar time periods. Meteorology and proximity to sources are the two most important factors in considering ambient concentrations; both the day-to-day and year-to-year variations in meteorology and source activity can affect concentrations.

3.III.2 MONITORING TO SUPPORT INTRA-URBAN EXPOSURE ASSESSMENT

In recent years, researchers have augmented urban- and regional-scale monitoring networks with local-scale networks to improve the understanding of intra-urban air-pollution exposures. Traffic emissions are the principal source of intra-urban variation in the concentrations of air pollutants in many cities, especially in cities where moderate or large point sources are located outside the city or are subject to strict emissions controls. As discussed in other parts of this chapter, the focus on the intra-urban scale has already demonstrated that for some air pollutants, particularly those in traffic emissions, the range of exposures can be larger within cities than between them. Table 3.2 (from Gilliland et al. 2005) shows the spatial scale of variability of the pollutants found in most urban environments. The characterization of variations in the concentrations of traffic-related pollutants within a small area requires monitoring at the scale appropriate to the area.

At present, most regional and urban monitoring networks have sites in urban areas that are 10 to 50 km apart. Monitoring locations are often selected to maximize regional representation and minimize the influence of local sources (e.g., traffic or point sources). Although the air quality in urban areas is often dominated by contributions from mobile sources, the sites in urban networks are too far apart to assess variations in intra-urban exposures from traffic in small areas. Central monitoring sites are important for characterizing short-term air-quality conditions, including the diurnal variation in contributions from traffic, long-term air-quality conditions, trends, and compliance with standards. Measurements of chemical and meteorologic factors at central monitoring sites with high temporal resolution are often invaluable for assessments of source attribution, including the identification of traffic-related sources. However, many sites lack the instruments, filter measurements, and analyses best suited to characterizing contributions from traffic. Augmentation of central monitoring sites with measurements that help distinguish traffic-related constituents both temporally and chemically (such as UFP; EC; OC; polycyclic aromatic hydrocarbons; various gaseous, semivolatile, and aerosol organic compounds; CO; and NO or NO_2) can be very helpful. Such measurements are highly desirable (perhaps necessary) but not sufficient for the characterization of local-scale variations in traffic-related pollution needed for epidemiologic investigations.

In this context, it should be noted that differences between jurisdictions in the criteria for selecting monitoring sites can complicate the interpretation of central monitoring in epidemiologic studies. In many areas of the United States, for example, roadside monitoring locations are avoided; but in Canada and some European countries, monitors are sometimes located specifically at or near roadsides in order to assess the effects of traffic. These differences in siting criteria might limit comparisons between locations. The location of the monitors in relation to traffic and other sources is a particular concern in large multinational studies seeking to compare health effects across countries (Götschi et al. 2004).

A number of approaches are available to collect local-scale air-quality data in saturation-monitoring network, in which, for example, 10 to 200 locations might be concurrently monitored to characterize traffic or other local-source-related pollutants. Most monitoring systems designed for microenvironmental sampling might be suitable for this application. Small, quiet, continuous monitors that do not require temperature-controlled shelters or much electrical power are well suited for use in residences, schools, businesses, and recreation facilities. Small aethalometers, water-based condensation particle counters, and PB-PAH monitors can be used to collect BC, make UFP counts, and measure concentrations of polycyclic aromatic hydrocarbons, all of which are surrogates for traffic emissions. Miniature nephelometers and beta-attenuation gauges can also be used to provide a surrogate measure of $PM_{2.5}$ mass. Samples can be collected with active and passive sampling systems over a period of time and then be subjected to laboratory analysis for determination of integrated aerosol and gas PM concentrations. Personal cascade impactors can be used to determine size and the chemical constituents of PM deposited on filters, such as OC, EC, trace metals, ions, and selected organic compounds (Singh et al. 2003; Lee et al. 2006). Active and passive samplers are also available to measure NO_x, ozone, sulfur dioxide (SO_2), and VOCs. Passive samplers for NO_2, NO_x, and VOCs are popular for saturation-monitoring studies

Table 3.2. Spatial Scale Variability of Ambient Air Pollutants[a]

Compound[b]	Regional Scale (100–1000 km)	Urban Scale (4–50 km)	Neighborhood Scale (50 m–4 km)	Household Scale (≤ 50 m) Outdoors and Indoors
Primary $PM_{2.5}$ constituents				
EC from combustion		X	X	X
Organics, including PAHs		X	X	
Metals, including chromium (VI), cadmium, lead, beryllium, nickel, arsenic, iron, and manganese		X	X	X
Other constituents from road dust, wood smoke, construction dust, and industrial sources		X	X	
Secondary $PM_{2.5}$ constituents				
Sulfate	X			
Nitrate	X	X		
Ammonium	X	X		
Secondary organics	X	X		
Primary $PM_{2.5–10}$ constituents				
Organics, including PAHs		X	X	X
Metals, including chromium (VI), cadmium, lead, beryllium, nickel, arsenic, iron, manganese		X	X	
Other constituents from road dust, wood smoke, construction dust, and industrial sources		X	X	
Primary $PM_{>10}$ constituents				
Pollen grains			X	X
O_3	X	X		
NO		X	X	
NO_2		X	X	
SO_2		X	X	
CO			X	X
Volatile organic compounds				
Benzene		X		X
1,3-Butadiene		X		X
Formaldehyde		X		X
Acetaldehyde		X		X
Acrolein		X		X
Vinyl chloride		X		X
Carbon tetrachloride		X		X
Chloroform		X		X
Propylene dichloride		X		X
Methyl chloride		X		X
Trichloroethylene		X		X
Tetrachloroethylene		X		X
Naphthalene		X		X
Mercury	X	X		

[a] Adapted from Gillibrand et al. 2005. Used with permission.

[b] Bioaerosols, including endotoxin, house dust allergens, fungal spores, and pollen grains, also vary considerably on the household and neighborhood scales; however, they were not included in this analysis.

because of their low cost and ease of deployment. The principal limitation of passive sampling technologies is the measurement precision, which might not be high enough to capture spatial variation. Active samplers are typically two or three times more precise than passive samplers.

Saturation-monitoring networks are usually established for 2-week cycles of two to eight rounds of monitoring during a year. Recent evidence has indicated that within-site variation in pollution measures over time is smaller than between-site variation, suggesting that saturation monitoring for approximately four 2-week periods might supply a good approximation to long-term annual averages (Gilliland et al. 2005). Moreover the spatial variability of traffic pollutants appears fairly constant over time (Lebret et al. 2000; Wheeler et al. 2006), which is essential for saturation-monitoring campaigns to represent chronic exposure to traffic pollution.

Traditional routine network monitoring conducted at a sufficient number of locations to model within-city variability is expensive. With the spatial variation of some common surrogates (such as UFP CO, and NO) within a range of 50 to 300 m (Hewitt 1991; Zhu et al. 2002), monitoring networks would have to approximate this scale of resolution to capture full information on the likely spatial variation of pollutants. Monitoring on this scale would require literally thousands of monitors in many cities. As shown earlier in Toronto, even a 500-m lattice of points results in 2537 potential monitor sites (Kanaroglou et al. 2005). Measuring on a 100-m grid would result in 60,545 locations and is therefore impractical. A lattice of this many samples is not only cost-prohibitive but would yield redundant information in, for example, large residential areas where pollution concentrations have less variability (Kanaroglou and Jerrett 2009). Efforts to sample such a large number of sites randomly in order to derive a representative sample would still require more than 500 sites. Such efforts are beyond the financial resources of most environmental health studies. In this context, the question of how to optimize sampling networks to capture spatial variation in air pollution with maximum efficiency takes on increasing importance.

When adding new monitors to an existing monitoring network, where some monitoring capacity is available initially, geostatistical approaches can be used to determine where they should be placed (Bailey and Gatrell 1995). These approaches rely on estimating the variance in the kriging prediction over the target spatial sampling field. Unfortunately the monitoring in most cities is inadequate to calibrate kriging models, which makes geostatistical approaches unfeasible. In the absence of detailed monitoring data, network assessments are commonly performed using data on traffic density, population density, and land use in suitability analyses.

Recently other optimization schemes have been developed for locating monitors effectively for saturation monitoring (Kanaroglou et al. 2005). These rely on the principle that the highest demand for monitors will be in places where pollution varies the most over small areas (usually in areas of variable or heavy traffic) and where the population density is highest. Weighting by population is necessary when resources are constrained for exposure assessment, as is often the case in health studies. If more sampling resources were available, it might be possible to ignore the human population targeted in a health study and to focus only on optimally modeling the variation in pollution. With finite resources, however, one strategy to ensure that errors are minimized in areas central to the health study (i.e., where the study population is likely to live) is to weight the statistical measure of pollution variation by the population density, thus ensuring that information content is highest where it is most useful for the assessment of health effects. As noted below, saturation monitoring can be combined with auxiliary information on land use and transportation characteristics to employ dispersion models and develop LUR models (Henderson et al. 2007) and integrated Bayesian interpolation models (Christakos et al. 2001) or other generalized linear models that account for time, space, meteorology, and traffic (Gryparis et al. 2006).

There are now at least 25 published papers documenting saturation monitoring with passive samplers and subsequent LUR models (Hoek et al. 2008). Because the sampling locations, numbers of samplers, monitoring instruments, basic land-use and traffic data, modeling strategies, and variables selected to predict the distribution contour of exposure (also known as the exposure surface) can all vary between studies, the comparative interpretation of such models in epidemiologic studies is challenging. Addressing these challenges will require establishing monitoring or measurement criteria for the characterization of intra-urban exposures and the development of methods to evaluate exposure models and performance standards. The most widely used exposure models are presented and discussed later in this chapter.

3.III.3 URBAN SPRAWL, INCREASED AUTOMOBILE DEPENDENCE, AND AIR-POLLUTION EMISSIONS

The form and structure of urban areas have changed dramatically over the past 150 years. Increased automobile use as the primary means of travel has increased the relative contribution of traffic to the urban pollution mixture. Compared with earlier settlements of small towns with

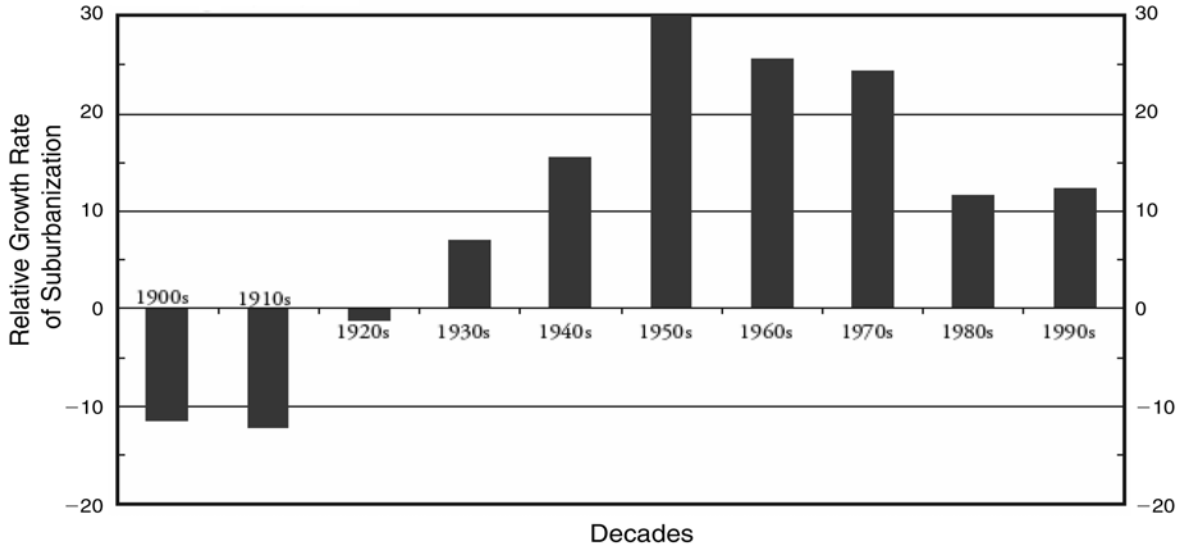

Figure 3.13. Suburbanization of American cities from 1900 to 2000. Relative growth rate of suburbanization expressed as difference between median suburban and city growth rates per decade. (Reprinted from Rappaport 2005. Used with permission.)

mixed land use and high levels of walkability, modern cities are sprawling complexes of residents who depend on automobiles. The reasons for the evolution of urban areas and the implications of the changes are multifaceted and interrelated. This section examines some of the major trends that have led to automobile dependence and their implications for VMT per capita and traffic-related air pollution.

3.III.3.A Automobile Dependency in Historical Perspective

Newman and Kenworthy (1996) identified three distinct phases of urban development that led to progressive automobile use in many urban areas. Settlement patterns that prevailed for thousands of years, until the Industrial Revolution of the 19th century, consisted of smaller settlements that mixed various types of land use. Because walking was the predominant mode of transport, these settlements were generally smaller than 5 km in diameter, had most commercial destinations within a half-hour walk of many residences, and relied more directly on local resources than modern cities do (Owen 1991).

The Industrial Revolution led to a migration of people from the countryside to the city, which often resulted in overcrowding, poor sanitation, and high concentrations of pollution from industries in proximity to residential areas (Mumford 1975; Hall 2002). In response to the ills of the industrial city, people moved away from the industrial urban core to suburban areas, which were usually connected by rail to the urban area (Howard 1946; Newman and Kenworthy 1996). This functional separation of industrial and residential land use reduced pollution exposure and overcrowding, which had often led to poor sanitation and outbreaks of infectious disease. The separation, however, also sowed the seeds of automobile dependence.

Beginning in the 1930s and 1940s and accelerating until at least the 1990s, many cities experienced rapid population growth in suburban areas. Figure 3.13 shows the relative growth of suburban areas compared with urban areas in American cities (Rappaport 2005). Urban sprawl, the haphazard spread of low-density development beyond a city's boundaries, is most pronounced in North American cities but has become a worldwide phenomenon that also characterizes land-use development in rapidly growing economies, such as in China and India. In these countries, increasing wealth has also generated demand for automobile travel (Molina and Molina 2004). In the absence of effective land-use planning, many cities are experiencing dramatic growth in private automobile use and in traffic-related air pollution.

Sprawl has four important characteristics that contribute to a syndrome of environmental and health costs, including increased air-pollution exposure (Frumkin 2005): (1) deconcentration (i.e., lower population density throughout much of the urban area than in earlier periods); (2) decentralization with more new development occurring in suburban than central areas (see Figure 3.14, for example, for a map showing the expansion of Mexico City during the 20th century); (3) large-scale development of subdivisions, industrial parks, and commercial centers; and, (4) as a result of this large-scale development, homogeneity in land-use

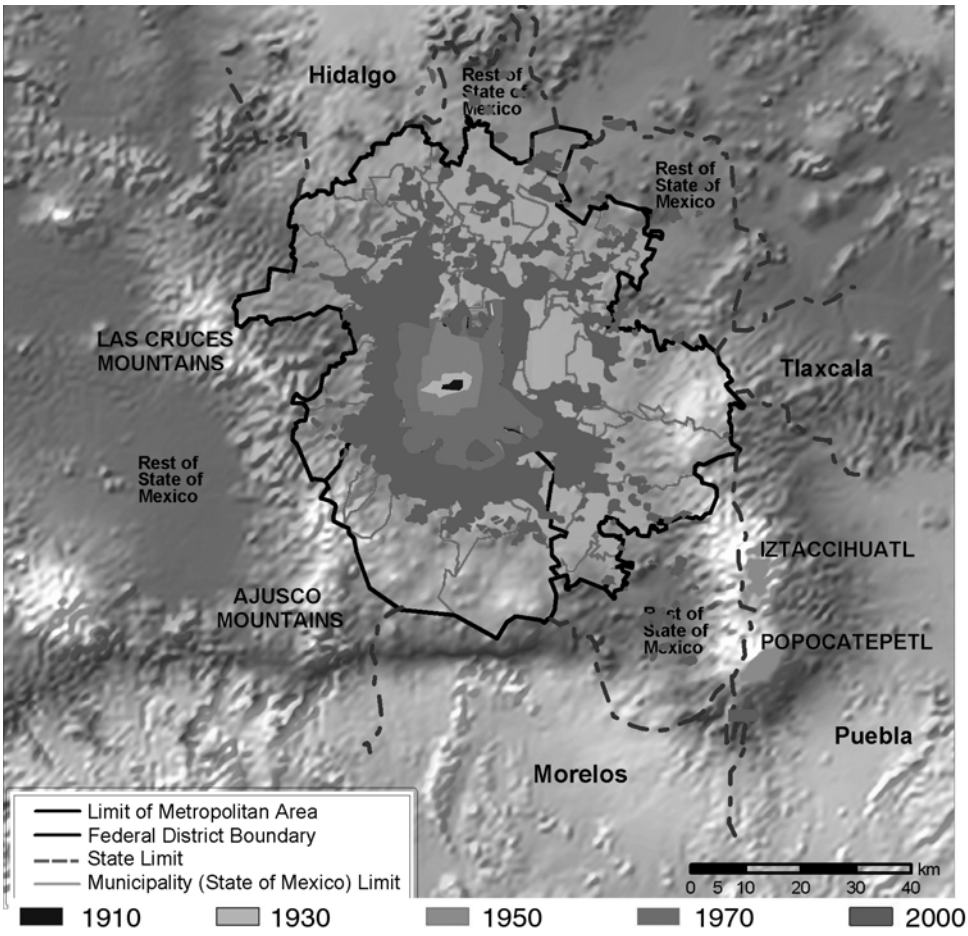

Figure 3.14. Topographic map of Mexico City Metropolitan Area showing expansion of metropolitan area from 1910 to 2000. (Reprinted from Molina and Molina 2004, with permission of the Air and Waste Management Association.)

mix and segregation of land-use types, creating a need for travel between, for example, residential and commercial sites.

Taken together, these characteristics create demand for travel, from residential sites, for example, to commercial sites. Moreover, sprawl increases the probability that this demand will be met with automobiles, because costs are too high to provide high-speed public transit to low-density developments. Transit supplied by buses without designated lanes is always slower than cars and therefore has low market penetration (Newman and Kenworthy 1989). Demand for automobile use leads to higher energy throughput in the regional environmental system and to numerous environmental problems (Hough 1995), including increased potential for air pollution from mobile-source emissions.

Because much more of the development and population growth has been occurring in suburban areas, growth in VMT has exceeded population growth by a large margin (Figure 3.15).

Earlier studies of cities from around the world (Kenworthy and Laube 2001; Kenworthy 2009) have demonstrated a strong inverse relationship between VMT per capita and simple measures such as urban density (see, for example, Figure 3.16). The most energy-intensive and automobile-dependent cities are the sprawling cities of the American Southwest (such as Houston, Tex., and Phoenix, Ariz.); densely populated cities in Asia, by contrast, have the lowest automobile dependency. Higher incomes in many areas of the newly industrialized world are contributing to more private automobile use and as a result the trend shown in Figure 3.16 might be changing although empirical data are not yet widely available. In the absence of aggressive emissions controls, increased automobile dependency leads to increases in pollutant emissions. One approach (described in detail in Sidebar 3.1) to link the impact of changes in emissions on population exposure is the determination of the intake fraction, defined as the proportion of emissions of a pollutant inhaled by an individual

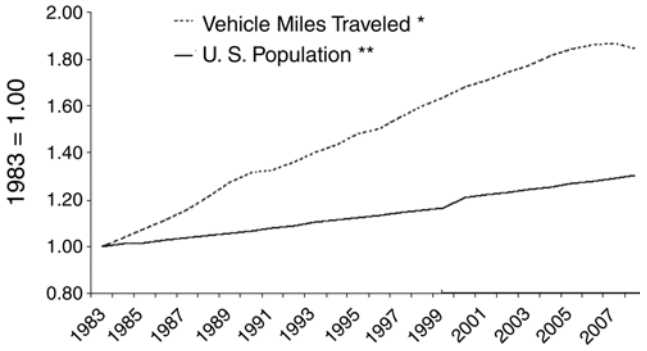

Figure 3.15. Growth in VMT and population from 1980 to 1997. Data sources: U.S. Department of Transportation, Traffic Volume Trends (12 Month Moving Average, April 1983 to April 2008) and U.S. Census Bureau, Annual Population Estimates. (Courtesy of the U.S. EPA. Developed using data from the *U.S. DOT [source for traffic volume trends: 12-month moving average, April 1983 to April 2008] and the **U.S. Census Bureau [source for annual population estimates]).

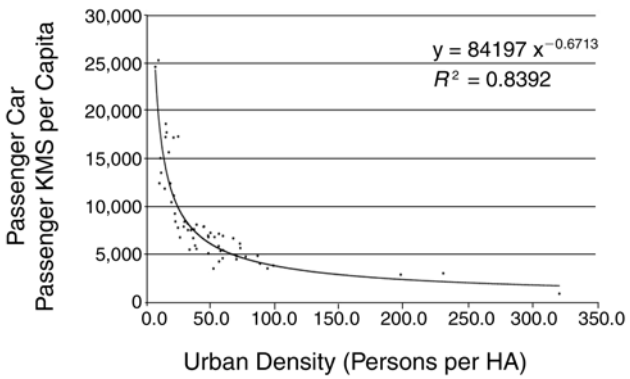

Figure 3.16. Relation between passenger-car travel (per capita) and urban density (persons per hectare) compared with in 1995. Data from 58 higher-income cities worldwide. (Reprinted from Kenworthy 2009, with permission of the author.)

Sidebar 3.1 Intake Fraction

The intake fraction of a pollutant is defined as the proportion of emissions of the pollutant inhaled by an individual or population and quantifies the "exposure efficiency" of an emission source (Bennett et al. 2002; Marshall et al. 2005).

Recent research has suggested that "the place makes the poison" as much as the ambient concentrations do, in the sense that the total proportion inhaled can be higher when the sources are closer to the exposed individuals or populations (Smith 1997). The inhalation of cigarette smoke, for example, has the highest intake fraction, i.e., nearly 100%. More remote sources, such as power plants that produce secondary pollutants, are thought to have among the lower intake fractions. Proximity to roads is thought to result in a higher intake fraction (and subsequent absorbed dose) than that of other sources that are farther away.

The intake fraction is another consideration in assessing the potential health effects that might accrue from having numerous traffic-related pollution sources in proximity to residential areas and areas with sensitive populations, such as schools. In essence, a higher intake fraction could result in higher body doses of pollutants even when ambient concentrations appear relatively similar in two places, if one is close to traffic sources and the other is farther away. The intake fraction is a tool for summarizing the extent to which emissions from a source might affect exposure (Greco et al. 2007). The equation for calculating intake fractions varies based on the method used but is generally the integrated incremental population-wide intake of a given pollutant, at any time, per unit of emitted pollutant. If data collected from monitoring stations and emissions inventories are available and the concentration of the pollutant is constant, then the equation is:

$$\mathrm{iF} = \frac{\mathrm{Br}P\Delta C}{\Delta E}$$

where iF is the intake fraction, Br is the average breathing rate in m^3/day, P is the total population affected, ΔC is the incremental change in exposure concentration over the population in μg/m^3, and ΔE is the change in emissions in μg/day (Stevens et al. 2007). The intake fraction does not account for real dosimetry or the toxicokinetic properties of the various physical and chemical species; it is therefore only a very rough approximation of the potential amount inhaled.

The change in ambient pollutant concentration can be estimated in several ways by models or measurements. Model complexity ranges from a simple one-compartment box model to more sophisticated models, such as urban air-shed models and atmospheric dispersion models that provide a distribution of individual exposures. Land-use regression analyses can be performed to explore the relationships between intake fractions and potential variables.

Although intake fractions vary across several orders of magnitude depending on population size, distance between the population and emissions source, and the persistence of the pollutant, a typical intake-fraction value for indoor and outdoor urban release is one per million, meaning that for every million grams of the pollutant emitted, one gram is inhaled.

The determination of intake fractions can assist with prioritization of pollutants because it allows clear comparison among various sources based on their exposure potential and can inform environmental-policy decisions and cost-effectiveness analyses. Several studies have determined the intake fraction of various pollutants in order to understand relationships between mobile-source emissions and exposure for a variety of pollutants and scenarios (Marshall et al. 2005; Greco et al. 2007; Stevens et al. 2007; Zhou and Levy 2008).

or a population. The intake fraction can quantify the "exposure efficiency" of a source of emissions.

As illustrated in the previous chapter, much of the projected increase in sales of automobiles and light-duty trucks will occur in rapidly industrializing economies. Although technologic innovations will help reduce emissions from motor vehicles, it appears unlikely that these, by themselves, will fully compensate for the increasing demand for motor-vehicle travel over the next 20 to 30 years.

3.III.4 SOCIAL DISTRIBUTIONS OF TRAFFIC-RELATED AIR-POLLUTION EXPOSURE AND THE ENVIRONMENTAL JUSTICE DEBATE

The concept of environmental "justice" or "equity" evolved in the 1980s into an important aspect of environmental exposure analysis. The field involves empirical analysis of the relationships of socioeconomic status, race, or both with moderate exposure to environmental contaminants and other potential sources of health effects, such as psychosocial stress. Environmental-justice research takes on a political dimension because the concept implies that not only have the poor and racial minorities been left behind in sharing the benefits of economic development, but also that they bear a disproportionate burden of the costs that arise from production and consumption (Buzzelli et al. 2003). Thus, environmental justice also encompasses issues of fairness in regulatory, planning, and other environmental-protection and economic decisions (Been 1993; O'Neill et al. 2003).

Research on environmental justice connects closely with health-effects research through what has been called the triple-jeopardy hypothesis. This hypothesis posits that three linked conditions affect the relationship between air pollution and human health, namely (1) that groups with lower socioeconomic status are exposed to higher concentrations of air pollution and other environmental hazards, (2) that these groups already suffer the burden of reduced health from social factors such as poverty and psychosocial stress, and (3) that the burden of reduced health from social determinants interacts with air pollution to produce more serious health effects in the groups (Jerrett et al. 2001; Levy et al. 2002). In other words, the groups most likely to suffer health effects from air pollution receive the highest exposure and are most likely to experience the health effects associated with air pollution. Some research supports the notion of more substantial health effects in groups with lower socioeconomic status. For acute effects, educational level in the neighborhood and manufacturing employment have both been related positively to the magnitude of health effects from air pollution (Jerrett et al. 2004); in a study of chronic effects, neighborhood income modified the health effects of air pollution (Finkelstein et al. 2003). Persons with both low income and high exposure were 2.5 times more likely to die during follow-up than those with high income and low exposure and were also nearly twice as likely to die as those in the same exposure group with high income.

Much of the earlier research focused on the distribution of toxic pollution from point sources (U.S. General Accounting Office 1983; United Church of Christ Commission for Racial Justice 1987; Anderton et al. 1994; Jerrett et al. 1997; Bolin et al. 2002). Earlier debates focused on two major issues: (1) whether the methods used to assess spatial inequities were adequate, considering the data and statistical limitations (Bolin et al. 2002), and (2) whether the existence of unequal exposure by social or racial group was proof of intentional discrimination (Bullard 1991) or an outcome of housing-market processes that tended to discount environmental externalities, such that people with lower incomes paid lower rents in areas with higher pollution (Been 1993).

More recent research has assessed whether pollution inequities have lessened or have been made worse by changes in land-use and pollution patterns over the 10-year period from 1986 to 1996 (Buzzelli et al. 2003). This work investigated how today's post-Fordist production system has modified the spatial distribution of pollution within cities — leading to smaller, more dispersed point sources and greater contributions from traffic emissions — and whether this leads to more equal distributions of pollution over a wider population base. The results showed that even in an industrial city with major point-source polluters, such as the city of Hamilton, Ont., pollution is becoming more dispersed and more equally distributed across the various social classes, probably as a result of the increased contribution of traffic sources to overall pollution in Hamilton.

There has been a recent heightened interest in directly examining the social distribution of traffic pollution, although this body of literature remains quite small in comparison with the broader literature on social processes and point sources. In the traffic-related literature, Apelberg and colleagues (2005) analyzed associations between the U.S. EPA's National Air Toxics Assessment (NATA) and census tract socioeconomic data in Maryland. Cancer risk from on-road vehicle emissions in the study was found to be higher in low-income and racial-minority tracts. Green and colleagues (2004) investigated whether elementary schools in socially disadvantaged parts of California were more likely to be exposed to heavy traffic. They found the highest traffic counts (vehicles per day) on nearby roadways (within a 150-m buffer) in areas that had high

proportions of economically disadvantaged and nonwhite groups. Other studies from Southern California have used emissions inventories (including NATA) to assess the health effects of a range of sources, reporting that transportation sources were the most important for lifetime cancer risk, especially for racial minorities (Morello-Frosch et al. 2001; Pastor et al. 2005). Houston and colleagues (2006) examined the question of whether day-care facilities were located close to areas of high exposure in California. The study found that 75% of the day-care facilities were in light-traffic areas and about 6% were in heavy-traffic areas. But the overall number of children potentially exposed was still large, more than 57,000 across California. Logistic-regression results indicated that each 10% increase in African-Americans living in nearby neighborhoods related to odds of about 1.10 of the day-care facility's being located in a heavy-traffic area (with a slightly smaller increase for Hispanic Americans).

In other countries, there has also been some evidence of unequal distributions of pollution by race and socioeconomic status, although the results are more mixed than in the United States. In a recent study from New Zealand, Pearce and colleagues (2007) used atmospheric dispersion modeling to demonstrate a relationship between likely levels of traffic and concentrations of air pollution and disadvantaged social groups. The authors reported evidence, similar to that from the American studies, of unequal distributions of pollution, with higher concentrations in areas of relative deprivation. In England, Brainard and colleagues (2002) found that CO and NO_2, both surrogates of traffic-related pollution, related strongly to racial- and ethnic-minority status and to social deprivation. Other factors that might influence near-source air pollution from dust resuspension, such as street cleaning and maintenance, have also been shown to be related to socioeconomic status in the United Kingdom (Hastings 2007). In Sweden, a country noted for its interest in social equality, Chaix and colleagues (2006) investigated the distribution of NO_2 in relation to young children. They reported higher concentrations of NO_2 for children living in poorer housing and neighborhoods. A recent Canadian study based on a land-use regression prediction of NO_2 in Toronto reported that markers associated with lower socioeconomic status were generally related to air-pollution exposures, but there were exceptions that contrasted with the U.S. findings. Racial-minority groups, for example, tended to be less exposed in Toronto than Caucasians, probably because of Toronto's role as a gateway city for highly educated immigrants (Buzzelli and Jerrett 2007). Housing values were also unexpectedly higher, which might be partly explained by the dense urban structure, relatively heavy traffic, and high land rents of the downtown area. The literature from other countries is thus suggestive, too, of differential exposures to traffic-related air pollution, although not as clearly linked to race and income as in the literature from the United States.

Although there have been some mixed results and the literature on air pollution from traffic is small, there is sufficient evidence to suggest an inverse association between socioeconomic status and exposure to air pollution from traffic. More recent studies also point to the possibility of other demographic groups being more highly exposed, including nonwhites, ethnic minorities, and children. The patterns observed seem to transcend the United States, where the majority of the research has been conducted, and generally support the presence of a universal phenomenon in which people of lower socioeconomic status experience higher exposures than people of higher socioeconomic status. The recent research has also shown a greater level of methodologic sophistication, with more advanced dispersion models and land-use regression estimates, and more subtle markers of social position or race. These methodologic advances have at least reduced if not eliminated some of the uncertainties in the earlier research. Assuming the body of evidence is sufficient to infer an association between socioeconomic status and air pollution from traffic, this conclusion merits consideration in the interpretation of epidemiologic findings and in the regulatory actions designed to protect public health.

3.III.5 SUMMARY

Factors influencing exposure surrogates are related to an individual's personal exposure, such as time and activity patterns, meteorologic conditions, land-use patterns, and socioeconomic status. Accurately measuring traffic exposure in both time and space is difficult and often impractical in large health studies. A potential solution is to deploy a large number of monitors in a geographic location, especially in places where concentrations of air pollutants are expected to be highly variable and the population density is high. The use of models that incorporate numerous factors to estimate exposures that are more spatially relevant to the individual's exposure can also be helpful. However, the accuracy of the inputs is critical to the usefulness of a given model.

With the expansion of cities and changes in land-use patterns, the patterns of population exposures have changed over time. In spite of technologic innovation and regulatory control, aggregate emissions from traffic in many urban locations have not been reduced as much as they might have been, largely because of the heightened demand for travel, which is prompted partly by urban structures that promote private automobile use over walking, cycling, and

public transit by rail or bus. Features of urban growth and sprawl might increase exposure for relatively large proportions of the populations. Another factor that can lead to unequal distribution of exposure is socioeconomic status. If, as the evidence suggests, groups of lower socioeconomic status experience higher exposures than groups of higher socioeconomic status, this needs to be taken into consideration in the interpretation of epidemiologic findings and also in the design of future studies.

3.IV. MODELING APPROACHES

There have been many advances in exposure modeling for traffic-related air pollution over the past decade, facilitated in part by the increased availability of GIS and associated modeling techniques (Briggs 2007). Such methods allow for relatively easy computation of distance from emissions sources, such as roadways, and for enhanced characterization of land use likely to influence the emissions or their dispersion. This section reviews modeling approaches currently used to characterize exposure to traffic-related air pollution in epidemiologic studies.

Following Jerrett and colleagues (2005a), this review divides the approaches into five major categories: (1) proximity-based models, (2) geostatistical interpolation, (3) LUR models, (4) dispersion models, and (5) hybrid models that combine one or more of the above four approaches with time–activity or personal monitoring data used to derive some measure of individual exposure (Jerrett et al. 2005a). Another class of models, integrated regional meteorologic models, is available for assessing regional impacts from traffic, but these are not reviewed here because of the focus on local traffic and near-source impacts. The section concludes with a summary of overarching data and methodologic issues that influence the accuracy of all traffic-exposure assessments and some of the emerging trends in the field, which arise from new geolocation, real-time biomonitoring, and remote-sensing technologies.

3.IV.1 PROXIMITY MODELS

The most basic exposure-assessment methods are proximity-based models, in which indicators, or surrogates, of the relative concentrations of motor-vehicle-related pollutants are used to estimate an individual's traffic exposure (see also section 3.II.3E). Examples of proximity-based models include self-reported measures of nearby roadway characteristics (such as stop-and-go truck traffic) or traffic volumes, matched to geographic coordinates to calculate distances to the nearest roadways, and spatially distributed link-based traffic-activity levels over a community using GIS-based density algorithms.

As noted earlier, proximity models assume that the distance to roadways (or traffic) from place of residence serves as a surrogate for exposure to traffic-related pollution. Proximity models used in several research papers were found to focus on the association between respiratory disease and traffic-related pollution (van Vliet et al. 1997; Ciccone et al. 1998; English et al. 1999; Wilkinson et al. 1999; Venn et al. 2000, 2001; Wyler et al. 2000; Janssen et al. 2001; Rijnders et al. 2001; Gauderman et al. 2007) or between mortality and traffic-related pollution (Hoek et al. 2002; Finkelstein et al. 2004). The majority of these studies were conducted in Europe; a few were conducted in North America (English et al. 1999; Finkelstein et al. 2004; Gauderman et al. 2005, 2007; McConnell et al. 2006a).

In most cases, data inputs consisted of traffic counts (using information on road buffers and distance from major roads). A few studies explicitly compared various measures of traffic exposures, including distance to roads and traffic volume. One study, for example, reported stop-and-go bus and truck traffic and traffic volumes in relation to respiratory health (Ryan et al. 2005).

A study that compared self-reported exposures in areas of Europe with modeled concentrations of pollutants reported overestimation of exposure based on subjective assessment (Heinrich et al. 2005). Another study from Europe reported only weak correlations between traffic-density measures, although basic distance measures were moderately correlated with measured concentrations of PM_{10} (Briggs 2007). A recent study by Molitor and colleagues (2007) investigated the predictive power of a range of exposure models in the context of lung-function decrements in children in Southern California. The findings here indicated the possibility of both inflated point estimates and variances in the estimation of health effects when using less refined exposure models.

Although these models can be useful, they do not typically consider the compounded influence at residences that might be affected by numerous roadways with different traffic levels, nor do they account for potential meteorologic influences. Systematic validation of proximity models has also been limited (although the gradient studies reviewed earlier might be informative in this regard).

3.IV.2 GEOSTATISTICAL INTERPOLATION MODELS

Interpolation models result in the creation of a pollution "surface," an attribute that varies continuously over space within the study domain, in which pollution concentrations z

at an unsampled location s_0 are estimated at neighboring measured sites denoted as s_1. The data required for this model include a network of sampling sites that were chosen based on factors such as the extent of analysis, topography of local area, local emissions, and degree of variability of the measured pollutant. Although such decisions on site location enhance the prediction surface, for the most part interpolation studies have relied on government monitoring surfaces, which might not have adequate spatial coverage to derive detailed estimates of traffic-pollution distributions. Linkages to traffic have to be achieved through indirect inference about the contribution of traffic to the observed concentrations. If dense networks of research monitors are employed, the interpolators can yield a good representation of the fine-scale variation typically associated with traffic-pollution gradients.

Wong and colleagues (2004) identified four interpolation models for air-pollution exposure assessment: (1) spatial averaging, (2) nearest monitor, (3) inverse distance weighting, and (4) kriging. The most advanced form of spatial interpolation is kriging, which produces the *best linear unbiased estimate* and allows for mapping of error variances. The variances can be used to view the location of errors for the predicted pollution surface (Mulholland et al. 1998) and can be incorporated into subsequent uncertainty models for health-risk assessment (Künzli et al. 2005).

The first method, spatial averaging, simply obtains all measurements within a given distance of the subject's home and computes an arithmetic average. The second method, nearest monitor, relies on the values of the monitor closest in space to the subject's home and assigns an exposure for the desired temporal averaging period. Although these two methods can supply useful information with a dense-enough monitoring network, routinely available government monitoring data are usually too sparse to support these basic methods. The third method, inverse distance weighting, allows more information to be captured from the available monitors by including more distant monitors and discounting their weight in the estimation as a function of distance from the target location. Inverse distance weighting makes use of the formula:

$$\hat{z}(s_o) = \frac{\sum_{i=1}^{n} z(s_i) \times d_{ij}^{-r}}{\sum_{i=1}^{n} d_{ij}^{-r}} \quad (1)$$

where $\hat{z}(s_o)$ is the interpolated value, $z(s_i)$ is the data value, d_{ij}^{-r} is the separation distance between the interpolated value and the data value, and r is the weighting value (Burrough and McDonnell 1998; Cliff 1981). Although this method is an improvement over spatial-averaging and nearest-monitor methods, it is also deterministic, offering no probabilistic assessment of the likely errors in the interpolated surface.

Kriging models, in contrast, exploit spatial dependence in the data to form estimates of the likely value for a random variable Z at unmeasured locations between sampling sites. The spatial dependence can be divided into two categories. First-order effects measure broad trends in all the data points, such as the global mean, and second-order effects measure local variations at short distances between the points (Bailey and Gatrell 1995; Burrough and McDonnell 1998). Breaking this down, the equation takes the following general form for a random variable Z at location s:

$$Z(\mathrm{s}) = \mu(\mathrm{s}) + \epsilon(\mathrm{s}) + \epsilon' \quad (2)$$

where $\mu(s)$ equals the deterministic function that describes the "structural," or first-order, component of Z at s; $\epsilon(s)$ is the stochastic second-order effect of the residuals from $\mu(s)$ that vary locally but are spatially dependent (sometimes called the regionalized variable); and ϵ' represents the residuals that are spatially independent normal terms with zero mean and constant variance. The search for a suitable interpolation model begins with deciding on a function for $\epsilon(s)$. If we assume that the variance of differences between sites depends solely on the distance between the sites, denoted as $\mathbf{h}$, then the equation for estimating $\epsilon(s)$, or the semivariance, is given as follows:

$$\begin{aligned} \gamma(\boldsymbol{h}) &= \hat{\mathrm{cov}}\left(Z(\mathbf{s}), Z(\mathbf{s}+\mathbf{h})\right) \\ &= \frac{1}{2n} \sum_{k=1}^{K_{\mathbf{h}}} \left\{Z(\mathbf{s}_k) - Z(\mathbf{s}_k + \mathbf{h})\right\}^2 \end{aligned} \quad (3)$$

where $K_{\mathbf{h}}$ equals the number of pairs k of sample points with values of the attribute of interest Z, which are separated by distance $\mathbf{h}$, and the semivariance is represented by $\gamma(\boldsymbol{h})$. While executing the interpolation of the point-attribute samples of pollution, experimental variogram models are fitted to theoretic distributions. The model can be adjusted to incorporate anisotropic wind patterns (Bailey and Gatrell 1995).

In regionalized variable theory, two conditions must be met to satisfy the "intrinsic hypothesis": (1) stationarity of difference and (2) stationarity of variance of differences. The intrinsic hypothesis states that once first-order effects

are accounted for, the remaining variation will be homogeneous. Any differences in attribute values between sites are then purely a function of the distance between the sites. If these conditions are fulfilled, the first equation can be written as follows to emphasize this hypothesis:

$$Z(\mathbf{s}) = \mu(\mathbf{s}) + \mathrm{E}\left[\epsilon(\mathbf{s}) \mid \{\epsilon(\mathbf{s}_i)\}, \gamma\right] + \epsilon' \quad (4)$$

where $\mathrm{E}[\epsilon(\mathbf{s}) \mid \{\epsilon(\mathbf{s}_i)\}, \gamma]$ is an average of the residuals at the measured sites, appropriately weighted by their distance from the point of interest *s* using the semivariance function.

There is an extensive literature on validation methods for kriging models. Although many cross-validation methods are applied, the most common approach in exposure modeling is to fit the kriging model to training sites, which constitute the majority of the data, and then to exclude some portion of validation sites, which are usually 10% to 20% of the total sample, as a means of externally validating the model predictions. Validation of this kind was conducted in London for PM_{10} (Briggs 2007). Results showed low correlations with measured values at the training sites. Ross and colleagues (2007), in contrast, compared kriging estimates with 15 validation sites and found them to be highly accurate when predicting $PM_{2.5}$ over an area of 28 counties centered on New York City. The relative success of the cross-validation in the study by Ross and colleagues might have resulted partly from the relative spatial homogeneity of $PM_{2.5}$.

Wong and colleagues (2004) compared all four methods of interpolation and reported that estimates were relatively insensitive to the interpolation method in areas with sparse monitoring. In areas of denser monitoring, however, results varied considerably between methods when predicting PM_{10} and ozone.

Studies using interpolation estimates have investigated associations between CO and birth outcomes (Ritz et al. 2002), SO_2 and the prevalence of wheezing in schoolchildren (Pikhart et al. 2001), ozone and asthma exacerbation in a pediatric sample (Mulholland et al. 1998), PM and a subclinical marker for atherosclerosis (Künzli et al. 2005), and mortality and particulate pollution (Finkelstein et al. 2003; Jerrett et al. 2005a,b). Unlike proximity models, interpolation models do not specifically relate the traffic source to the health outcome.

3.IV.3 LAND-USE REGRESSION MODELS

LUR models treat the pollutant of interest as the dependent variable and proximate land-use, traffic, and physical environmental variables as independent predictors. As a result, they predict pollution concentrations at a given site based on surrounding land use and traffic characteristics. Specifically, this method uses measured pollution concentrations $Z(s)$ at locations *s* as the response variable and land-use types, *W(s)*, within circular areas around *s* (called buffers) as predictors of the measured concentrations (see Figure 3.17). The incorporation of land-use variables into the interpolation algorithm detects small-area variations in air pollution more effectively than standard methods of interpolation such as kriging, discussed earlier (Briggs et al. 1997, 2000; Lebret et al. 2000).

The first LUR studies of criteria air pollutants were conducted in Europe. Two studies (Briggs et al. 1997; Lebret et al. 2000) were part of the SAVIAH (Small Area Variation in Air pollution and Health) project, which examined traffic-related air pollution in four European cities (Amsterdam; Huddersfield, U.K.; Prague; and Poznań, Poland).

An updated model described by Briggs and colleagues (2000) investigated traffic-related air pollution in four urban areas in the United Kingdom [Huddersfield, Sheffield, Northampton, and parts of London (boroughs of Hammersmith and Ealing)]. The independent variables used for the prediction of mean NO_2 concentrations were road-traffic volume, land-use type, and elevation. These variables produced good predictions, with coefficient of determination (R^2) values ranging from 0.79 to 0.87.

Brauer and colleagues (2003) compared traffic-related $PM_{2.5}$ models in multiple European cities using land-use regression. In each of the study cities, investigators fitted two types of models: one available through a GIS and another that included additional variables not available in the GIS. The results obtained for cities in the Netherlands, Munich, and Stockholm using the GIS showed R^2 values of 0.81, 0.67, and 0.66, respectively, for particle filter absorbance. The alternate, or "best," model included variables such as heavy-traffic locations and street canyons and produced results with better R^2 values of 0.90, 0.83, and 0.76 for the three locations, respectively.

Similar modeling predictions in North America have been produced for NO_2 and for $PM_{2.5}$. For NO_2, R^2 values ranging from 0.64 to 0.76 were achieved (Kanaroglou et al. 2005; Ross et al. 2006; Sahsuvaroglu et al. 2006; Henderson et al. 2007; Jerrett et al. 2007). Two studies using $PM_{2.5}$ in North America have been published: one in the New York City region (Ross et al. 2007) and another in Los Angeles (Moore et al. 2007). Both found traffic counts within 300 to 500 m, population density, and areas of industrial or institutional land use to be significant predictors of $PM_{2.5}$ concentrations. Here industrial land use served as an indicator of point source or area emissions; institutional land use was intended to capture major

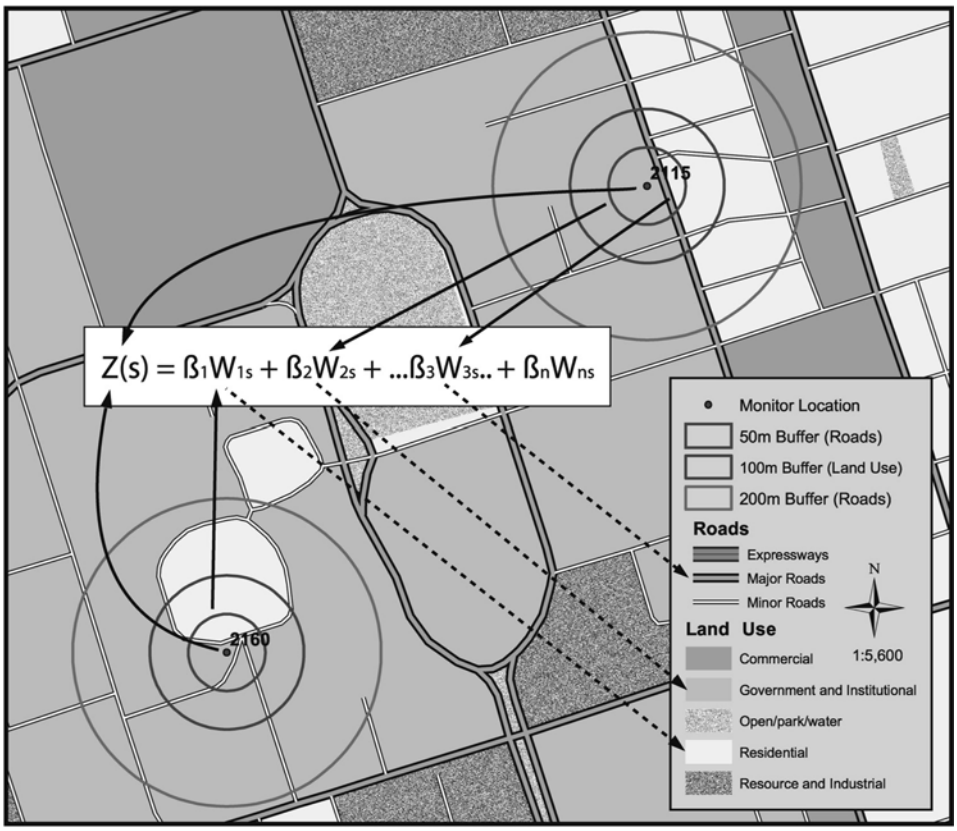

Figure 3.17. Illustration of elements of a LUR model. (Reprinted from Jerrett 2007, with permission of Taylor & Francis Group, *www. informaworld.com*.)

mobile-source destinations that might have inadequate traffic counts (such as schools or hospitals). Another study from Vancouver used $PM_{2.5}$ absorbance and produced good predictions in the range of $R^2 \approx 0.6$ (Henderson et al. 2007).

Validation of these models has shown that they generally perform as well as or better than dispersion models in areas of Europe for NO_2 prediction (Briggs et al. 2000). In a more recent study, LUR outperformed kriging, inverse distance weighting, proximity models, and dispersion models for predicting PM_{10}, although as noted by the authors the comparison was limited by the lack of spatial variation in PM_{10} across the study area (Briggs 2007). In North American studies, LUR has generally achieved predictions in the range of $R^2 = 0.56$ to 0.79, and models appeared to predict well at validation locations excluded from the training data sets. Ryan and colleagues (2007) compared proximity to LUR models that predicted EC concentrations. Although the authors' earlier studies had shown associations with proximity measures (as noted above), their more recent study concluded that LUR predictions of EC had the potential of reducing exposure error and producing more accurate estimates of health effects. Recent attempts to incorporate wind direction into land-use predictions have shown modest improvements in model fit (Arain et al. 2007), but in general there has been much less emphasis on working meteorologic data into these model predictions. In comparison with dispersion models that explicitly account for wind direction, these models rely more on the density and quality of land-use and traffic data to derive empirical estimates of exposure.

The use of LUR in health studies has been limited to date. Brauer and colleagues (2007) used LUR to model $PM_{2.5}$, NO_2, and PM absorbance in the Netherlands for a study focused on incidence of childhood respiratory disease. Associations were also assessed with other respiratory health outcomes, including asthma onset. Morgenstern and colleagues (2007) used methods similar to Brauer's to assess similar outcomes. Finkelstein and Jerrett (2007) used LUR for predicting NO_2 concentrations in Hamilton and Toronto, Ont. These exposures were used as surrogates of traffic pollution to assess possible links between airborne manganese from the gasoline additive methylcyclopentadienyl manganese tricarbonyl (MMT) and Parkinson's disease or treatment with L-dopa medication. Jerrett and colleagues (2008)

used the same models in Toronto to predict mortality effects of traffic-related air pollution.

3.IV.4 DISPERSION MODELS

Air-quality dispersion models have been used for decades to estimate ambient concentrations from emission sources (Gifford Jr 1961, 1968; Pasquill 1961; Turner 1970). Dispersion models have been developed for the regional (100–1000 km), urban (4–100 km), neighborhood (0.5–4 km), middle (100–500 m), and micro (10–100 m) scales and for reactive and nonreactive pollutants (Seinfeld and Pandis 1998). Near-field impacts are generally assessed using nonreactive steady-state Gaussian dispersion models employing coefficients that vary with downwind distance and atmospheric stability. Although Gaussian point-source models have received the most attention, significant work was conducted in the 1970s and 1980s to refine Gaussian line-source dispersion models for estimations of ambient concentrations resulting from mobile-source emissions (Benson 1989).

Similar to LUR models, Gaussian line dispersion models require data for air quality, geophysical locations, meteorologic conditions, and, in addition, for emissions. Data on pollution concentrations, also referred to as *background concentrations,* are usually obtained from air-monitoring stations near the study area and are used for model calibration (Clench-Aas et al. 1999). The geophysical data consist of terrain heights and surface roughness (determined from land use). Meteorologic data provide information about wind speed, wind direction, ambient temperature, solar radiation, and atmospheric stability (Gualtieri and Tartaglia 1998). On-road motor-vehicle emissions are usually estimated by traffic counts and composite emissions factors for various types of vehicles and speeds using mobile-source emissions-factor models, such as MOBILE6 or EMFAC2002. After the data requirements have been met and the model calibrated, the dispersion model computes the pollution concentrations at receptor locations on an hourly basis. Model-performance evaluations indicate that line-source Gaussian models are typically able to estimate ambient concentrations of inert pollutants, such as CO, within −50% to +100% when given accurate input data (Fox 1981, 1984; U.S. EPA 1984).

Dispersion models have been used in health-effects assessments. Hrubá and colleagues assessed associations between modeled long-term exposure to total suspended-particulate concentrations and asthma symptoms and prevalence (Hrubá et al. 2001). Bellander and colleagues (2001) estimated neighborhood-scale pollutant concentrations with a dispersion model and extrapolated these over time to estimate NO_2 and SO_2 concentrations for all years between 1955 and 1990 in Stockholm. Using 10,800 addresses matched to geographic coordinates, they assessed individual-level pollution-exposure averages, based on indices of complex air-pollution mixtures derived from house heating and traffic-related pollution sources. Estimated NO_2 values from their model correlated very well ($r = 0.96$) with site measurements. They concluded that, although the technique has practical application for epidemiologic studies, it might be limited to study sites that possess historical traffic and other emissions data. McConnell and colleagues (2006a) and Gauderman and colleagues (2007) used California Line Source Dispersion Model (CALINE) estimates to assess associations with childhood asthma prevalence and adolescent lung-function growth, respectively (see below).

Recently, Gaussian dispersion models have been used in conjunction with GIS. This combination has allowed information from empirical monitoring systems and data on population distribution in the study area to be analyzed together. A more realistic representation of the problem is formed with the addition of data on the topography of the study area, a model of the road network, and traffic observations. These models have been used for various kinds of pollutants, such as total suspended particles (Bartonova et al. 1999), NO_x (Bartonova et al. 1999; Bellander et al. 2001; McConnell et al. 2006a), and CO (Benson 1989).

3.IV.5 HYBRID INDIVIDUAL-EXPOSURE MODEL

An individual-exposure model has been applied to seven of the 12 communities in the Children's Health Study, in Southern California (Wu et al. 2005). The model relies on measured concentrations of pollutants in microenvironments (residential outdoor, residential indoor, school outdoor, school indoor, and in-vehicle), where children spend most of their time, to compute the time-weighted average exposure TX_i for each child:

$$TX_i = X_i / T = \Sigma_m X_{im} \Delta t_{im} / \Sigma_m \Delta t_{im} \quad (5)$$

where X_{im} is the pollutant concentration in subject i's microenvironment m, and Δt_{im} is the time spent by subject i in microenvironment m.

In the seven-community study, CALINE4 (CALINE version 4) dispersion model was used to estimate local-scale pollutant concentrations of motor-vehicle emissions. Background concentrations and local non-mobile sources were taken into account by applying the Surface Meteorology and

Ozone Generation (SMOG) airshed model developed by Lu and colleagues (1997) and updated to include the MM5 prognostic meteorology model. The SMOG model is a regional air-quality modeling system that has been applied in simulations of surface air-pollutant concentrations and elevated pollution layers observed over the South Coast Air Basin in California (Lu et al. 2002). Indoor and in-vehicle concentrations were computed using standard mass-balance equations with appropriate penetration and decay factors (Koutrakis et al. 1992; Thornburg et al. 2001) and typical in-vehicle-to-ambient concentration ratios for the California environment (Rodes et al. 1998; Fitz et al. 2003; Fruin 2003) .

In the Children's Health Study (Wu et al. 2005), a time–activity survey was administered twice a year to each of the children, asking them how much time (using five categories) they spent outdoors in the afternoon (12 noon to 6 p.m.) on weekdays, on weekends, and during the summer. It also asked the children about travel mode and time between school and home. The survey was more useful for classifying individual subjects by their time activities than for providing quantitative time–activity data for use in exposure modeling. The Consolidated Human Activity Database (CHAD) developed by the U.S. EPA provides 24-hour time–activity patterns based on recall diaries (U.S. EPA 1997). A time–activity submodel was developed to create a 24-hour time–activity series (with 15-minute intervals) for each child in the Children's Health Study cohort by using information from both the Children's Health Study survey and the CHAD database.

When integrated, these model components produce a comprehensive estimate of potential individual exposure. Although limited by the quality of data inputs (such as in the CALINE model noted above and the limitations of time–activity data), the individual-exposure model combines and quantifies individual, rather than ambient, exposure, avoiding the problems of representativeness usually associated with personal-monitoring studies that rely on small samples. With accurate data inputs, these hybrid individual-exposure models have the potential to parse the various components of personal exposure (e.g., in a vehicle compared with ambient outdoors at home) for inclusion in health-effects assessments. As with many of the preceding models, the underlying data quality and accuracy are constraints that limit the accuracy of the resulting model output. In the next section, we outline some of the limitations in data quality that can limit the accuracy and reliability of modeled traffic-pollution exposures.

3.IV.6 VALIDATION STUDIES COMPARING MODELED TRAFFIC EXPOSURES WITH AMBIENT AND PERSONAL-EXPOSURE MEASUREMENTS

Understanding how well various models of traffic exposure explain variations in personal exposure to various traffic-related air pollutants is important for interpreting the results of epidemiologic studies. Several studies have cross-validated exposure models against ambient measurements. Most commonly, the cross validation involved dispersion models (Reungoat et al. 2003; Beyea et al. 2006). For some common pollutants, such as CO and NO, these cross-validations suggested fairly good model performance in predicting ambient concentrations of traffic-related pollutants. Similar cross-validations have been done for LUR and kriging models. In most instances, when adequate levels of data support exist, the models were able to predict ambient concentrations well (Briggs et al. 2000; Lebret et al. 2000; Jerrett et al. 2007).

Only a few studies have examined how well traffic-related exposure predicts personal exposure to air pollutants. Such assessments are complicated by a variety of factors, including the time–activity patterns of the individual, housing-stock characteristics and related indoor–outdoor penetration of various pollutants, and the relative contribution from near-source traffic to the total concentration of pollutants in the atmosphere. Other sections of this report deal with time–activity and mobility as well as with the case of in-vehicle exposures. Here we examine the studies that have compared personal exposure to some measure of traffic intensity (or density) or a modeled traffic exposure.

Three relevant published studies were conducted in the Netherlands (Van Roosbroeck et al. 2006, 2007, 2008). These studies investigated whether personal measurements of $PM_{2.5}$ absorbance (what the authors termed "soot"), NO, NO_2, and NO_x correlate with traffic measures. The authors investigated correlations between traffic exposures and personal measurements in both children and adults. In a smaller pilot study involving 14 children who were measured for four periods of 48 hours, researchers investigated whether personal exposures to soot, NO_x, and $PM_{2.5}$ were elevated when the home location was near a busy road (Van Roosbroeck et al. 2006). The children were selected from the same school to control for possible school influences on personal exposure. Students living in the areas of highest traffic intensity were found to have exposures to soot that were 35% higher than those living in the areas of lowest traffic intensity. The same investigators (2007) examined relationships between personal exposure and exposures at both the children's schools and their residences. Schools within 100 m of a major road had

soot concentrations that were 75% higher than those in background locations. The personal exposure of children attending the schools near roads was 30% higher than that of the children living in background locations. For NO_x the ambient concentrations were 30% higher in the near-road schools, and personal exposure was 37% higher. Differences between near-road and background sites were smaller and statistically insignificant for NO_2 and $PM_{2.5}$. Differences for NO, NO_2, and NO_x were in the range of 14% to 15% higher for children living in the areas of greater exposure. In the larger study of adults, traffic intensities predicted personal exposures to soot but not to $PM_{2.5}$ or NO_x (Van Roosbroeck et al. 2008). Personal exposure to soot for adults living on heavy-traffic streets was 15% higher than that for adults living on light-traffic streets. This increase was found to be significant. Other pollutants such as NO_x had elevated ratios when comparing areas with greater and lesser exposures, but these were not significantly different. The results suggested that absorbance measures of $PM_{2.5}$ tended to show the most pronounced differences when comparing high- and low-exposure areas. For other species, elevated ambient concentrations were found, but the association between traffic and personal exposure was not as consistent as it was for soot measures (Van Roosbroeck et al. 2007). This is not surprising, because NO_2 and NO_x also have indoor sources that have been shown to relate significantly to personal exposure. Breysse and colleagues (2005) and others (Lai et al. 2004; Rotko et al. 2001), for example, found significant associations between personal NO_2 and gas stoves in the home.

In our review, we were unable to identify research specifically comparing models of traffic exposure to soot, NO_2, or other traffic-species measures of personal exposure. This gap in the literature tempers findings from epidemiologic studies because, with the exception of the Dutch studies mentioned above, there is little evidence that surrogates or models of traffic pollution influence personal exposures. Future research aimed specifically at traffic-pollution constituents likely to have few indoor sources and with the capacity to discriminate near-source traffic and background traffic is needed to interpret the epidemiologic studies attempting to link traffic to adverse health outcomes.

3.IV.7 DATA LIMITATIONS IN MODELS

This section reviews some of the major data limitations that currently add uncertainty to traffic-exposure models. These limitations concern geographic accuracy of input data, incompleteness and errors in traffic data, errors in geocoding, and variability in activity spaces and residential mobility.

3.IV.7.A Geographic Accuracy of Road, Land-Use, and Pollution-Monitoring Data

All of the models discussed above rely on accurate geographic representation of roads, land use, and pollution-monitoring locations. Although few studies are published, there is sufficient field evidence to indicate that in older studies the spatial accuracy of all necessary data inputs might be questionable. Many of the pollution monitors run by government organizations, for example, did not have locations marked by global positioning systems (GPS) until recently. Road networks were often translated from digitized paper maps that did not agree well with digital orthophotography (aerial photography geometrically corrected so that the scale is uniform) or control sites. Land-use classifications and spatial boundaries had large errors compared with the actual landscape. In developing countries, many of these issues are exacerbated by poorly funded government organizations and by a general lack of resources to develop the geographic-information infrastructure. Recent studies conducted in Mexico, for example, were limited to proximity and nearest-monitor measures for predicting exposure even though researchers had collected large volumes of multi-pollutant measurements. In this instance, lack of land-use and traffic data prevented the researchers from producing more accurate predictions of pollutant concentrations with LUR models (Holguin et al. 2006). Moreover, in many developing countries such as China, there is no Wide Area Augmentation System or its equivalent to improve GPS performance. Without a Wide Area Augmentation System, GPS accuracy can decline dramatically, at less than 50 m, which limits the capacity for conducting small-area studies linking air pollution from traffic to health outcomes. Researchers in these areas can use differential GPS, but this often increases the cost and might not be available in low-income areas.

In wealthier, data-rich countries, these issues are being resolved with better maps of roads and land use, which are often based on highly accurate global-positioning field surveys or satellite imagery. The National Land Cover Database created by the Multi-Resolution Land Characteristics Consortium of the U.S. federal government (*www.mrlc.gov/index.asp*), for example, is based on enhanced Landsat images that classify land use nationally at 30-m resolution. In most instances now, many of the government-run pollution-monitoring sites have been marked with GPS that are usually accurate to within 6 m of the true position. The introduction by the U.S. Department of Transportation of new location technologies based on land beacons promises to reduce GPS errors to less than 1 m. Readily available satellite imagery through publicly available Web sites has increased access to orthocorrected images that can be

used to quickly assess the spatial accuracy of aberrant field measurements. Despite these advances, there are continuing issues about integrating multiple data sources. Commercially available networks of roads, for example, can show minor differences in spatial locations caused by digitizing or other errors. When these road networks are combined, there can be obvious spatial discontinuities that require considerable manual correction. The same problem exists when combining land-use and road networks from different sources in some locations.

Often, while accurate spatial data might be available, the government agency managing the data might attempt cost recovery that effectively prohibits researchers from accessing the data. In California, for example, the counties of Los Angeles and Santa Clara have detailed land-parcel GIS coverage, but they have typically charged for providing them. In the case of Los Angeles, the charge is $2.00 per parcel, and with 12 million parcels, the land-use data are virtually unattainable by health researchers. New York City's Planning Department, in contrast, provides accurate parcel data to researchers for approximately $3000.00, and such data have improved the spatial prediction of air pollution there (Ross et al. 2007). Further improvements in institutional data access will need to be made to resolve potential issues related to data accuracy and reliability.

3.IV.7.B Traffic-Data Resolution and Accuracy

Two main problems are associated with the resolution and accuracy of traffic data. The first is the tendency for agencies to count traffic more thoroughly in more heavily trafficked areas. leading to missing data and undercounts in light-traffic areas. The second problem relates to time and includes issues such as data sets containing unrepresentative counts that might span 20 years of measurements or more and traffic-count bias caused by the time of year in which the short-term counts were made. One approach to help overcome these problems in traffic data is to use traffic-demand models, which are usually based on multinomial nested logit, tobit, or probit models of all possible origins and destinations. These are based in turn on cordon counts between origin and destination traffic zones (known as microsimulation travel-demand models). Such models use travel origins and destinations to predict likely flows through the entire street network, which unlike traffic counts, are usually only available for larger streets or streets where special studies were undertaken in response to circulation planning, resident concerns, or new construction (Figure 3.18). In some regions, academic centers also implement these models for research purposes. Generally the models are not widely available and, where they are available, are often based on simplified street networks (Figure 3.19) (see section 2.VI.1.C for details about travel-demand models).

The use of traffic-demand models to predict air pollution has been limited (see, for example, Kanaroglou and Scott 2002). Even when counts are available from demand models, they might not include complete information on likely driver behavior, and this too becomes problematic for predicting pollution concentrations, given the relatively higher emissions from cold starts, stop-and-go acceleration, and hard acceleration (CARB 2007). In addition, information on the movement of goods, particularly trucking logistics and trip generation, is also generally unavailable.

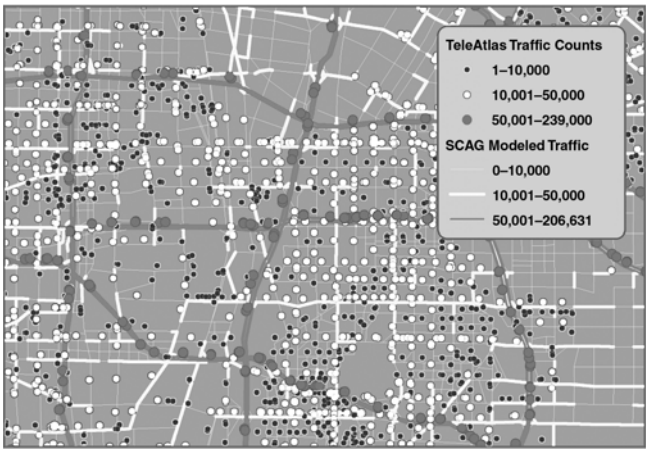

Figure 3.18. Map showing traffic counts (annual average daily traffic) in an area of Los Angeles obtained from a commercial provider compared to estimates generated with a traffic-prediction model. The commercial provider was Tele Atlas of Lebanon, NH, and the traffic-prediction model was implemented by the Southern California Association of Governments (SCAG). Note the wider coverage of the modeled traffic. (Courtesy of Zev Ross and Michael Jerrett.)

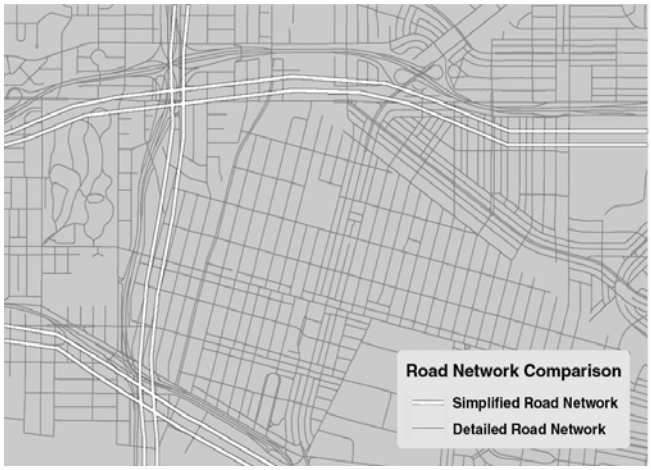

Figure 3.19. Map comparing detailed road network to the simplified network used to generate traffic-prediction models. Detailed network shown in gray; simplified network shown in white. (Courtesy of Zev Ross and Michael Jerrett.)

When dealing with traffic counts, efforts to correct temporal inconsistencies, spatial gaps, and seasonal biases in traffic counts in epidemiologic and exposure studies usually (1) impute some average for missing data links (based on similar speed or road type where counts are available), (2) leave these data as missing with the understanding that light-traffic areas are likely to be less important, or (3) augment the predictions with road types and other metrics for land use likely to correlate with traffic flows (e.g., commercial or institutional land use that generates many trips or road-length densities can also act as a surrogate for counts). The latter approach is used in LUR, and this additional information might account for some of the success of the method in predicting counts at unmeasured locations. Nonetheless, the issue of undercounts and inaccuracies in the traffic input data remains a source of uncertainty in exposure estimation. As noted below, new remote-sensing techniques, based on object recognition, might be able to supply useful information for alleviating this problem in future research.

3.IV.7.C Assignment to Individual Address

Once a predictive model for exposure is developed through the methods reviewed above, estimates are generally assigned to home addresses and occasionally to workplace or school locations. Exposure surfaces can be assigned through raster-grid cells or as points in a vector-based lattice. The result is a high-resolution estimate of potential ambient exposure across the entire urban area that can be assigned to the subjects' address through the geocoder file that converts alphanumeric street addresses to a longitude–latitude coordinate or equivalent projected coordinate system, such as the Universal Transverse Mercator system. Several researchers have raised questions about potential errors introduced by geocoding coordinates. Studies from Canada indicated that although only small proportions of total cases had been erroneously geocoded, in local areas these errors can increase to unacceptably high levels, which might change the spatial structure of the health-outcome data and subsequently affect the analytic results of air-pollution or other exposure studies (Burra et al. 2002).

Others have questioned whether the geocode algorithms currently available offer sufficient accuracy to conduct small-area analyses assessing air-pollution exposures. Zandbergen (2007) outlined the three typical sources of error in "street" geocoders (which identify a street link and then linearly interpolate along the block face based on the house number): (1) completeness in the match rate, meaning the percentage that can be successfully linked to the geocoder; (2) repeatability, indicating the sensitivity of the specified locations to changes in street network or other inputs; and (3) positional accuracy of the assignment in relation to the true position on earth.

Using data from Orange County, Fla., Zandbergen (2007) also compared the more common street-geocoder method with a presumably more accurate geocoder method based on the parcel point of specific residences. Median errors from the actual location for the street geocoder were between 36 and 43 m, while they were only 3 m for the parcel compared with the actual building centroid. The 95th-percentile positional error was in the range of 133 to 140 m of error. Further analyses suggested a high potential to falsely classify high-exposure children (with short buffer distances to the road) using the street-geocoder method compared with the parcel geocoder. Strickland and colleagues (2007) conducted similar tests of positional accuracy in Atlanta and found that median errors between the geocoders and the parcels were approximately 100 m. In some instances, subjects were placed in the wrong census tract, which would further complicate efforts to control for neighborhood confounders, such as poverty and unemployment (see, for example, Jerrett et al. 2005a).

Whether these differences would affect the outcome of a health-effects study remains an open question. However, the nondifferential errors would seem to be instances of Berkson error, with the possibility of inflating the variance of the health effect estimates; if the effects are nondifferential, the errors would follow the classical structure and likely bias toward the null. As a result, the risk estimates could have the potential both to be biased toward the null and to overestimate the variance. Reducing this concern is the fact that many of the errors observed by Zandbergen (2007) and Strickland and colleagues (2007) were the result of parallel displacement along the road network, with relatively little perpendicular error from the street center line. Assigned exposure would not be expected to change much as a function of parallel displacement 100 m along a road, and in LUR or dispersion models we might expect to see only minor errors in the model's continuous surface of pollution. Residences at the end of the road link might be influenced if the geocoding displacement resulted in increased distance from perpendicular roads, but this would influence only a relatively small number of the exposure assignments. As more parcel-level geocoders become available, along with improved exposure models that take the continuous nature of the pollution distribution into account, these errors appear less likely to influence statistical results.

3.IV.7.D Activity Spaces and Residential Mobility

Beyond these positional errors, most studies have not assigned exposures based on the "activity space" occupied by individuals. Studies conducted by Kwan (2004) indicated high variability in the likely distances from home during the day. At this stage, much of the research has focused on residential addresses, but this results in differential degrees of accuracy for commuters versus noncommuters, for children walking versus being bussed to school, and for retirees versus working people. Elgethun and colleagues (2007) compared parent diary reports with data from GPS units worn by children 3 to 5 years of age and found a 48% disagreement between the two methods, with some areas of exposure being significantly underestimated (e.g., time in transit and time outdoors at home). Emerging technologies, such as GPS, and related activity-measuring devices, such as accelerometers, offer possibilities for reducing such errors in the exposure assignment of individuals in health studies.

Many studies have assumed that baseline addresses are sufficient to characterize exposure. Longer-term cohort studies, in particular, have relied on the baseline addresses of their respondents (e.g., Hoek et al. 2002); the potential for movement within and between cities has rarely been directly assessed. One recent study using the American Cancer Society Cohort (Jerrett et al. 2007) indicated that relatively large percentages of the study subjects moved during the follow-up and that these movements were partly dependent on age, educational attainment, and marital status. The nondifferential mobility errors in exposure might also create additional uncertainties in health-effects assessments.

3.IV.7.E Summary

In this section, we provided a synthesis of the various traffic-exposure models, based on comparative criteria that evaluate which model best suits the needs of health-effects assessments, while considering resource constraints associated with the various study designs (adapted from Jerrett et al. 2005). Table 3.3 summarizes the results of this evaluation; each row characterizes one of the models. From the top to the bottom row, the models are arranged in terms of increasing complexity with respect to three sets of evaluation criteria. The first set evaluates the specific requirements of each model, such as the amount of data, data updates, and the software or expertise needed. The second set of criteria concerns the matching of the method to theory and the utility of the model for health studies. The third set of criteria includes the overall limitations and marginal benefits of implementing the model compared with the proximity models, which were taken here as the base case. The time required for the implementation of a model is also an important criterion included in this third set of criteria. Model-implementation time varied significantly in the examined literature, depending on data availability and collection method. In some instances, especially when the design of the study required that data be collected for various seasons of the year, the implementation time of the project was long (i.e., greater than two years). Because of the lack of a common basis for comparison between projects, we decided against including model-implementation time as one of the evaluation criteria. The last criterion for evaluating the models in Table 3.3 is transferability, meaning the extent to which a model can still provide reliable results if implemented (with minor adjustments) at a different location.

Proximity models usually provide a relatively crude but quick evaluation of the impact of traffic pollution on health. Their main disadvantage is that factors affecting the dispersion and physico-chemical activity of pollutants are not considered. These models are limited to the statistical investigation of traffic activity in relation to the risk of respiratory illness. Statistical and GIS tools are often used to assess traffic volume on the relevant road network and the distance of subjects from the network. In addition, survey data are collected from the population under study. The time required to develop a proximity model is generally short if the necessary data are available. The studies might have to be repeated at various time periods to capture seasonal variations.

Geostatistical models can be implemented in conjunction with a dense, well-distributed monitoring network. These models allow the estimation of pollution concentration over several time intervals, but this estimation is limited by the duration of the measurement periods. Improved hardware, spatial statistics software, and appropriate expertise are mandatory for the implementation of a geostatistical model, thus increasing the cost relative to a proximity model.

LUR models are relatively inexpensive to implement and can provide reliable estimates of traffic-related air pollution when adequate land-use, transportation, and pollution-monitoring data are available. In most cases, greater reliability is achieved when the number of observations over the study area is increased. In some instances, geostatistical techniques are used as supplementary tools. These models typically make use of independent variables (such as land-use, elevation, and traffic variables) that are known to affect the concentration of pollutants. The cost can be higher for this model than for proximity and geostatistical models, especially if a dense set of observations is sought for traffic flow and other measures.

Table 3.3 Summary of a Comparison and Evaluation of Models[a]

Model	Requirements			Utility to Health Studies	Extrapolation	Limitations	Marginal Benefits
	Data Requirements	Expertise	Software				
Proximity models	Traffic counts, density, distances of the measurement point, questionnaire data	GIS, statistics	GIS (Arcinfo) or equivalent	Low, crude, error prone	Low	Possibility of large errors in complex meteorology and terrain	Base case
Geostatistical interpolation	Topography, socioeconomic data, location of monitors, monitoring data	GIS, statistics, monitor experts	Spatial statistics, GIS	Depends on the density of the monitoring network	Low	Monitoring networks rarely available to support model estimation	Quantification of error structure
Land use regression	Traffic volumes, land cover, meteorologic data, monitoring data	GIS, statistics, monitor experts	GIS, statistical software	Depends on the density of monitoring and land-use data	Medium	Interpretation of traffic effects complicated by inclusion of other variables (e.g., population density)	Highly resolved exposure prediction if data are available
Dispersion	Meteorologic data, traffic volumes, topography, background concentrations, emission data from point and line sources	GIS, statistics, operators for measurement equipment	GIS, statistical software, specialized dispersion software	Often lacks adequate data to support; depends on data input	High	Rarely have data support required to calibrate model	Easily transferable and conceptually well matched
Hybrid (personal monitoring and one of the preceding methods)	Questionnaire (socioeconomic data, activities), monitoring data, other data depending on the combination	Depends on the method combined with personal monitoring	Depends on the combination	Very good	Low	Usually very expensive and limited to small samples of subjects, making it difficult to use in epidemiologic studies	Higher validity in epidemiological studies

[a] The models are arranged from top to bottom in terms of increasing complexity with respect to various evaluation criteria. See text for details. (Adapted from Jerrett et al. 2005.)

Dispersion models are considered more sophisticated because they explicitly incorporate meteorologic data. If calibrated correctly, these models are potentially more reliable than the three models described earlier but are more expensive to implement and often lack the data resolution necessary to make accurate, reliable predictions. They require a substantial amount of data on emissions and meteorology; improved management tools and specialized software (such as GIS, dispersion software, and integrated software) and hardware capable of handling, storing, and processing these data; and specialized personnel trained in GIS, statistics, mathematics, and computer science. As a result, the cost of implementation is significantly higher than with previous models. The reward comes in the form of a better representation of the process under study.

Personal monitoring offers the most direct way of measuring the exposure of subjects to air pollutants. The drawback of this approach, however, is the high cost of implementation and the associated small number of observations, which tends to produce sample biases. This is because only specific types of subjects can be relied on to carry monitors and record their daily activities for a relatively long period of time. For this reason, personal monitoring is often used as a complement to one of the other model types, creating what we have termed hybrid models. The hybrid models are associated with a high theory-to-method match because they allow direct exposure measurements. In the absence of subjects willing to partake in a personal monitoring program, however, the use of regional monitoring in conjunction with another modeling scheme allows researchers to secure additional validation for their model.

Recent advances in Bayesian modeling enable integrated and complete fusion of personal-monitoring methods with central-site and intra-urban models. These models simultaneously estimate measurement models (based on predicting personal exposures), exposure models that assume a true exposure with measurable error, and health-effects models (Molitor et al. 2007). In so doing, they offer the promise of usefully integrating personal-monitoring data with the other models and, more important, with health-effects estimation. They require extensive statistical expertise, specialized programming software, and a relatively small sample because of the computational intensity. An in-depth presentation of Bayesian modeling and its applications can be found in Appendix C, available on the HEI Web site.

3.IV.8 SOURCE APPORTIONMENT IN HEALTH STUDIES

Few research groups have used source apportionment in epidemiologic studies of air pollution to attribute risk of exposure to emissions from specific types of sources. Most analyses have focused on risk from a specific pollutant or individual chemical component rather than from a mixture of pollutants emitted by various source types. Results from source-apportionment health analyses could be particularly informative for policy decisions (Laden et al. 2000; Mar et al. 2000).

A workshop was held in 2003 to assess the reliability of source-apportionment health-effects methods by analyzing daily mortality with existing PM data sets from Phoenix, Ariz., and Washington, D.C. (Thurston et al. 2005; Hopke et al. 2006; Ito et al. 2006; Mar et al. 2006). As noted in Chapter 2, source-apportionment analyses by various research groups generally resulted in the detection of consistent identification of the same major sources of PM (e.g., soil, secondary sulfate, and traffic), but estimates of traffic and wood burning, when detected, varied considerably. Also, some source categories for each city were not identified by each research group, and the source category of traffic could not reliably be partitioned into gasoline-fueled and diesel motor vehicles. After the source-apportionment analyses were completed, a standardized approach was used for time-series analyses of mortality in the two cities. For each set of source-apportionment results, the source components were individually tested for associations with mortality. The time-series analyses using these data resulted in a large variation in attribution of risk to individual PM-source components. The variability in the results suggested that much additional research is needed to refine the methods and determine whether this approach will be useful for the scientific and regulatory communities.

Grahame and Hidy (2007) recently reviewed studies in which source-apportionment factors derived from receptor modeling were combined with regression techniques using human-health endpoints to infer source influences on health effects. The authors noted that factor-based analyses have been used successfully for both epidemiologic and toxicologic studies. Although the methods are useful in many ways, they also have important limitations that include failure to identify specific sources, misidentification from commingled source factors, and inconsistency or implausibility of results from the same locations when using different factor techniques. Concerns arose from the failure to distinguish statistically based factors from actual sources and from health impacts inferred from measurements from single centrally located air monitors, which are assumed to represent actual exposure for large regional populations. These concerns further emphasized the need for additional research to refine the methods and determine whether this approach will be useful for the scientific and regulatory communities.

3.IV.9 EMERGING METHODS AND TOOLS: REMOTE SENSING

Remote sensing has emerged as an important innovation in the exposure sciences. Remote sensing is defined as "the acquisition and measurement of data/information on some property(ies) of a phenomenon, object, or material by a recording device not in physical, intimate contact with the feature(s) under surveillance" (*http://rst.gsfc.nasa.gov/Intro/Part2_1.html*). The field of remote sensing encompasses the capture, retrieval, analysis, and display of information on surface and atmospheric conditions collected using satellite, aircraft, or other technologies designed to sense energy, light, or optical properties at a distance. Here we review the potential uses of remote sensing for studying

exposures to traffic-related pollution in three categories: (1) as a means of estimating the concentrations of pollutants, potentially generated by traffic, that might be associated with health effects; (2) as a direct data input to models used to predict air pollution from land-use, traffic, or other ground-level information; and (3) as a means of cross-validation for land or atmospheric data captured by ground or traditional meteorologic devices.

3.IV.9.A Remote Sensing for Predicting Surface Concentrations

Most satellites collect data with distance resolutions that are generally not sufficiently fine to meet the 500-m distance from traffic identified in this report as the zone impacted. However, a few direct applications of remote sensing that are capable of estimating the fine-scale variations in traffic pollutants at resolutions relevant to health-effects assessment have been identified. The Moderate-resolution Imaging Spectroradiometer (MODIS), which operates from the Terra and Aqua satellites (*http://modis.gsfc.nasa.gov/about/*), currently has the capacity to measure aerosol optical thickness and, when combined with appropriate processing and analysis, to predict particle concentrations in the troposphere. Some of the better retrievals and predictive models have been for relatively large areas on, for example, 1×1 degree grids, which translate into a resolution of about 110 km at the equator (see, for example, van Donkelaar et al. 2006). The minimum grid size currently available from MODIS is 10×10 km, with global coverage on a two-day cycle. Liu and colleagues (2005) demonstrated a method for retrieving and reprocessing the MODIS images to a 1-km resolution. Based on a three-day comparison against 11 to 14 ground-level measurements of PM_{10}, correlations ranged from 0.55 to 0.86. Although the predicted values were for areas slightly larger than the 500-m resolution recommended in this report, further refinements to scales useful for assessing health effects of traffic appear likely. An additional limitation is temporal availability. At best, most satellites have only daily coverage, and usually less because of cloud conditions.

The Multi-angle Imaging SpectroRadiometer (MISR) is another space-based instrument capable of estimating aerosol optical thickness. The instrument can resolve a minimum grid size of 17.6×17.6 km and provide full coverage of the earth every nine days (*www-misr.jpl.nasa.gov/mission/minst.html*). Recent studies have used MISR to predict PM_{10} surface concentrations in Beijing, China (Jiang et al. 2007). The authors found moderately high correlations between measured concentrations and MISR predictions in the fall, winter, and spring (ranging from $r = 0.59$ to $r = 0.72$) but a weaker correlation in summer ($r = 0.32$). Although the MISR predictions characterized the spatial pattern of aerosol optical thickness fairly well over the broad metropolitan area of Beijing, the authors noted that the minimum grid size might nevertheless be too large for assessing spatial variation in areas with high levels of heterogeneity in particle concentrations in the city.

Special studies using Light Detection and Ranging (LIDAR) have been used to augment other meteorologic and ground-level data for understanding spatial and temporal dimensions of aerosols (Brook et al. 2004). In theory, LIDAR sensors observe all particles in the atmosphere and are capable of producing images of particle scattering (and estimated particle concentrations) with resolutions down to 1 m, but they are more sensitive to coarse particles (Brook, personal communication, August, 2007) and likely only estimate fine-particle concentrations (i.e., ≤ 2.5 μm). Future studies using LIDAR might allow for highly refined estimates of exposure from traffic pollution.

In 2005, the Ozone Monitoring Instrument was launched aboard the Aura satellite. The instrument measures the ozone column in the atmosphere but also has the potential for estimating tropospheric ozone and NO_2 concentrations on 13 km $\times$ 24 km grids. It has been used in conjunction with integrated meteorologic models to produce ground-level estimates (Lamsal et al. 2008). Figure 3.20 illustrates the correlation coefficients between measured and modeled NO_2 across North America.

Correlation coefficients were greater than 0.4 in most locations and exceeded 0.8 in some locations. Although the instrument's resolution is coarser than the 500-m guideline adopted for the purposes of this report, its potential to characterize larger regional patterns appears very promising.

3.IV.9.B Remote Sensing as Data Input

Increasingly, land-cover information is derived partly or wholly from remotely sensed imagery. For example, as mentioned earlier, the U.S. Multi-Resolution Land Characteristics Consortium of federal agencies has purchased and processed Landsat 7 images to classify land cover for the National Land Cover Database, which encompasses the entire U.S. (*www.mrlc.gov/index.asp*). This database provides land-use data in a grid cell format at a 30-m resolution. Earlier versions of this data were used to calibrate a LUR model in New York City for predicting small-area variations in $PM_{2.5}$ (Ross et al. 2007); similar information is available for the rest of the country, which will enable large-area models of many cities to be calibrated where the pollution-monitoring data exist or are collected for studies.

In addition to applications in classifying land use, digital orthophotography has been used to improve traffic

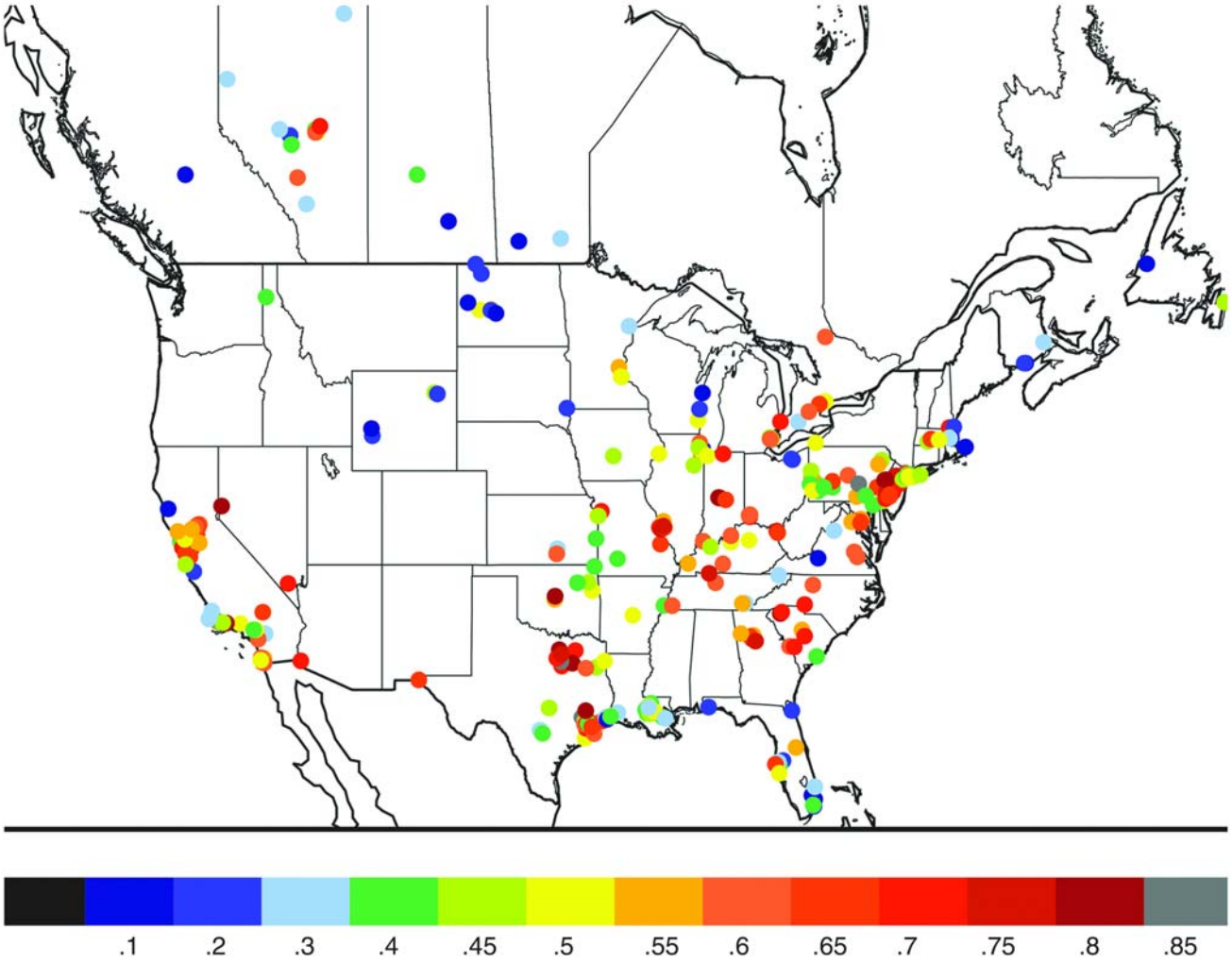

Figure 3.20. Correlation coefficients between in situ measurements and estimates derived from Ozone Measuring Instrument (onboard the Aura satellite) of surface NO_2 for the year 2005. (Reprinted from Lamsal et al. 2008. Copyright 2008, American Geophysical Union. Reproduced/modified by permission of American Geophysical Union.)

counts. Object-oriented programming might be used to refine traffic counts by vehicle type, enabling better estimation of the flow of light- versus heavy-duty vehicles (McCord et al. 2003). Vehicle-flow information might also be augmented with ground-level horizontal LIDAR, which can accurately assess speeds. LIDAR was also discussed in Chapter 2 for across-road measurement of vehicle emissions.

In addition, processed images might supply useful information as input to exposure models. As an example, the Normalized Difference Vegetation Index (NDVI) can be used to derive estimates of vegetative cover (Defries and Townshend 1994). These have been used as predictors in LUR models, and because the "green cover" supplies an alternate estimate of the areas likely to have fewer mobile sources, future applications of the NDVI and other processed images might serve as important data inputs to traffic-exposure assessments.

3.IV.9.C Remote Sensing for Cross-Validation

Many of the current exposure models used to predict pollutant concentrations at a fine scale utilize ground-based information on pollutant concentrations, land use, and traffic. In some instances, the geographic accuracy of these ground data can be of variable or questionable quality. Remotely sensed images of high resolution can be used as cross-validation against which to compare the ground data. Some examples include the location of pollution-monitoring stations operated by government entities.

Although these sites are increasingly marked with GPS coordinates, errors in the GPS coordinates can occur, and reliance on coordinates assigned by paper maps can introduce large errors. Digital orthophotographs or high-resolution images from the IKONOS or QuickBird satellites, at resolutions of 1 to 5 m, can increase the spatial accuracy of the data used as input for LUR models (see, for example, Moore et al. 2007; Ross et al. 2007). Similar comparisons can be made with land-use classifications and road networks. The advent of Google Earth and its extensions has made such cross-validation more accessible for many researchers, and reductions in spatial errors have probably increased the prediction accuracy of ground-level concentrations.

3.IV.10 SUMMARY

Many improvements in exposure modeling for traffic-related air pollution have occurred over the past decade. Much of the improvement has relied on GIS and associated modeling techniques. Such methods allow for relatively easy computation of distances from emissions sources, such as roadways, and for enhanced characterization of land use likely to influence the emission or dispersion of pollutants. The modeling section reviewed five major categories of methods currently used to characterize exposure to traffic-related air pollution in epidemiologic studies: (1) proximity models, (2) geostatistical interpolator models, (3) LUR models, (4) dispersion models, and (5) hybrid models (which combine one or more of the other four approaches with time–activity or personal-monitoring data). All of these approaches are represented in the epidemiologic literature, with a recent trend toward more sophisticated models in the latter categories. The emergence of remote-sensing technologies based on satellite imagery has contributed to a further refinement of the data inputs, although at this time direct estimates of ground-level pollution from remote sensing are at scales generally coarser than those of near-source impacts.

Although there have been notable advances, fundamental data-input problems continue to raise questions about the validity of traffic-exposure estimates. Three specific problems have been reviewed in this report: First, the accuracy of the geographic locations used for individuals in health studies, based on geocoding algorithms currently available, is affected by the occurrence of locational errors, some of which might be nondifferential. This problem could potentially lead to a bias toward the null in health studies. Second, the traffic-data inputs used to calibrate LUR and dispersion models are of varying quality and completeness. Similarly, information on emissions under various driving conditions also seems prone to error. Third, information on the actual "activity space" of individuals in health studies is rarely available, and home addresses are generally used as the surrogate for total exposures, when in fact a high percentage of an individual's total exposure can accrue from relatively short periods of time spent in high-exposure microenvironments such as in transit. Failure to capture data on time spent in these microenvironments may introduce errors into exposure estimates.

Relatively few studies have attempted to compare the various models against one another or to assess the importance of measurement error. Those that have assessed measurement error appear to indicate that the more advanced dispersion and land-use models do predict exposures more accurately and produce more stable estimates in health studies (Molitor et al. 2007), although much depends on the quality and resolution (both spatial and temporal) of the underlying data.

Overcoming the fundamental limitations will require international efforts to improve the quality of geocoding, to refine and complete traffic counts and emissions estimates through a consistent method, and to estimate more completely the spatiotemporal activity of individuals in health studies. The spatial heterogeneity and high variation over small areas in traffic-related air pollution necessitates such refinements, beyond what would have been needed in earlier air-pollution studies that focused on background or community-level air-pollution contrasts. Further research will also be needed to integrate the rich data available from remote sensing into ground-based estimates. Finally, more studies comparing the use of various exposure models and their associated errors will be necessary to alleviate concerns about the potential for error in traffic-exposure studies caused by small-area variation.

3.V. SUMMARY AND CONCLUSIONS

Emissions of air pollutants from mobile on-road sources comprise numerous organic and inorganic compounds in both the particle and gas phases. Many of these compounds undergo both physical and chemical transformations after being emitted. The type and quantity of emissions are a function of several variables (such as the mix of light- and heavy-duty vehicles, fuel type, vehicle speeds, and vehicle densities). The impact of vehicle emissions extends beyond the local scale to the urban, regional, and international scales against a background of similar contaminants from other sources. Resulting ambient concentrations are determined by emission rates in combination with vehicle use conditions (including traffic

characteristics) and meteorologic conditions, topography, and land use. What individuals are exposed to is influenced by their proximity to sources, the rate at which chemical transformations take place, other ambient and microenvironment sources, and individual time–activity patterns.

Given these issues, assessing exposure to traffic-related air pollutants poses significant challenges. Over the years, several air pollutants have been used as surrogates to represent the contribution of mobile-source emissions. The principal surrogates used include CO, NO_2, PM, PM_{10}, $PM_{2.5}$, UFP, EC, and benzene.

Measurements of outdoor air quality on roadways indicate that concentrations of these pollutants are high, compared with ambient concentrations measured at air-monitoring stations, and are highly variable. In-vehicle concentrations are higher than ambient concentrations and lower than roadway concentrations for most traffic-related gases and aerosols. In the United States, adults spend an average of 81 minutes per day in vehicles. Individuals are likely to be exposed to the highest concentrations of traffic-related pollutants when traveling in or near vehicles and to receive a disproportionate (up to 50%) amount of their daily exposures to traffic-related pollutants in this microenvironment.

Gradient studies have indicated that exposure zones for traffic-related air pollution range from 50 to 1500 m from highways and major roads. Meta-analyses have suggested a range of 300 to 500 m, depending on the likely background concentrations of air pollution and other meteorologic factors. Meteorology plays an important role in determining the size and diurnal and seasonal stability of affected zones. Examining various assumptions with respect to two large North American cities suggested that 30% to 45% of the total population is found in such zones.

When traffic-pollution surrogates are considered at the urban scale, none of the surrogates meet all the requirements for validity and practicality. Emissions of surrogates from both light- and heavy-duty vehicles have varied greatly over time, as have emissions of surrogates from other source materials. Data are not available to assess the ratio of surrogates to total emissions over time. On-road vehicle emissions of CO, benzene, and NO_x (as well as the reaction by-product NO_2) are all major contributors to emissions from all sources, accounting for 40% or more of total emissions into the atmosphere. All three compounds have significant ambient and microenvironmental sources, making it extremely difficult to disentangle the motor-vehicle contribution. Primary on-road vehicle emissions of PM represent a small contribution, typically around 3%, to emissions from all sources in the United States. When considering secondary-aerosol formation, motor vehicles can account for 15% or more of ambient PM concentrations. As is the case with CO, NO_2, and benzene, there are many sources of PM outdoors and indoors, making the assessment of the contribution of traffic PM difficult, particularly for PM_{10} and $PM_{2.5}$. Although UFPs are emitted in large concentrations from vehicles, they decay rapidly within short distances of the roadway and hence are of limited utility as a surrogate. In recent years, EC has been used as a surrogate, primarily for DE, but further studies are needed to account for other non-mobile sources of EC, as well as for gasoline-fueled motor vehicles, and to calibrate the various sampling methods. The current IMPROVE and STN networks provide data on 24-hour average EC concentrations for predominantly regional and urban-oriented monitoring sites. Monitoring sites designed to measure traffic-related EC — as well as other chemical species mentioned above — are few in number. There is no national database on EC and there is only limited data on the concentrations and sources of carbonaceous aerosol. Inexpensive passive monitors exist at this time only for NO_2.

Few studies link traffic volume to concentrations of surrogates near roadways or at homes. The few available studies are difficult to interpret because they used different measures of traffic volume and vehicle mix, measured different pollutants, monitored pollutants at varying distances from the roads, and were conducted under variable meteorologic conditions and over varying sampling periods.

Factors influencing an individual's personal exposure to a surrogate pollutant include time–activity patterns, meteorologic conditions, land-use patterns, and socioeconomic status. Accurately measuring traffic exposure in both time and space is difficult and often impractical in large health studies. A potential solution is to deploy a large number of monitors in a geographic location, especially in places where air pollutants are expected to be highly variable and the population density is high. The use of models that incorporate numerous factors as inputs to estimate exposures that are more spatially relevant to the individual's exposure can also be helpful. However, the accuracy of the inputs is critical to the usefulness of the model.

With the expansion of cities and changes in land-use patterns, the patterns of population exposures have changed over time. In spite of technologic innovation and regulatory control, emissions from traffic in many places have not been reduced as much as they might have been, largely because of the heightened demand for travel, which is prompted partly by urban structures that promote private-automobile use over walking, cycling, and public transit. Features of urban growth and sprawl can increase exposure for relatively large proportions of the populations. Another factor that can lead to unequal distribution

of exposure is socioeconomic status. If, as the evidence suggests, groups of lower socioeconomic status experience higher exposures than groups of higher socioeconomic status, this needs to taken into consideration in the interpretation of epidemiologic findings and also in the design of future studies.

There have been many advances in exposure modeling for traffic-related air pollution over the past decade, precipitated in part by the increased availability of GIS and associated modeling techniques. These methods allow for relatively easy computation of distances from emissions sources, such as roadways, and for enhanced characterization of land use likely to influence the emission or dispersion of traffic-related air pollution. The models currently used to characterize exposure to traffic-related air pollution in epidemiologic studies fall into five major categories: (1) proximity models, (2) geostatistical interpolator models, (3) land-use regression (LUR) models, (4) dispersion models, and (5) hybrid models (which combine one or more of the above four approaches with time–activity or personal-monitoring data). All of these approaches are represented in the epidemiologic literature, with a recent trend toward the more sophisticated models. The emergence of remote-sensing technologies based on satellite imagery has contributed to a further refinement of the data inputs, although at this time direct estimates of ground-level pollution from remote sensing are generally at scales coarser than estimates obtainable on the ground.

Although there have been notable advances, fundamental data-input problems continue to raise questions about the validity of traffic-exposure estimates. Three specific problems have been reviewed in this chapter: First, the accuracy of the geographic locations used for individuals in health studies, based on geocoding algorithms, is currently affected by the appearance of locational errors, some of which might be nondifferential. This problem could potentially lead to a bias toward the null in health studies. Second, the traffic-data inputs used to calibrate land-use and dispersion models are of varying quality and completeness. Similarly, information on emissions under various driving conditions also seems prone to error. Third, information on the actual "activity space" of individuals in health studies is rarely available, and home addresses are generally used as the surrogate for the total exposure experience, when in fact a high percentage of an individual's total exposure can accrue from relatively short periods of time spent in high-exposure microenvironments (such as during transit). Failure to capture data on time spent in such microenvironments might introduce errors into exposure estimates.

Relatively few studies have attempted to compare the various models against one another or attempted to assess the importance of measurement error. Those that have assessed measurement error appeared to indicate that the more advanced dispersion and land-use models do predict exposures more accurately and produce more stable estimates in health studies, although much depends on the quality and resolution (both spatial and temporal) of the underlying data.

Overcoming the fundamental limitations will require international efforts to improve the quality of geocoding, to refine and complete traffic counts and emissions estimates through a consistent method, and to estimate more completely the spatiotemporal activity of individuals in health studies. The spatial heterogeneity and high variation over small areas of traffic-related air pollutants necessitates such refinements, beyond what was needed in earlier air-pollution studies, which focused on contrasting background or community-level air-pollution concentrations. Further research will also be needed to integrate the rich data available from remote sensing into ground-based estimates. Finally, more studies comparing the various exposure models, and their associated errors, will be necessary to alleviate concerns about the potential for error in assigning exposure in epidemiologic studies of traffic-related pollution caused by small area variation of pollutants and concerns about how that error might affect the results of these studies.

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Appendix A.1. Data for Nitrogen Dioxide[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (µg/m^3) Mean	Concentration (µg/m^3) Maximum	Description
In-Vehicle (in Traffic)						
Behrentz et al. 2005 Los Angeles	22	Gas chromatography	~70 min	137	209	6 school buses on 2 routes
Chan et al. 1999 Hong Kong	25 32 64	Chemiluminescence	20–90 min 14–38 min 20–41 min	131 110 131	396 319 430	8 cars; during peak commuting times 4 light buses; during peak commuting times 8 buses; during peak commuting times
Lewné et al. 2006 Stockholm	39 42 40	Chemiluminescence	9 hr, 50 min 8 hr, 20 min 8 hr, 35 min	48 60 68	82 109 190	39 taxis; 1 working day 42 buses; 1 working day 40 trucks; 1 working day
Riediker et al. 2003 North Carolina	50	Ogawa monitor	9 hr	59.7	1042	10 police cars during work shifts (extreme value of 1042 µg/m^3 not included in average)
Sabin et al. 2005 Los Angeles	31	Gas chromatography	60 min	116	220	Mean of 7 school buses on urban bus routes. Calculated from Table 3 of Sabin et al. 2005.
van Wijnen et al. 1995 Amsterdam	31 18	SKC monitor	60 min	111 103	267 165	18 cars (Averages calculated from Table 1 of van Wijnen et al. 1995.) 31 bicycles (Averages calculated from Table 1 of van Wijnen et al. 1995.)
Westerdahl et al. 2005 Los Angeles	5	Chemiluminescence	120 min	66.5 (median) 58.9 (median) 104.5 (median) 100.7 (median)		4 runs in a car mostly on freeways

Table continues next page

[a] Mean concentrations are plotted in Figure 3.9.

Appendix A.1 (*Continued*). Data for Nitrogen Dioxide[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (µg/m^3) Mean	Concentration (µg/m^3) Maximum	Description
Roadside						
Cape et al. 2004 Scotland	84 54 54 84	Palmes tubes	2 mo	2.7–50.1 11.0–48.3 9.3–44.5 2.9–39.8		1 m from 14 roads with variable traffic volume 2 m from 9 roads 5 m from 9 roads 10 m from 14 roads
Chan et al. 1999 Hong Kong	70	Chemilumin-escence	60 min	141	304	16 pavement monitors in central business districts
da Silva et al. 2006 São Paulo	17 16	Palmes tubes	1 wk	64 48	~90 ~67	Heavy traffic sites (average of 2 periods) Low traffic sites (average of 2 periods)
Gilbert et al. 2003 Montreal	31	Ogawa monitor	1 wk	56 23	65	Different distances (0–1310 m) from roads. Upper and lower range of means of all locations. Maximum value from Figure 1 in Gilbert et al. 2003.
Janssen et al. 2001 the Netherlands	84	Palmes tubes	1 wk	39.2	76.6	Outside 24 schools within 400 m of motorways (mean distance from motorways = 206 m)
Lam et al. 1999 Hong Kong	60	Palmes tubes	15 days (monthly average)	~150	245	15 sites 1 m from road. Estimated from Figure 6 of Lam et al. 1999.
Lewné et al. 2004 Munich the Netherlands (3 areas) Rotterdam Stockholm	 68 48 24 24	Palmes tubes	2 wk	 33.0 37.9 39.8 28.8	 50.6 50.8 49.7 44.7	 Urban traffic sites
Marconi et al. 2007 Rome	661	Not available	24 hr	44.9	89.2	20 m from street
Namdeo and Bell 2005 London	Continuous monitoring	Not available	Yearly average Summer average Winter average	75.5 (geometric mean) 72.4 (geometric mean) 78.5 (geometric mean)		1 m from a busy road (Marylebone Road)

Table continues next page

[a] Mean concentrations are plotted in Figure 3.9.

Appendix A.1 (*Continued*). Data for Nitrogen Dioxide[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (µg/m^3) Mean	Concentration (µg/m^3) Maximum	Description
Roadside (*Continued*)						
Raaschou-Nielsen et al. 1996 Central Copenhagen	156	Palmes tubes	1 wk	39.3		Outside 26 urban homes on streets with high traffic
Riediker et al. 2003 North Carolina	50	Ogawa monitor	8.4 hr	95	403	Four-day rotating locations near major traffic routes
Roorda-Knape et al. 1998 Delft and Overschie	51	Palmes tubes	2 wk	36.0		Different distances at six residential sites within 300 m from a major road. Calculated from Table 2 in Roorda-Knape et al. 1998.
Smargiassi et al. 2005 Montreal	15	Ogawa monitor	24 hr	62.3	105	10 m from expressway with > 160,000 vehicles/day
van Roosbroeck et al. 2006 the Netherlands	68	Ogawa monitor	48 hr	37	51	Outside homes near busy roads
van Wijnen et al. 1995 Amsterdam	12	SKC monitor	1 hr	106	229	Pedestrians walking near busy urban street
Westerdahl et al. 2005 Los Angeles	5	Chemilumin-escence	2 hr	23 (median) 65 (median) 67 (median) 74 (median)		From primarily on freeways

Table continues next page

[a] Mean concentrations are plotted in Figure 3.9.

Appendix A.1 (*Continued*). Data for Nitrogen Dioxide[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (µg/m^3) Mean	Concentration (µg/m^3) Maximum	Description
Urban						
Behrentz et al. 2005 Los Angeles	18	Gas chroma-tography	10–120 min	93		Cabin of school bus (parked, windows open) in areas with varying levels of traffic (representing urban background)
Carr et al. 2002 Munich	216 192	Palmes tubes	4 wk (annual means)	65.8 32.2	85.4 43.8	18 locations affected by traffic 16 schools affected by traffic
Lewné et al. 2004 Munich the Netherlands (3 areas) Rotterdam Stockholm	 32 44 24 44	Palmes tubes	2 wk	 29.7 28.0 30.2 21.0	 35.1 35.4 35.4 26.9	 8 urban background sites 11 urban background sites 6 urban background sites 11 urban background sites
Namdeo and Bell 2005 London	Continuous measure integrated over season and year	Not available	Yearly average Summer average Winter average	45.8 (geometric mean) 39.4 (geometric mean) 52.3 (geometric mean)		Urban center away from curb (Bloomsbury)
Riediker et al. 2003 North Carolina	50	Ogawa monitor	8 hr	58	132	Fixed ambient site collocated with state monitoring site
Rijnders et al. 2001 the Netherlands	53 192 150 33 56 43	Palmes tubes	1 wk (annual means)	37.5 29.6 25.1 37.0 29.7 25.6	71.4 49.5 43.5	Very urban homes; yearly averages Fairly urban homes; yearly averages Non-urban homes; yearly averages Very urban schools Fairly urban schools Non-urban schools
Smargiassi et al. 2005 Montreal	15 15 15	Ogawa monitor	24 hr	37.7 43.5 47.2	59.8 63.4 64.8	< 10 m from curb, quiet residential street < 10 m from curb, major residential artery < 10 m from curb, major residential artery
van Roosbroeck et al. 2006 the Netherlands	27	Ogawa monitor	48 hr	33.8 (geometric mean)	50.5 (geometric mean)	Outside children's homes in urban background location

Table continues next page

[a] Mean concentrations are plotted in Figure 3.9.

Appendix A.1 (*Continued*). Data for Nitrogen Dioxide[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (µg/m^3) Mean	Concentration (µg/m^3) Maximum	Description
Suburban						
Lewné et al. 2004						
Munich	60	Palmes tubes	2 wk	23.4	28.9	15 locations
the Netherlands (three areas)	20			25.2	37.5	5 locations
Rotterdam	8			31.2	37.5	2 locations
Stockholm	24			20.5	23.9	6 locations affected by traffic
Stockholm	40			15.5	21.7	10 locations
Rural						
Lewné et al. 2004						
the Netherlands (3 areas)	48	Palmes tubes	2 wk	22.3	29.9	12 locations
Rotterdam	16			27.6	29.2	4 locations
Sweden	36			10.6	13.8	9 locations
Namdeo and Bell 2005 London	Continuous measure integrated over season and year	Not available	Yearly average	16.4 (geometric mean)		Outside London (Rochester)
			Summer average	12.8 (geometric mean)		
			Winter average	18.1 (geometric mean)		
Raaschou-Nielsen et al. 1996 Copenhagen	144	Palmes tubes	1 wk	13.7		Outside 24 homes
In Homes						
Raaschou-Nielsen et al. 1996	156	Palmes tubes	1 wk	14.8		Bedrooms of 26 children in homes near traffic
Copenhagen	144			4.9		Bedrooms of 24 children in homes in rural areas
van Roosbroeck et al. 2006 Amsterdam	15	Palmes tubes	48 hr	46.6 (geometric mean)	151.7	Homes near high traffic road (some may have had gas stoves)
	27		48 hr	38.2	131.9	Homes near low traffic roads

Table continues next page

[a] Mean concentrations are plotted in Figure 3.9.

Appendix A.1 (*Continued*). Data for Nitrogen Dioxide[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (µg/m^3)		Description
				Mean	Maximum	
In Schools						
Janssen et al. 2001 the Netherlands	192	Palmes tube	1 wk	19.1	44.7	24 schools within 400 m of motorways (mean distance from motorways = 206 m)
Rijnders et al. 2001 the Netherlands	33	Palmes tubes	1 wk	23.1		Schools near very busy highway
	56			12.5		School near fairly busy highway
	43			10.9		School near nonbusy highway
Roorda-Knape et al. 1998 the Netherlands (6 city districts)	12	Palmes tubes	2 wk	9.2 13.0 23.6 14.8 9.2 14.7 16.0 32.8 27.7 30.0 22.0 21.5		12 schools near a motorway (35 to 645 m) in 6 city districts
Personal Exposures						
Rijnders et al. 2001 the Netherlands	81	Palmes tubes	1 wk	31.2	163.1	Mean of 4-seasons measurements for 14–26 children in school in very urban areas
	199			19.8	58.9	Mean of 4-seasons measurements for 47–53 children in schools in fairly urban areas
	157			15.9	30.8	Mean of 4-seasons measurements for 35–42 children in nonurban areas
van Roosbroeck et al. 2006 Amsterdam	15	Ogawa monitor	48 hr	46.2 (geometric mean)	118.1	Children living near busy road
	26			39.7 (geometric mean)	89.3	Children living in background area

[a] Mean concentrations are plotted in Figure 3.9.

Table A.2. Data for $PM_{2.5}$[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (µg/m³) Mean	Concentration (µg/m³) Maximum	Description
In-Vehicle (in Traffic)						
Adams et al. 2001 Central London	40	Gravimetric	5–48 min	30.7 (geometric mean)		Bicycle; summer, on 3 fixed routes
	36			34.0 (geometric mean)		Bus; summer, on 3 fixed routes
	42			35.0 (geometric mean)		Car; summer, on 3 fixed routes
	56			20.1 (geometric mean)		Bicycle; winter, on 3 fixed routes
	32			30.9 (geometric mean)		Bus; winter, on 3 fixed routes
	12			23.7 (geometric mean)		Car; winter, on 3 fixed routes
	105			28.4 (geometric mean)		Commuter bicyclists; summer, on non fixed routes
Behrentz et al. 2005 Los Angeles	22	DustTrak, continuous	~70 min	43.0	62.0	School bus driving on two bus routes
Gomez-Perales et al. 2004 Mexico City	28	Gravimetric	1 hr	68.0	106.0	Mini-buses; rush-hour concentrations
	16			71.0	137.0	Bus; rush-hour concentrations
	18			61.0	99.0	Metro; rush-hour concentrations
Kaur et al. 2005 Central London	56	Gravimetric	> 18 min	27.5	64.4	Walking
	48			33.5	77.5	Cycling
	42			34.5	64.6	Bus
	29			38.0	58.5	Car
	22			41.5	71.8	Taxi
Riediker et al. 2003 North Carolina	50	Gravimetric	~9 hr	23.0	58.7	10 police cars; workshift measurement

Table continues next page

[a] Mean concentrations are plotted in Figure 3.10.

Table A.2 (*Continued*). Data for $PM_{2.5}$[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (µg/m³) Mean	Concentration (µg/m³) Maximum	Description
Roadside						
Cyrys et al. 2003						
Munich	24	Gravimetric	2 wk	14.3		10 m from traffic, 6 locations
the Netherlands	16			19.9		6 m from traffic, 4 locations
Stockholm	8			13.8		19 m from traffic, 2 locations
Fischer et al. 2000	18	Gravimetric	24 hr	25.0	50.0	Outside homes near high-density traffic
Amsterdam	18			21.0	54.0	Outside homes near low-density traffic
Funasaka et al. 2000	8	Gravimetric ($PM_{2.0}$)	48–72 hr	37		Outside homes 5 m from high traffic road in urban district A
Osaka	6			23		Outside homes 5 m from high traffic road in suburban district B
Giugliano et al. 2005	6	Gravimetric	48 hr	27.1	56.9	Curbside in urban residential area — spring
Milan	16			20.3	54.4	Curbside in suburban area — spring
Harrison et al. 2004a	101	*Tapered element* oscillating microbalance	24 hr	22.3	330	5 m from heavily traveled roads, 4 locations
Harrison et al. 2004b				16.0		Roadside (Selly Oak)
London				25.9		Roadside (High Holborn)
	< 84	Gravimetric	24 hr	24.2		Roadside (Elephant and Castle)
				21.2		Roadside (Park Lane sampled from the roof of six-story building)
				14.6		Roadside (Park Lane, westerly wind)
				42.0		Roadside (Park Lane easterly wind)
Janssen et al. 1997	28	Gravimetric	8 hr	42.9	99.0	0.5 m from road
Arnhem, the Netherlands						
Janssen et al. 2001	181	Gravimetric	1 wk	24.8	60.8	Outside 24 schools within 400 m of motorways (mean distance from motorways = 206 m)

Table continues next page

[a] Mean concentrations are plotted in Figure 3.10.

Table A.2 (*Continued*). Data for $PM_{2.5}$[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (μg/m³) Mean	Concentration (μg/m³) Maximum	Description
Roadside (*Continued*)						
Kinney et al. 2000 New York City	4	Gravimetric	8 hr	45.7		Intersection with high number of diesel trucks and buses
	4			47.1		Near bus depot
	4			36.6		Intersection with high number of cars
	4			38.7		Quiet street
Lam et al. 1999 Hong Kong	204	Gravimetric	24 hr	~100	~200	Conducted at 15 sites during December, 1996 Estimated from Figure 5 in Lam et al. 1999.
Lam et al. 2007 Taiwan	55	Gravimetric	15 hr	141	210	5 m from busy road.
Lena et al. 2002 Bronx, New York	6	Gravimetric	10–12 hr	29.9		Truck route (site 1)
	6			21.1		Non-truck route (site 2)
	6			18.2		Residential street (site 3)
	3			28.2		Truck route (site 4)
	2			20.7		Truck route (site 5)
Marconi et al. 2007 Rome	387	Gravimetric	24 hr	24.0 (geometric mean)	87.9	20 m from street
Martuzevicius et al. 2004 Cincinnati	219	Gravimetric	24 hr	28.6	48.3	Highest average of 11 sites near major highway
Namdeo and Bell 2005 London	Continuous measure integrated over season and year	*Tapered element* oscillating microbalance	Yearly average	21.8 (geometric mean)	58.7	1 m from a busy road (Marylebone Road)
			Summer average	21.0 (geometric mean)		
			Winter average	22.7 (geometric mean)		
Riediker et al. 2003 North Carolina	50	Gravimetric	8.4 hr	29.9	69.1	Four-day rotating locations near major traffic routes

Table continues next page

[a] Mean concentrations are plotted in Figure 3.10.

Table A.2 (*Continued*). Data for $PM_{2.5}$[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (µg/m³) Mean	Concentration (µg/m³) Maximum	Description
Roadside (*Continued*)						
Roorda-Knape et al. 1998 Delft and Overschie	18	Gravimetric	1 wk	19.1	20.8 (maximum site mean)	Locations at 50, 115, 165, and 310 m from a motorway. Average of means for all distances from Table 2 of Roorda-Knape et al. 1998.
Smargiassi et al. 2005 Montreal	34	Gravimetric	24 hr	15.4	39.5	10 m from curb of collector artery
Urban						
Behrentz et al. 2005 Los Angeles	18	DustTrak, continuous	10–120 min	20.0		Locations with varying levels of traffic (representing urban background (measured inside school bus with engine off)
Cyrys et al. 2003 Munich the Netherlands Stockholm	 24 16 28	Gravimetric	2 wk	 13.3 17.8 10.2		Locations with no major roads or other sources within 50 m radius (6 locations) Locations with no major roads or other sources within 50 m radius (4 locations) Locations with no major roads or other sources within 50 m radius (7 locations)
Fromme et al. 2005 Berlin	50	Gravimetric	7–8 hr	28.5	70.6	Outside apartments
Funasaka et al. 2000 Osaka, Japan	8 6 6	Gravimetric ($PM_{2.0}$)	48–72 hr	22.0 26.0 18.0		Outside 4 homes 60–150 m from high traffic road in urban district A Outside 4 homes 60–150 m from high traffic road in suburb B Outside 4 homes 60–150 m from high traffic road in suburb C
Giugliano et al. 2005 Milan	 18 40 16 24	Gravimetric	48 hr	 23.4 18.2 43.6 58.7	 39.7 40.3 70.1 128.1	One location not directly exposed to traffic Spring Summer Autumn Winter

Table continues next page

[a] Mean concentrations are plotted in Figure 3.10.

Table A.2 (*Continued*). Data for $PM_{2.5}$[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (μg/m³) Mean	Concentration (μg/m³) Maximum	Description
Urban (*Continued*)						
Harrison et al. 2004b London	< 84	Gravimetric	24 hr	9.4 17.9 13.0 12.1 10.0 18.6		Roadside (Selly Oak) Roadside (High Holborn) Roadside (Elephant and Castle) Roadside (Park Lane sampled from the roof of six-story building) Roadside (Park Lane, westerly wind) Roadside (Park Lane easterly wind)
Janssen et al. 1997 Arnhem, the Netherlands	28	Gravimetric	8 hr	35.0	92.0	200 m from busy road in city center
Lena et al. 2002 Bronx, New York	9	Gravimetric	10–12 hr	19.0		Outside home in urban residential street
Namdeo and Bell 2005 London	Continuous monitoring over a 1-yr period	*Tapered element* oscillating microbalance	Yearly average Summer average Winter average	11.3 11.2 11.4		Urban center away from curb (Bloomsbury)
Riediker et al. 2003 North Carolina	50	Gravimetric	8.3 hr	35.4	96.0	Fixed ambient site collocated with state monitoring site
Smargiassi et al. 2005 Montreal	33 30 35	Gravimetric	24 hr	12.4 13.7 13.4	35.0 35.8 33.0	< 10 m from curb, quiet residential street < 10 m from curb, major residential artery < 10 m from curb, major residential artery
Rural						
Cyrys et al. 2003 the Netherlands Stockholm	 ~16 ~12	Gravimetric	2 wk	 17.3 8.4		 4 locations 3 locations
Lin et al. 2007 Taiwan	~55	Gravimetric	15 hr	60.5	67.0	1 location
Martuzevicius et al. 2004 near Cincinnati	Not available	Gravimetric	24 hr	~19.0		1 location (average of 2 measurement cycles)

Table continues next page

[a] Mean concentrations are plotted in Figure 3.10.

Table A.2 (*Continued*). Data for $PM_{2.5}$[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (µg/m³) Mean	Concentration (µg/m³) Maximum	Description
In Homes						
Fischer et al. 2000 Amsterdam	16 16	Gravimetric	24 hr	27.0 12.0	78.0 23.0	Homes near high-density traffic Homes near low-density traffic
Fromme et al. 2005 Berlin	27 16 73	Gravimetric	7–8 hr	28.0 27.9 53.8	46.6 58.6 128.4	Apartments of non-smokers Apartments of non-smokers Nursery schools
Funasaka et al. 2000 Osaka	8 14 6	Gravimetric ($PM_{2.0}$)	48–72 hr	20.0 18.0 22.0		4 homes 5 m from high traffic road in urban district A 4 homes 60–150 m from high traffic road in urban district A 4 homes 5 m from high traffic road in suburb B
Schools						
Janssen et al. 2001 the Netherlands	178	Gravimetric	6–8 hr	24.8	60.8	24 schools within 400 m of motorway (mean distance from motorways = 206 m)

[a] Mean concentrations are plotted in Figure 3.10.

Table A.3. Data for Elemental Carbon or Black Carbon[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (µg/m^3) Mean	Concentration (µg/m^3) Maximum	Description
In-Vehicle (in Traffic)						
Adams et al. 2002 London	21	Nephelometer	16-59 min	15.4	32.1	Bicycle; summer, 3 fixed routes
	15			16.3	33.3	Bus; summer, 3 fixed routes
	22			26.1	58.6	Car; summer, 3 fixed routes
	50			19.2	62.8	Bicycle; winter, 3 fixed routes
	31			24.7	79.8	Bus; winter, 3 fixed routes
	11			34.4	88.8	Car; winter, 3 fixed routes
	99			21.0	48.4	Bicycle; commute, non fixed route
Behrentz et al. 2005 Los Angeles	22	Aethalometer	~70 min	8.0	19.0	2 school buses driving on 2 bus routes
Fitz et al. 2003 Los Angeles	32	Aethalometer	60–90 min	2.7	10.0	School bus driving on bus routes windows open (suburban/rural) and closed (urban)
Fruin et al. 2004 Los Angeles	917	Aethalometer	~2 hr	~4.4		Following non-diesel vehicles. Averaged from Table 2 in Fruin et al. 2004.
Sacramento	927			~2.7		Following non-diesel vehicles. Averaged from Table 2 in Fruin et al. 2004.
Los Angeles	501			~14.2		Following diesel vehicles. Averaged from Table 2 in Fruin et al. 2004.
Sacramento	259			~9.7		Following diesel vehicles. Averaged from Table 2 in Fruin et al. 2004.
Riediker et al. 2003 North Carolina	50	Nephelometer	9.1 hr	2.3	5.0	10 police cars, during workshift
Sabin et al. 2005 Los Angeles	31	Aethalometer	~60 min	6.7	19.0	School buses driving on urban bus routes (overall mean from several commutes)

Table continues next page

[a] Mean concentrations are plotted in Figure 3.11.

Table A.3. (*Continued*) Data for Elemental Carbon or Black Carbon[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (μg/m³) Mean	Concentration (μg/m³) Maximum	Description
Roadside						
Cyrys et al. 2003		Thermal oxidation analysis	2 wk			
Munich	12			3.1		10 m from traffic, 6 locations
the Netherlands	12			3.9		6 m from traffic, 4 locations
Fischer et al. 2000		Absorbance of $PM_{2.5}$ on filter from reflectometer	24 hr			
Amsterdam	18			2.8[b] ($\times 10^{-5}$/m)	4.9[b] ($\times 10^{-5}$/m)	Outside homes near high-density traffic
	18			1.5[b] ($\times 10^{-5}$/m)	2.7[b] ($\times 10^{-5}$/m)	Outside homes near low-density traffic
Funasaka et al. 2000		Thermal oxidation analysis	48–72 hr			
Osaka	8			7.5		Outside 4 homes 5 m from high traffic road in urban district A
	6			11.0		Outside 4 homes 5 m from high traffic road in suburb B
Harrison et al. 2004a						
London	101	Thermal oxidation analysis	24 hr	8.4		4 roadside locations
Hies et al. 2000						
Berlin	361	Thermal oxidation analysis	24 hr	7.6		1 near traffic location
Janssen et al. 1997						
Arnhem, the Netherlands	28	Absorbance of $PM_{2.5}$ on filter from reflectometer	8 hr	51.0	83	0.5 m from road
Janssen et al. 2001						
the Netherlands	179	Absorbance of $PM_{2.5}$ on filter from reflectometer	1 wk	12.2	24.5	Outside 24 schools within 400 m of motorways (mean distance from motorways = 206 m)
Kinney et al. 2000		Thermal oxidation analysis	8 hr			
New York City	3			6.2	7.9	Intersection with high number of diesel trucks and buses
	2			3.7		Near bus depot
	3			2.3		Intersection with high number of cars
	2			1.5		Quiet street

Table continues next page

[a] Mean concentrations are plotted in Figure 3.11.

[b] Concentration expressed as $\times 10^{-5}$/m indicates absorbance. (Absorbance values not included in the figure.)

Table A.3. (*Continued*) Data for Elemental Carbon or Black Carbon[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (μg/m³) Mean	Concentration (μg/m³) Maximum	Description
Roadside (*Continued*)						
Lena et al. 2002 Bronx, New York	6 6 6 3 2	Absorbance of $PM_{2.5}$ on filter from reflectometer	10–12 hr	5.9 2.6 2.6 7.3 3.8		Truck route Non-truck route Non-truck route Truck route Truck route
Riediker et al. 2003 North Carolina	50	Nephelometer	8.4 hr	4.0	6.6	Four-day rotating locations near major traffic routes
Roorda-Knape et al. 1998 Delft and Overschie	54	Absorbance of PM_{10} on filter from reflectometer	1 wk	9.9	14.9 (maximum site mean)	Locations at 50, 115, 165, and 310 m from a motorway (average of means for all distances from Table 2 in (Roorda-Knape et al 1998))
Smargiassi et al. 2005 Montreal	34	Absorbance of $PM_{2.5}$ on filter from reflectometer	24 hr	2.5[b] ($\times 10^{-5}$/m)	4.74[b] ($\times 10^{-5}$/m)	10 m from curb of collector artery
Urban						
Behrentz et al. 2005 Los Angeles	18	Aethalometer	10–120 min	2.0		Cabin of school bus (parked, windows open) in areas with varying levels of traffic (representing urban background)
Carr et al. 2002 Munich	216 192	Coulometric analysis after solvent extraction and thermal desorption of OC	4 wk (annual mean)	12.9 5.7	20.7 7.1	18 locations impacted by traffic 6 schools impacted by traffic
Cyrys et al. 2003 Munich the Netherlands (3 areas) Stockholm	24 16 28	Thermal oxidation analysis	2 wk	2.1 2.1 1.4		6 locations 4 locations 7 locations

Table continues next page

[a] Mean concentrations are plotted in Figure 3.11.

[b] Concentration expressed as $\times 10^{-5}$/m indicates absorbance. (Absorbance values not included in the figure.)

Table A.3. (*Continued*) Data for Elemental Carbon or Black Carbon[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (µg/m³)		Description
				Mean	Maximum	
Urban (*Continued*)						
Fromme et al. 2005 Berlin	56	Thermal oxidation analysis after solvent extraction of OC	7–8 hr	2.8	13.4	Outside apartments
Funasaka et al. 2000 Osaka	8	Thermal oxidation analysis	48–72 hr	4.0		Outside 4 homes 60–150 m from high traffic road in urban district A
	6			7.4		Outside 4 homes 60–150 m from high traffic road in suburb B
	6			4.1		Outside 4 homes 60–150 m from high traffic road in suburb C
Harrison et al. 2004a London	151	Thermal oxidation analysis	24 hr	2.2		4 urban locations
Hies et al. 2000 Berlin	328	Thermal oxidation analysis	24 hr	4.0		Urban residential location
Janssen et al. 1997 Arnhem, the Netherlands	28	Absorbance of $PM_{2.5}$ on filter from reflectometer	8 hr	22.7	45.0	200 m from a busy road in city center
Lena et al. 2002 Bronx, New York	9	Absorbance of $PM_{2.5}$ on filter from reflectometer	10–12 hr	2.6		Outside home in urban residential street

Table continues next page

[a] Mean concentrations are plotted in Figure 3.11.

Table A.3. (*Continued*) Data for Elemental Carbon or Black Carbon[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (μg/m³) Mean	Concentration (μg/m³) Maximum	Description
Urban (*Continued*)						
Riediker et al. 2003 North Carolina	50	Nephelometer	8.3 hr	1.7	3.7	Fixed ambient site collocated with state monitoring site
Smargiassi et al. 2005 Montreal	33	Absorbance of $PM_{2.5}$ on filter from reflectometer	24 hr	1.18[b] ($\times 10^{-5}$/m)	2.95[b] ($\times 10^{-5}$/m)	< 10 m from curb, quiet residential street
	30			1.42[b] ($\times 10^{-5}$/m)	3.34[b] ($\times 10^{-5}$/m)	< 10 m from curb, major residential artery
	35			1.63[b] ($\times 10^{-5}$/m)	3.30[b] ($\times 10^{-5}$/m)	< 10 m from curb, major residential artery
Rural						
Cyrys et al. 2003 the Netherlands	~16	Thermal oxidation analysis	2 wk	1.9		4 locations
Stockholm	~12			1.3		3 locations
Hies et al. 2000 Outside Berlin	352	Thermal oxidation analysis	24 hr	2.4		Outside city center in area affected by long-range transport
	343			2.2		Outside city center in area affected by long-range transport
In Homes or In Schools						
Fischer et al. 2000 Amsterdam	16	Absorbance of $PM_{2.5}$ on filter from reflectometer	24 hr	2.1[b] ($\times 10^{-5}$/m)	3.1[b] ($\times 10^{-5}$/m)	Homes near heavy traffic
	16			1.1[b] ($\times 10^{-5}$/m)	1.8[b] ($\times 10^{-5}$/m)	Homes near low traffic
Fromme et al. 2005 Berlin	60	Thermal analysis	7–8 hr	2.2	4.6	Inside apartments
	73			3.1	8.1	Inside schools

Table continues next page

[a] Mean concentrations are plotted in Figure 3.11.

[b] Concentration expressed as $\times 10^{-5}$/m indicates absorbance. (Absorbance values not included in the figure.)

Table A.3. (*Continued*) Data for Elemental Carbon or Black Carbon[a]

Study / Location	Observations (*N*)	Measurement Method	Average Sampling Time	Concentration (μg/m^3) Mean	Concentration (μg/m^3) Maximum	Description
In Homes or In Schools (*Continued*)						
Funasaka et al. 2000 Osaka	8	Thermal oxidation analysis	48–72 hr	4.6		4 homes 5 m from high traffic road in urban district A
	6			9.2		4 homes 5 m from high traffic road in suburb B
	8			3.6		4 homes 60–150 m from high traffic road in urban district A
	6			6.8		4 homes 60–150 m from high traffic road in suburb B
	6			3.4		4 homes 60–150 m from high traffic road in suburb C
Janssen et al. 2001 the Netherlands	177	Absorbance of $PM_{2.5}$ on filter from reflectometer	8 hr	14.7	35.4	24 schools within 400 m of motorways (mean distance from motorways = 206 m)
Roorda-Knape et al. 1998 the Netherlands (6 areas)	12	Absorbance of PM_{10} on filter from reflectometer	1 wk	10.0	20.8 (maximum site mean)	12 schools 35 to 645 m from motorways
Personal						
van Roosbroeck et al. 2006 Amsterdam	20	Absorbance of $PM_{2.5}$ on filter from reflectometer	48 hr	1.7[b] ($\times 10^{-5}$/m)	2.9[b] ($\times 10^{-5}$/m)	Children living near a busy road
	35			1.2[b] ($\times 10^{-5}$/m)	2.6[b] ($\times 10^{-5}$/m)	Children living in urban background area

[a] Mean concentrations are plotted in Figure 3.11.

[b] Concentration expressed as $\times 10^{-5}$/m indicates absorbance. (Absorbance values not included in the figure.)

REFERENCES

For references cited in this appendix, see the reference list at the end of Chapter 3.

APPENDICES AVAILABLE ON THE WEB

Appendices B and C contain supplemental material not included in the printed report. They are available on the Health Effects Institute (HEI) Web site *http://pubs.healtheffects.org*. They can also be requested by contacting HEI at 101 Federal Street, Suite 500, Boston, MA 02110, +1-617-488-2300, fax +1-488-2335, or e-mail (*pubs@healtheffects.org*). Please include (1) the full title and number of the Special Research Report and (2) the title of the appendix requested.

APPENDIX B. Summary of Studies for Section 3.III.2

APPENDIX C. Bayesian Hierarchical Modeling

ABBREVIATIONS AND OTHER TERMS

BC	black carbon
BS	black smoke
CALINE4	California Line Source Dispersion Model, version 4
CHAD	Consolidated Human Activity Database
CO	carbon monoxide
DPM	diesel-exhaust particulate matter (referred to as DEP in Chapter 5)
EC	elemental carbon
GIS	geographic information system
GPS	global positioning system
IMPROVE	U.S. Interagency Monitoring of Protected Visual Environments network
LIDAR	Light Detection and Ranging
LUR	land-use regression
MISR	Multi-angle Imaging SpectroRadiometer
MMT	methylcyclopentadienyl manganese tricarbonyl
MODIS	Moderate-resolution Imaging Spectroradiometer
NATA	National Air Toxics Assessment
NDVI	Normalized Difference Vegetation Index
NEI	National Emissions Inventory
NO	nitric oxide
NO_2	nitrogen dioxide
NO_x	nitrogen oxides
PB-PAHs	particle-bound polycyclic aromatic hydrocarbons
PM	particulate matter
$PM_{2.5}$	PM with aerodynamic diameter $\leq$ 2.5 μm
PM_{10}	PM with aerodynamic diameter $\leq$ 10 μm
SAVIAH	Small Area Variation in Air pollution and Health
SMOG	Surface Meteorology and Ozone Generation
SO_2	sulfur dioxide
STN	U.S. EPA Speciation Trends Network
TEOM	tapered-element oscillating balance
UFP	ultrafine particles
U.S. EPA	U.S. Environmental Protection Agency
VMT	vehicle miles traveled
VOCs	volatile organic compounds

Chapter 4

Health Effects: Epidemiology of Traffic-Related Air Pollution

CONTENTS

Chapter 4

Health Effects: Epidemiology of Traffic-Related Air Pollution

CONTENTS (*Continued*)

Chapter 4

Health Effects: Epidemiology of Traffic-Related Air Pollution

4.I. INTRODUCTION

This chapter reviews and synthesizes the evidence for the associations of exposure to traffic-related air pollution with adverse human health effects. The review is organized around health outcomes. Generally speaking, it evaluates the epidemiologic evidence for associations between roadway-traffic* exposure and adverse health effects and, where possible, the consistency of the estimated associations across various traffic-exposure measures.

The synthesis is confined to primary emissions from roadway traffic and excludes those from other mobile sources, such as diesel locomotives, construction vehicles, or other off-road vehicles, because the bulk of the epidemiologic data pertain to roadway-traffic emissions. Our goal is to provide a comprehensive summary of studies that met the predetermined inclusion criteria but not to give detailed descriptions and critiques of each. We do include comments on the major strengths and limitations of particular studies.

4.I.1 CRITERIA FOR INCLUSION OF STUDIES FOR REVIEW

As described in Appendix 1 of Chapter 1, the literature searches yielded 275 potentially relevant published studies. These were considered carefully for abstraction by HEI staff. Of these, a total of 107 studies were excluded because they were not in English, were not primary-research publications (such as review articles, editorials, and policy briefs), or lacked emphasis on traffic or evidence about health effects in exposure-assessment studies. This left 168 eligible studies for abstraction. Subsequently, another 36 studies were excluded by this review's primary authors on methodologic grounds, primarily the inadequate or nonspecific estimation of traffic exposure (e.g., self-reporting; reporting of nitrogen dioxide [NO_2†] or particulate-matter [PM] concentrations, for example, without specific documentation of a traffic source; or the absence of exposure estimates on a local scale, such as those found in Air Pollution and Health: A Combined European and North American Approach [APHENA] or the National Morbidity, Mortality, and Air Pollution Study [NMMAPS]). After these exclusions, 137 studies remained. Finally, an additional 30 studies published or accepted for publication between July 2007 and October 2008 were included, providing a total of approximately 170 studies as the basis for this review.

Table 4.1 presents the criteria used for the inclusion of studies in this review based on the characterization of traffic exposure in each study. The relation between these exposure surrogates and the actual exposures of interest — i.e., ambient pollutants derived from emissions from motor vehicles, both fresh and aged — has been discussed at length in Chapter 3. Criteria 1 through 4 are quite specific and could be applied readily and unambiguously. Criterion 5 required some subjective interpretation, in that no single rule could be established to classify a monitoring site as "reasonably related to traffic" in the absence of a concomitant traffic-specific measure. In general, the proximity of the monitoring site(s) to the individuals or population and roadways of interest was often a primary determinant. An example of a study that met criterion 5 was that of Schwartz and colleagues (2005), who studied all subjects living within 1 km of a fixed monitoring site in a city where black carbon derived largely from traffic sources. An example of a study that did not meet criterion 5 was that of Grazuleviciene and colleagues (2004), which used NO_2 concentrations from municipal fixed monitors as a traffic surrogate without providing (1) information on the distances of the monitors from residences, (2) direct or cited evidence to support a specific association with traffic in the study location, or (3) an explicit statement to the effect that other sources (e.g., fuel combustion from power plants or industrial sources) had not contributed to the emissions inventory for NO_2 in the study areas. Studies with measures of traffic exposure based solely on subject self-reporting without other, more direct measures were also excluded.

4.I.2 CRITERIA FOR CAUSAL INFERENCE

An issue of central importance for the review was the establishment of an acceptable set of criteria by which to evaluate the overall quality of the evidence presented in

* Referred to as "traffic" throughout the chapter.

† A list of abbreviations and other terms appears at the end of this chapter.

the various studies for the association between exposure to air pollution from traffic and health outcomes, particularly with respect to whether the associations were causal. Meta-analytic summaries have been used, indirectly, to infer causality — inferences that derived from Hill's "consistency" criterion (Hill 1965) — but although this chapter makes use of forest plots to summarize data, formal meta-analytic summaries have not been provided. The main reason for not using meta-analysis was the lack of equivalence among the exposures and populations studied (see below). The frequent report of heterogeneity in meta-analytic summaries of air-pollution-related health effects (Bell et al. 2004, 2005; U.S. Environmental Protection Agency [U.S. EPA] 2004; Ito et al. 2005; Levy et al. 2005) and the extensive heterogeneity among the findings and populations in the publications reviewed here indicated that the criteria for exposure and population equivalence had not been met, a finding that raises questions about the content validity and interpretation of any meta-analytic summary. Therefore, we relied on a more qualitative summary of the available data. A discussion of issues related to pooling association estimates is presented in Sidebar 4.1.

Table 4.1. Traffic Exposure Metrics Used in the Studies Included in this Review[a]

1. Measures based on distance or length
   Maximum distance to nearest main road or highway
   Distance to street canyons
   Length of main streets within buffer zones around homes or schools
2. Measures of traffic density
   Density on nearest road
   Average density estimated from road networks within buffer zones around homes or schools
   Note of street canyons within buffers
3. Modeling
   Dispersion modeling of traffic exposure
   Other modeling techniques for estimating of traffic exposure (e.g., a land-use regression model)
   Traffic-specific source apportionment
4. Subjects in occupations characterized by exposure to traffic
5. Pollutant surrogates of traffic exposure such as NO_2, CO, EC (or BS); other (e.g., benzene, diesel exhaust, lead, etc.) included as a criterion in the absence of a specific metric, if the monitors or other sources of measurement used to estimate the pollutant-exposure surrogate could reasonably be related to traffic (e.g., roadway-specific monitoring or subjects lived within short distances of fixed monitors)

[a] Studies in which traffic exposure was based on subject self-report, and direct measurements were not included.

Sidebar 4.1. POOLING ASSOCIATION ESTIMATES

Pooling improves precision but accumulates bias; it is of most use when the bias in individual studies is expected to be much lower than the uncertainty in the effect estimates. Pooling of estimates is thus standard practice for randomized trials but is more controversial for observational studies even under ideal circumstances. Even for health-effect estimates based on similar measures of exposure, it is reasonable to assume that there will be substantial heterogeneity in effects for different populations and patterns of exposure, as has in fact been reported for other sets of air-pollution studies (and as discussed in this chapter).

Heterogeneity in and of itself does not exclude the possibility of carrying out a meta-analysis, but it does imply that a single summary of the average effect, as produced by standard fixed or random-effect meta-analysis, would be of limited usefulness. In addition, the estimated health effects in the papers we examined were based on a variety of estimates that cannot be placed on a common scale (e.g., traffic density and proximity to roadways). Meta-analytic approaches exist (Conlon et al. 2006) that rely on the direction of the effects and allow for scale differences, but these approaches are neither standard nor straightforward to apply. The panel considered developing a more sophisticated meta-analysis (see Appendix C in Chapter 3, on Bayesian modeling) that would summarize the variability across studies as well as provide point estimates, but in the end concluded that the number of studies for any given exposure metric was too small to support reliable modeling of the between-study variability.

Our approach to evaluating the evidence is an adaptation of that used in the 2004 U.S. Surgeon General report, *Health Consequences of Smoking*, which based its updated methodology (compared with that of earlier reports) for evaluating the causality of associations on a combination of assessments of study quality and consistency (U.S. Department of Health and Human Services 2004). This approach acknowledged the importance of the combination of theoretic concepts of causality (e.g., the role of counterfactuals) with statistical analysis, inference, and judgment, the latter best represented by Hill's well-known criterion (1965). To this, we have added elements of the coherence criterion proposed by Bates (1992), which is deductive in the sense that it indicates that, if a given set of associations has been observed, then another set of associations should be found that follows directly from the first set. Bates illustrated his concept by analyzing various published papers that had related air pollution to adverse respiratory-health outcomes (see Table 1 in Bates 1992). The Bates coherence criterion has been invoked repeatedly in summaries of air-pollution-related health-effects studies (see, for example, U.S. EPA 2004). The criteria adopted in this chapter to establish the strength of the evidence for causal associations are given in Table 4.2a; they are a modification of those employed in the report of the Veterans and Agent Orange Task Group (Veterans Administration 1991) and the 2004 report of the Surgeon General (U.S. Department of Health and Human Services 2004). Table 4.2a adapts these criteria to reflect the Bates coherence criterion (Bates 1992). The criteria stipulate the quality issues that often temper causal inference in epidemiologic studies.

Four fundamental concepts lie behind these criteria: (1) absence of bias, (2) minimization of the effects of measurement error, (3) minimization of the effects of chance (precision of estimates of exposure associations), and (4) consistency in magnitude and direction of effect estimates. In epidemiologic studies of the health effects of traffic-related air pollution, absence of bias relates primarily to control of individual- and group-level confounding and temporal trends and meteorologic factors; the latter two are particularly important in time-series studies related to acute exposures. Selection bias with respect to subjects who actually participate in studies is of obvious importance but is addressed inconsistently across studies. Measurement errors generally relate to differences between

Table 4.2a. Criteria for Strength of Causal Inference Based on Available Data[a]

A: Sufficient evidence to infer a causal association

The evidence was deemed sufficient to conclude that an association observed between a metric of traffic exposure and a disease (or biomarker of disease) risk was causal, in studies where chance, bias, and confounding could be ruled out with reasonable confidence. For example, if several small studies that are free from bias and confounding show an association that is consistent in magnitude and direction, this may constitute sufficient evidence for an association.

B: Suggestive but not sufficient evidence to infer a causal association

The evidence was deemed suggestive but not sufficient to conclude that an association between a metric of traffic exposure and a specific disease (or biomarker of disease) risk was causal, in studies where chance, bias, and confounding could not be ruled out with reasonable confidence. For example, if at least one high-quality study shows a positive association but the results of other studies of good quality are inconsistent, this may constitute limited/suggestive evidence of an association.

C: Inadequate and insufficient evidence to infer the presence or absence of a causal association

The evidence was deemed inadequate and insufficient when the available studies were of insufficient quality, consistency, or statistical power to conclude whether a causal association was present or absent. For example, if studies fail to control for confounding or have inadequate sample size, this may constitute inadequate and insufficient evidence to determine whether an association exists.

D: Evidence is suggestive of no causal association

The evidence was deemed suggestive of no causal association when there were several adequate studies, covering the full range of human exposure levels, that were consistent in not showing a positive association, at any level of exposure, between exposure to a metric of traffic exposure and a disease outcome. (Of course, a conclusion of "no association" is inevitably limited to the conditions, level of exposure, and length of observation covered by the available studies. In addition, the possibility of a very small elevation in risk at the levels of exposure studied can never be excluded.)

[a] We do not use gradations of "exposure–response" as specific criteria for any component of the table because in virtually all epidemiologic studies it is difficult to infer meaningful exposure–response gradations from the types of exposure metrics used or from the data as presented.

Table 4.2b. Traffic-Specific Criteria for Strength of Inference for a Given Disease

A: Sufficient evidence to infer a causal association

Criterion "A" was met when all studies were of the appropriate quality, at least one study measured traffic density or modeled traffic exposure[a], measures of socioeconomic status were taken into account in distance-only studies, and the studies' results were consistent.

B: Suggestive but not sufficient evidence to infer a causal association

Criterion "B" was met when all the criteria for classification A were met except that only studies that used distance-based metrics were available,

Or when all the criteria for classification A were met except that not all the studies that used distance-only metrics took into account measures of socioeconomic status or the studies took into account measures of socioeconomic status but the results were not consistent.

C: Inadequate and insufficient evidence to infer the presence or absence of a causal association

Criterion "C" was met when the results from studies that used distance-only metrics were not consistent

Or when the results of all studies using distance-only metrics were consistent, but all those studies failed to include measures of socioeconomic status

Or when the results from at least one study based on traffic density or modeled traffic exposure were inconsistent with those from distance-only studies

Or when the number of distance-only studies was too small.

D: Evidence is suggestive of no causal association

Criterion "D" was met when studies were of adequate quality (using distance-only metrics or at least some measures of traffic density or modeled traffic exposure) and were consistent in failing to find an association.

[a] In some cases, this criterion was met when modeling or source-apportionment data were cited to show that a pollution surrogate in the study was reasonably accurate in representing the traffic sources in the study area.

measures of personal exposures to pollution and measures from fixed monitoring sites or modeled ambient concentrations at specific locations or across surfaces used to represent these exposures. Errors in the measurement of other covariates, such as smoking histories or occupational exposures, are rarely if ever considered. Minimization of chance generally relates to sample size. Consistency is taken to mean that the magnitude and direction of the effect estimates (most often measured as odds ratios, relative risks [RRs], or relative hazards* are similar across the different populations (i.e., their population characteristics and geographic locations) and different times, after proper handling of confounding, measurement error, and chance. The assumption of the latter concept is that it would be unlikely that the same confounding factors would be responsible for consistent results across a broad range of study settings (i.e., population, geography, and meteorology) and pollutant mixtures. Lastly, it should be noted that this classification makes a clear distinction between having insufficient evidence to infer the presence or absence of causal relations and having evidence that is suggestive of no causation — the latter would be subject to criterion D in the table.

Table 4.2b reflects the application of an additional traffic-specific coherence criterion to the criteria already presented in Table 4.2a. Not all traffic-exposure measures in Table 4.1 have equivalent validity; traffic density and modeled exposures, for example, are generally considered to be better surrogates, at least in theory, for actual (personal) exposures to pollutants derived from traffic. Simple measures of distance from roads or road length and of pollutant surrogates without specific traffic data are the least specific. Such surrogates, particularly those based on distance measures, are most likely to introduce confounding (evaluated either by way of regression modeling or stratified analysis) by socioeconomic status (O'Neill et al. 2003) and noise, the latter caused by the fact that a non-combustion pollutant source might have contributed to the observed associations (Ising et al. 2004). Exposure estimates based on traffic density or measures of flow would be more specific, particularly if they were combined with a pollutant known to have a high association with traffic in a given location — for example, black carbon (BC) or elemental carbon (EC). A

* Risk differences, despite their importance and relevance to public health and risk assessment, are presented only very rarely.

priori, modeled estimates of exposure to pollution from traffic should be more valid than traffic-density estimates alone because they account for other factors that can impact exposure, such as geography, land use, and meteorology, when making estimates for particular locations. In addition, the validity of estimates can be enhanced by modeling strategies that estimate the contribution of traffic to personal exposure separately from the contributions of regional and background pollution (Janssen et al. 2001). At the same time, however, the uncertainties inherent in modeling may offset any theoretic advantages with respect to traffic-density estimates, insofar as the estimates may be more uncertain because of the model assumptions and the data available to input into the model.

For these reasons, criterion A in Table 4.2b includes a requirement that at least one of the studies showed an association with a specific health outcome using traffic density or exposure modeling to estimate exposures — in addition to all of the components included in the criterion A, in Table 4.2a — in order to ensure that more than one type of study design led to the similar inferences. Criterion B in Table 4.2b acknowledges that studies based on simple distance measures are subject to concerns about unmeasured confounding caused by socioeconomic factors; markers for other exposures; and lifestyle factors, such as noise pollution and stress that might be associated with residential proximity to major roadways and highways. (Criterion B, in Table 4.2a, had already combined the concerns of residual confounding with the consistency criterion.) Criterion C in Table 4.2b is more stringent about precisely what types of studies need to be consistent*; that is to say, inconsistency of findings in studies based on measures of traffic density or exposure modeling carried the most weight in placing the inference into this category. In the application of the criteria in Table 4.2b, issues in Table 4.2a that related to the quality of the epidemiologic studies took precedence over the quality of the traffic measures when it came to the final classification.

4.I.3 SUMMARY ESTIMATES OF EFFECTS

While it may seem straightforward to combine estimates from various studies to arrive at a summary estimate for an association (e.g., through meta-analytic methods) and to assess the studies using the consistency criterion, summarization of this kind is fraught with difficulties. Kundi (2006) has addressed this problem through two concepts related to the unfolding of the causal chain in a disease process in relation to an environmental exposure. Although related to the issues of consistency and coherence, the two concepts discussed by Kundi are tied most closely to issues that go beyond the usual consideration of the consistency or coherence criteria for the purposes of evaluating evidence with respect to causal inference:

1. *Environmental equivalence*: Are the conditions to which the study populations are exposed sufficiently similar, except for traffic exposure? This concept question pertains to all other exposures in the ambient, indoor, and social environments in which exposure to traffic-related pollution occurs and, by implication, the many unmeasurable additive and multiplicative ways in which these, in conjunction with exposure to traffic-related pollution, can lead to the causation of a disease outcome. Qualitative and quantitative differences in traffic exposure undoubtedly exist for two different populations whose exposures are estimated using distance-, traffic-density-, or model-based surrogates of exposure.
2. *Population equivalence*: Are the features of the populations that differ with respect to traffic-related air pollutants sufficiently similar, except for this exposure? This concept pertains to the counterfactual construct for causality (Maldonado and Greenland 2002) and to concepts of what has been called "complete exchangeability" (Greenland and Robins 1986). Simply put, it requires that the underlying propensity to develop a given disease is the same in two or more populations, in the absence of any exposure to traffic-related pollutants or, perhaps more practically, when exposed to identical traffic-related pollutants (qualitatively and quantitatively). It is highly unlikely that complete exchangeability could ever be achieved (Oakes 2004), because it requires the comparability of the multiple determinants of disease risk other than the exposure under investigation. Even partial exchangeability (in which the exposed population would experience the same distribution of outcomes as some other, less exposed population) is not very likely, given the large differences between and within populations over long periods of time (i.e., period and cohort effects within populations); the latter is a particular issue for cohort or repeated cross-sectional studies in a given area.

Meta-analytic summaries that identify heterogeneity across studies provide prima facie evidence that one or both of these theoretic conditions have not been met (under the assumption that the statistical model chosen is properly specified). The implications of such heterogeneity on the validity of summary estimates were illustrated dramatically in a study by Janes and colleagues (2007),

* As used here, "consistent" includes the consistent presence of an association, a consistent range of exposure estimates, and a consistent direction in the association (including associations that are consistently null).

who demonstrated that, in the face of heterogeneity, average point estimates may not be relevant to any one location and that the direction of location-specific associations can be opposite that of the mean estimate (see Figure 1 and 2 in Janes et al. 2007).

The use of RRs (relative-hazard) can add to heterogeneity when derived from models estimating effects that are conditional on fixed measures for other covariates: (1) models from different studies often have different sets of covariates and different definitions for the same covariates (or functional forms), and (2) in the presence of interactions, these estimates cannot be interpreted as population marginal estimates (under the assumption of a properly specified model and of sufficient control of confounding); to obtain a population-level estimate, other approaches are required.* Two RR estimates with the same value from two populations in which interactions have been found (such as an increase in the hazard of death from an interaction between a given pollutant exposure and, say, underlying diabetes) are therefore not likely to have the same quantitative meaning with respect to the marginal influence of the traffic exposure on the two populations. In the face of heterogeneity, differences in definitions of the covariates and traffic measures just add to this problem of interpretation.

These criticisms do not mean that summaries of the effects estimates are not desirable or possible; they might be desirable and even needed for assessments of risk and health impact. What the criticisms do indicate is that, in order to reflect the innumerable uncertainties related to comparisons between studies, summaries should take a more qualitative approach. This latter consideration was an important factor in the adoption of the criteria in Table 4.2a.

In the sections that follow, qualitative and quantitative summaries are provided for the estimates of associations between exposure to primary traffic-generated air pollution and various health outcomes from individual studies.† The results are discussed with respect to the weight of evidence (as noted in the section above on inference) along with comments on specific issues or inconsistencies within studies. Figures are provided showing the distributions of selected estimates of traffic-exposure effects on each health outcome. Associated tables with more complete information can be found at the end of this chapter.

* We note that failure to consider important interaction effects can affect the interpretation of the main effects. For example, there might be no observed "significant" main (marginal effect) of a covariate because the subgroup in which there was a response is a small fraction of the population studied. Investigation of an interaction in this case could reveal such a subgroup.

† Primary traffic-generated pollution refers to pollution emitted directly from the tailpipes of motor vehicles and to its rapidly formed near-source physical and chemical transformation products.

4.II. TRAFFIC EXPOSURE AND MORTALITY‡

The magnitude of impact estimates of the overall health effects of exposure to ambient air pollutants is largely driven by the impacts of mortality in terms of its costs to society. Mortality is considered a "hard" endpoint, with the advantage of being easily measured and almost completely ascertainable at the population level in many developed countries, primarily as a result of the high degree of completeness of mortality data over extended periods of time in these countries. It is therefore not surprising that the assessment of the health effects of exposure to traffic-related pollution rightfully begins with its impact on mortality.

4.II.1 ALL-CAUSE MORTALITY

Although studies of all-cause mortality lack specificity with respect to possible mechanisms and physiologic systems through which exposure to traffic-related pollutants affect health, consideration of all-cause mortality has its appeal because of the large numbers of data that can be amassed.

4.II.1.A Long-Term Exposure

Figure 4.1 shows some of the RR estimates of all-cause mortality for studies based on long-term exposures that met our selection criteria (see also Table 4.3, at the end of the chapter). All of the studies considered multiple individual-level confounders (such as age, sex, smoking, underlying medical conditions, and socioeconomic status [SES]), although not all included the same set. All studies included age and sex (the latter where relevant); but Finkelstein and colleagues (2004) did not include smoking and Hoek and colleagues (2002) did not include underlying medical conditions. The Lipfert studies (2006a,b) included only indirect measures of SES based on ZIP code level variables on racial distribution and income on the assumption that, overall, veterans all had the same SES. Smoking was often treated as a confounder; although it might be an empirical confounder (residence near major roads, for example, is often associated with lower SES, which is in turn associated with increased smoking prevalence), it also is likely to be an effect modifier. The same can be said for underlying medical conditions (which might also be on the causal pathway, in some cases), as evidenced by a number of studies that have evaluated factors such as diabetes (Bateson and Schwartz 2004), underlying chronic pulmonary disease (Zeka et al. 2006), and cardiac disease (Bateson and Schwartz 2004) in studies of mortality related to air pollution. The extent to which the omission of such

‡ In this section, *mortality* refers to premature mortality (i.e., the advancement of the time of death by days or years) rather than to absolute increase in mortality.

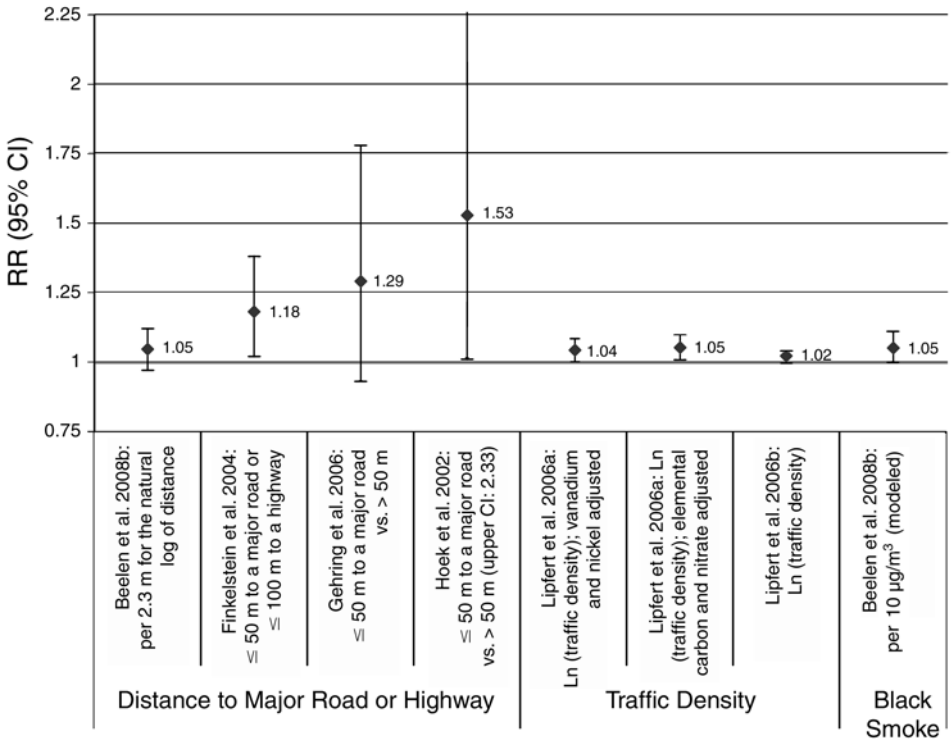

Figure 4.1. Studies of long-term exposure to traffic pollution and all-cause mortality (by exposure metric). See Table 4.3 for data. Vertical lines indicate 95% confidence intervals.

potential modifiers biased the effect estimates reported cannot be determined without data on the distribution of the modifiers. Several issues are not evident in Figure 4.1. First, the population sources in the studies are very different. For example, Finkelstein and colleagues (2004) included subjects from a referral clinic in Ontario, Canada, and Gehring and colleagues (2006) included only women, who were generally younger than participants in the other studies. Lipfert and colleagues (2006a,b) included only men. Differences in the epochs of follow-up and therefore the actual cohort experiences of the study samples mean that there were likely differences in terms of past pollutant exposures, survivor bias, and other lifetime exposures embodied in the covariate adjustments. These issues apply to data for all of the disease categories reviewed later in this section but are not referred to in every case.

Two of the studies provided additional estimates that are of interest. Finkelstein and colleagues (2004) estimated the rate-advancement period* in order to calculate additional deaths per year. The estimated rate-advancement period for all-cause mortality for a residence within 50 m of a major urban roadway or 100 m from highways was 2.5 years (95% CI, 0.2–4.8), compared with 3.1 years (95% CI, 0.5–5.4) for a diagnosis of chronic ischemic heart disease. Based on interpolation in the Ontario life tables, the rate-advancement period for the traffic measure translated to estimated rates of additional deaths per year ranging from 0.4 per 1000 for persons 40 years old to 10.9 per 1000 for persons 70 years old. The estimate of the all-natural-cause mortality risk associated with residential exposure to traffic (defined as living near a major road) was 1.18 (95% CI, 1.02–1.38) (see Figure 4.1).

Hoek and colleagues (2002) estimated a RR of 2.38 for total deaths (95% CI, 1.58–3.57) for a smoker of 25 pack-years who lived within 100 m of a freeway or 50 m from a major urban road compared with a similar smoker who lived outside the buffer. The comparable estimate for those who never smoked was 1.41 (95% CI, 0.94–2.11), an observation that provides evidence that smoking was an effect modifier in this study of subjects 55 to 69 years old at intake. The study was based on a sample of 4492 subjects from the Netherlands Cohort Study on Diet and Cancer (NLCS). A more recent publication that used data from the 10-year follow-up of the full NLCS cohort (120,852 subjects) reported

* The rate-advancement period is an estimate of how much older a reference population would have to be to experience the same "attrition rate" as subjects who reside within a given road buffer. The rate-advancement period is derived from a linear model of the form log(hazard) = ($b_1 \times$ exposure) + ($b_2 \times$ age) + covariates, where b_1 and b_2 represent the change in hazard associated with one unit change in the exposure or the age variables. From this model, a point estimate of the rate-advancement period is b_1/b_2 per unit increase in exposure (see Brenner et al. 1993).

estimates of all-natural-cause mortality associated with living near a major road of 1.05 (95% CI, 0.97–1.12) (Beelen et al. 2008b), much lower than those reported by Hoek and colleagues (2002). However, statistically significant associations were observed for NO_2 (1.08; 95% CI, 1.00–1.16) and black smoke (BS) (measured as light absorbance of PM on filters)* (1.05; 95% CI, 1.00–1.11). The analysis also considered cigarette smoking as well as measures of socioeconomic status and included a large number of such individual-level covariates as educational status, occupational history, and diet. Exposure was based on a background-exposure variable plus a local traffic variable from a detailed traffic model (including vehicles/24 hr, proximity to roadways with 10,000 vehicles/day, distances of 50 and 100 m from major roads and BS and NO_2 measurements near these roads). The investigators also estimated total NO_2 and BS from background and local traffic combined.

The two studies by Lipfert and colleagues (2006a,b) were based on the Washington University–EPRI Veterans' Cohort Mortality Study that was established in the mid-1970s and continued through 2001. Both studies included only men and assessed the effects of county-level traffic density per unit area, defined as the difference between the mean density estimate for all counties and an arbitrary minimum density. In the first study (Lipfert et al. 2006a), correlations of traffic density and long-term mortality were compared with those determined using metals in PM with an aerodynamic diameter $\leq$ 2.5 μm ($PM_{2.5}$) and gaseous pollutants in single- and multi-pollutant models. One model combined the sum of markers of combustion (SO_4^{2-}, NO_3^-, C_{total}, and EC). In virtually all cases in which traffic density per unit area was included with combustion-related metals (vanadium and nickel) and the combustion index, the traffic-density measure was significantly associated with mortality. Three examples chosen from the large number of estimates in the paper are given in Figure 4.1. The second study (Lipfert et al. 2006b) considered the effects of population and housing density to determine the extent to which estimated associations with traffic were attenuated. Estimates of traffic associations were robust to control for these factors (see Table 4.3).

A study reviewed but not included in Table 4.3 is that by Jerrett and colleagues (2005), which provided only an indirect and somewhat incomplete assessment of traffic exposure (it only considered residences within either 500 or 1000 m of a freeway) for members of the American Cancer Society's Cancer Prevention Study II population who lived in Los Angeles, Calif. The study also considered exposures to $PM_{2.5}$, which were assessed based on a smooth $PM_{2.5}$ surface. The association of $PM_{2.5}$ with mortality (after correcting for 44 individual covariates and 11 census variables) did not change when the freeway-distance indicator was included in the model. There are several possible, but unresolved, explanations other than there being in fact no effect: (1) inaccurate exposure assignments, (2) lack of traffic data, and (3) model overfitting with covariates that are highly associated with traffic exposure. Because of these potential unresolved issues, the inferential value of this study is limited with respect to effects on mortality related to exposure to traffic pollutants; the study is therefore not shown in Figure 4.1.

Based on the criteria in Tables 4.2a and b, these studies were considered to provide "suggestive but not sufficient evidence to infer a causal association" between mortality and long-term exposure to traffic-related air pollutants, largely because of the paucity of studies that met our criteria for inclusion in the review. While the study by Hoek and colleagues (2002) and, secondarily, the studies by Lipfert and colleagues (2006a,b) provided the strongest support for inferring a causal association, based on the quality of their exposure assessments, these studies have their limitations. Hoek and colleagues also reported associations of mortality with other measures of traffic-related pollution, such as BC; but did not fully separate out the local component from the background. The associations with all traffic-exposure measures in their study were larger than in the follow-up study of the full cohort by Beelen and colleagues (2008b). The studies (2006a,b) by Lipfert and colleagues estimated traffic density (density per unit area) at the county level, which, although nominally unbiased, might not have provided adequate spatial representation of the subjects' locations and potential exposure. Consequently the findings were limited with respect to causal inference, because near-road exposure to BC is a local-source exposure that needs to be differentiated from exposure to background sources. All three studies tried to separate a traffic-component association from a more general ambient component, although with different techniques.

Finally, it is evident from the substantial differences in populations, time periods, and somewhat different sets of confounders and modifiers considered that it is difficult to provide a composite estimate of association from these studies. Moreover, we note that findings from the Gehring study (2006), which was based solely on a sample of women, cannot be used to suggest that women might be at greater mortality risk from exposure than are men.

* The measurement of light absorbance of suspended PM or PM deposited on filters has been used in many of the studies cited in this chapters as a measure of combustion soot and a surrogate of traffic-related pollution (as discussed in chapter 3). The absorbance measure has been referred to as soot, black carbon (BC), black smoke (BS), or PM absorbance. These terms will be used as reported in each study.

4.II.1.B Short-Term Exposure

Only four time-series studies (Laden et al. 2000; Roemer and van Wijnen 2001; Ito et al. 2006; and Maynard et al. 2007; not presented in a table) met our criteria. Qualitatively and quantitatively, the findings of these studies were somewhat unclear with respect to associations between short-term exposure to pollutants derived from traffic emissions and all-cause mortality. Although all of them used acceptable methods to control for meteorologic factors and time trends, the complexities of the studies were such that any single summary estimate from each could in fact be misleading, as would a combined estimate from all of the studies. In addition to problems of different time periods, there were differences in the studies' populations and exposure environments.

Using data from the Harvard Six Cities Study from 1979 to 1988, Laden and colleagues (2000) reported a summary estimate of 3.4% (95% CI, 1.7%–5.2%) for the percentage increase in daily deaths associated with a 2-day mean 10-μg/m^3 increase in concentrations of a mobile-source factor (using lead as the marker), based on standardized daily factor scores (Figure 4.2). The mobile-source factor was determined by apportioning selected tracer elements to known sources and consisted predominantly of lead, which was still present in gasoline at the time. However, the degree to which lead loaded on the mobile-source factor and to the total $PM_{2.5}$ mass in each of the six cities did not track very closely with the percentage increases in mortality. It is thus difficult to be sure just how accurate the source allocations in each city were and the proper weights to assign to the mobile-source-related exposures in relation to deaths in each city.

A study by Ito and colleagues (2006) of deaths in the Washington, D.C., area from 1988 to 1997, also based on source-apportioned exposures, is equally problematic. The data on PM composition used for source apportionment were obtained from the Interagency Monitoring of Protected Visual Environments (IMPROVE) network and included trace metals, sulfate, nitrate, ammonium, elemental carbon, and organic carbon. The data were collected only on Wednesdays and Saturdays, which means that the lag days studied (0 to 4 days) were fixed days of the week and not the full set of lags, a situation that the authors acknowledged likely biased their results. Equally important, when nine different approaches to source apportionment were applied to the data, no consistent pattern emerged over the 0-to-4-day lags (see Figure 3 in Ito et al. 2006); the median correlation between methods was ~0.45, with a range of 0.00 to 0.90 (Hopke et al. 2006) as discussed in Chapter 2, section 2.VIII and Chapter 3, section 3.IV.8.

In contrast to the Laden and Ito studies, in which exposure estimates were based on data from central monitors, the two other studies that met our criteria for inclusion were based on estimates of exposure at the residence level and thus provided a greater degree of exposure specificity. Roemer and van Wijnen (2001) obtained data from a sample of Amsterdam residents (N = 4352) who lived "along roads with more than 10,000 motorized vehicles per day" (actual distance from the roads not specified) from 1987 to 1998. Ambient-pollutant data from "traffic-influenced" sites and "non-influenced" sites (criteria not specified)

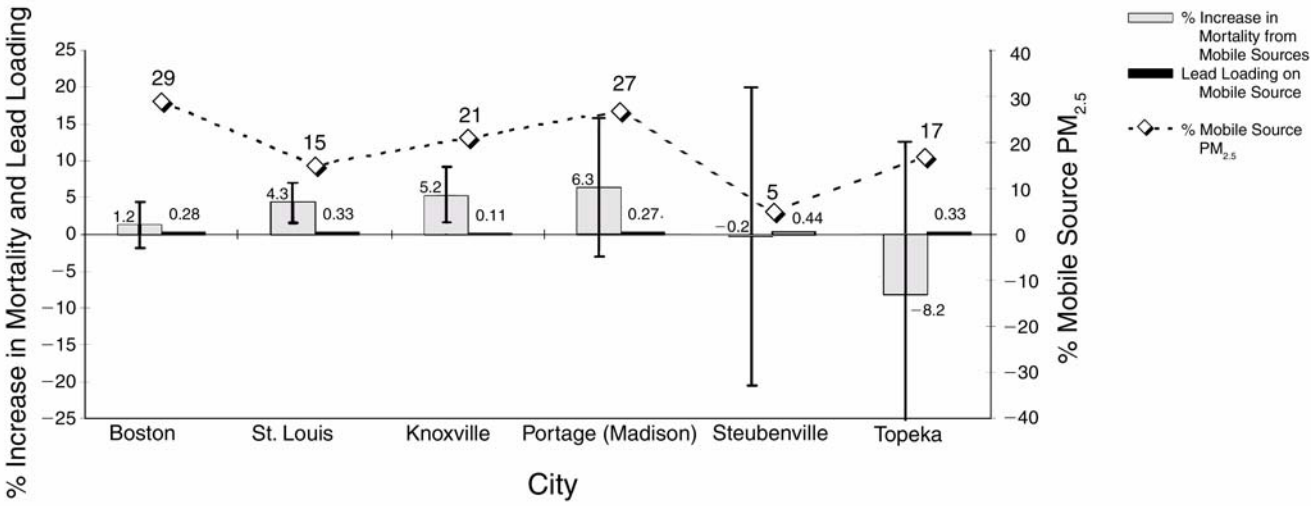

Figure 4.2. Percent increase in all-cause mortality, lead loading, and mobile-source contribution to $PM_{2.5}$ in each of the cities in the Harvard Six Cities Studies. Increase in mortality is expressed as percent increase (with 95% confidence interval) associated with a 10-μg/m^3 increase in $PM_{2.5}$ from the mobile-source factor and lead loading on mobile source. The percent contribution of $PM_{2.5}$ from the mobile source to total $PM_{2.5}$ is also shown. Vertical lines indicate 95% confidence intervals. (Figure based on data from Laden et al. 2000.)

were obtained for BS, PM with aerodynamic diameter ≤ 10 µm (PM_{10}), and gaseous pollutants (CO, NO_2, SO_2, and O_3). Background sites were used to estimate "background" exposure to BS.

Table 4.4 (at the end of the chapter; adapted from Table 3 in Roemer and van Wijnen 2001) demonstrates the difficulty of selecting a single estimate to summarize the data from this study. For each of the BS lags, there is an overlap between the mortality estimates based on background-related versus traffic-related pollutant concentrations and the population chosen (i.e., the total population versus the population living along the busy roads). Moreover, the 100-µg/m^3 increments of BS used to calculate the RR estimates is greater than the range of the entire BC distribution. In addition, there was a suggestion of overall seasonal heterogeneity in the association of background BC with mortality: summer and winter, lag day 1, were 1.64 (95% CI, 1.08–2.49) and 1.31 (95% CI, 1.07–1.610), respectively; a clear explanation is not provided for this finding. NO_2 from the background site, lag day 1, was the only other pollutant associated with mortality.

A case–crossover study by Maynard and colleagues (2007) provided stronger support for the existence of an association between exposure to traffic pollutants and all-cause mortality. The study employed a spatial–temporal land-use regression model to map BC concentrations to residential locations of out-of-hospital deaths in the Boston, Mass., metropolitan area, based on death certificates from the Massachusetts Department of Health. The variables included in the model were day of the week, meteorologic data (temperature and relative humidity), traffic density within 100 m of the homes, latitude and longitude, and BC measurements at a stationary monitoring site. The cross-validated R^2 between the modeled BC concentrations and the daily BC measurements taken outside residential locations was 0.36, compared with 0.09 when concentrations from the central site monitor were used for the comparison with the measured concentrations. An interquartile-range (IQR) increment of modeled BC (0.757 µg/m^3) was associated with a 2.3% increase (95% CI, 1.2%–3.4%) in all-cause mortality (N = 107,925 deaths from 1995 to 2002). An analysis of cardiovascular death in the same population showed that despite a sample size of 33,785 deaths, there was only weak evidence for an association between BC and cardiovascular deaths (1.5%; 95% CI, –0.4% to 3.4%) (see section 4.II.2.B). Multiple causes of death were not considered.

In summary, although it appears that time-series studies do support associations between various surrogates of traffic exposure and all-cause mortality, the evidence, based largely on the Maynard study, was at best only "suggestive but not sufficient to infer a causal relation." Bias and confounding were handled reasonably well in all of the studies. However, the two studies with formal source apportionment were problematic, either in terms of the quality of the source apportionment (Laden et al. 2000) or the structure of the data and lack of robustness to alternative methods of source apportionment (Ito et al. 2006). Moreover, these two studies used exposure estimates based on area-wide monitors that might have failed to adequately capture spatial heterogeneity related to traffic exposures. Our "suggestive" designation, then, is based largely on the Maynard study, which provided a reasonable level of spatial specificity in an area where sources of BC other than traffic were not large (Schwartz et al. 2005). Moreover, when background concentrations of sulfate (a surrogate of transported PM) were included in the analyses, the BC associations remained, and the sulfate associations were not significant (Maynard et al. 2007). In general, although BC is a reasonable marker for traffic-related emissions, the source-apportionment data from Laden and colleagues (2000) and Ito and colleagues (2006) make it clear that considerable uncertainty is attached to risk estimates based on any single surrogate.

4.II.2. MORTALITY FROM CARDIOVASCULAR DISEASE

Cardiovascular-disease outcomes are the most consistently cited adverse human health effects associated with exposure to ambient pollutants (Brook et al. 2004). We used the causal inference paradigm based on the coherence criterion established by Bates (1992) to set the order for evaluation — in other words, we evaluated, in order, mortality, morbidity, and the physiologic factors thought to place individuals at risk for increased cardiovascular morbidity and mortality. A number of studies grouped cardiac and pulmonary deaths into a single "cardiopulmonary" category. We included these deaths in the discussion, although in many cases it was not possible to separate the unique contribution of cardiovascular disease.

4.II.2.A Long-Term Exposure

Most of the mortality estimates for cardiovascular disease were derived from studies considered in the earlier section on all-cause mortality and summarized in section 4.II.1.A. Their results are shown in Figure 4.3 below and summarized in Table 4.5 (at the end of the chapter). The study by Finkelstein and colleagues (2005) used the same population for its analysis of all-cause mortality as was used in their earlier study (Finkelstein et al. 2004) but included a social deprivation index (DI) (derived from census data on income, unemployment rate, and the percentage of residents who were not high school graduates). Although not statistically different, the cumulative hazard

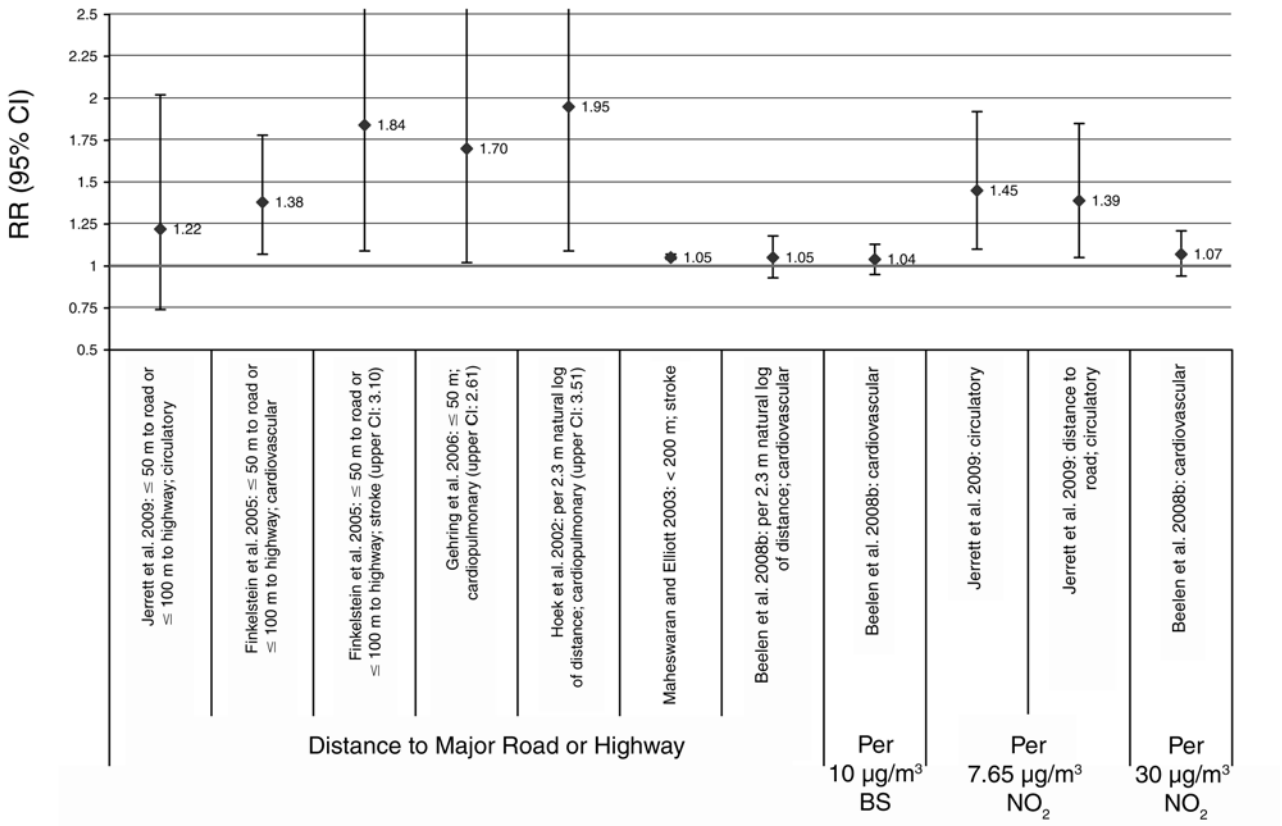

Figure 4.3. Studies of long-term exposure to traffic pollution and cardiovascular and cardiopulmonary mortality (by exposure metric). See Table 4.5 for data. Vertical lines indicate 95% confidence intervals.

curve for those who were exposed to traffic-related pollution (home within 100 m of a highway or 50 m of a major road) and whose DI was less than the median diverged markedly from the findings for the other three groups (who had a DI below the median and were not exposed to traffic pollution or had a DI above the median and were either exposed or not exposed to traffic pollution). In fact, most of the association appears to be among those with a lower DI.

Gehring and colleagues (2006) evaluated total and cause-specific mortality in a cohort of German women. Traffic exposure was defined as living within 50 m of a major road and based on NO_2 and PM_{10} concentrations estimated at the home address from air-monitoring-station data. Many confounding variables were considered, including risk factors for cardiopulmonary mortality (asthma and hypertension). Cardiopulmonary mortality was associated with living close to major roads and also with long-term exposure to NO_2 and PM_{10}.

A study by Jerrett and colleagues (2005), described earlier in more detail, found that cardiopulmonary death was associated with increased exposure to $PM_{2.5}$ concentrations. Chronic exposure to $PM_{2.5}$ was more strongly associated with ischemic heart disease than with either all-cause or cardiopulmonary mortality. As discussed earlier, the mortality results from this study have limited inferential value because of inaccurate exposure assignments, lack of traffic data, and model overfitting with covariates that are highly associated with traffic exposure. This study is not shown in Figure 4.3.

An ecologic study by Maheswaran and Elliott (2003) evaluated stroke incidence in census enumeration districts in England and Wales. Traffic exposure was based on the shortest distance between the centroid of each enumeration district and "main" roads (traffic volumes not provided). The only individual-level data were age and sex; ecologic variables included income, urbanization, deprivation index, and region. Although little difference was found in the rate ratios for the various categories of distance of residences to the nearest main road (up to 1000 m), a comparison of the highest and lowest quintiles of the deprivation index showed that those less than 75 years old had a high risk of stroke compared with older subjects. However, no interactions between SES and traffic exposure were reported. The authors pointed out that they could not

exclude noise from traffic as a contributing factor to the apparent increased RR associated with proximity to a roadway.

Two very recent studies have added to the evidence base. The Dutch NLCS cohort provided data from a case–cohort and full-cohort analysis of cardiopulmonary mortality (Beelen et al. 2008b). Results on a subset of this cohort were reported by Hoek and colleagues (2002). The full-cohort analysis considered a limited number of covariates (cigarette smoking and SES); the case–cohort analysis also considered a large number of such individual-level covariates as educational status, occupational history, and diet. Exposure was based on a background-exposure variable and a local variable from a detailed traffic model (vehicles/24 hr, proximity to roadways with 10,000 vehicles/day, distances of 50 m to a major road and 100 m to a motorway, and BS and NO_2 measurements near the roads). The investigators also estimated total NO_2 and BS from background and traffic-related sources combined (Beelen et al. 2008b). Across all disease categories, RR estimates based on the full cohort were greater than 1.00. However, with one exception (respiratory mortality and traffic intensity in a 100-m buffer), all the estimates included 1.00 in the 95% CIs. For the case–cohort analysis, many of the RR estimates for these pollutants were < 1.00 for cardiovascular mortality. BS and NO_2 were associated with increased respiratory mortality, but the lower-bound 95% CIs were < 1.00 (see Figure 4.3 and Table 4.5). Beelen and colleagues extended their full-cohort analysis to investigate the effect of confounding by noise on their estimates of traffic-related associations (Beelen et al. 2008a). Traffic noise was evaluated with a validated model that included traffic intensities on the nearest roadway, distance to roads, land use, and location of noise barriers. Estimated RRs for all cardiovascular-mortality groups and noise in regressions adjusted only for age, sex, smoking, and SES* were very similar to those that included traffic intensity and noise (four categories). Traffic noise above 65 dB(A) alone was associated with overall cardiovascular mortality (RR = 1.25; 95% CI, 1.01–1.53) and heart-failure mortality (RR = 1.99; 95% CI, 1.05–3.79) (Beelen et al. 2008a), which suggested that high levels of noise could be a confounder in analyses in some studies (although, in the Beelen analysis, it was not).

Jerrett and colleagues (2009) studied 2360 patients recruited from a pulmonary clinic in a hospital in Toronto. Traffic-exposure estimates were based on a land-use regression model that predicted NO_2 concentrations based on a dense network of passive NO_2 samplers deployed to capture the variability of concentrations (R^2 = ~ 0.7). However, the contribution of traffic variables per se in the model was not given. Covariates included smoking history and a social deprivation index. An IQR increase in NO_2 (~4 ppb or 7.5 μg/m^3) was associated significantly with an increase in the relative hazard of mortality from circulatory disease (Table 4.5), and the NO_2 exposure appeared to have a greater association than a distance-to-roadway measure.

With respect to the causal criteria in Table 4.2a, the issues here are similar to those raised for all-cause mortality and long-term exposure. Given the concerns raised above with respect to the parsing of the local component of BS in the Hoek and colleagues study (2002) and to the data from the two newest studies (Beelen et al. 2008b; Jerrett et al. 2009), a classification of "suggestive but not sufficient evidence to infer a causal relation" seems to be the most reasonable for the category of mortality from cardiovascular disease as a whole. There were too few studies to classify specific categories, such as cardiac, circulatory, and cerebrovascular (including various types of cerebrovascular events), separately.

4.II.2.B Short-Term Exposure

Only two time-series studies provided data on cardiovascular mortality (Ito et al. 2006 and Maynard et al. 2007; not included in Figure 4.3 and Table 4.5). The data from the study by Ito and colleagues (2006) had all of the problems and lack of consistency noted earlier in connection with the studies of all-cause mortality. In fact, the lag effects were even less consistent among the nine source-apportionment approaches than for the all-cause-mortality studies (compare Figures 3 and 4 in Ito et al. 2006). The case–crossover study by Maynard and colleagues (2007) discussed earlier also provided cause-specific mortality data. The study made use of data on 33,785 cardiovascular deaths in the metropolitan Boston area over the period from 1995 to 2002. The percentage increase in cardiovascular disease mortality for an IQR increment in BC (0.8 μg/m^3) was 1.5 (95% CI, −0.4 to 3.4). The percentage increase in mortality due to stroke (a smaller number of N = 6070) for an IQR increment in BC was 4.4 (95% CI, −0.2 to 9.3). Thus, despite the strength of this study, there were insufficient data to make any statement with respect to the magnitude of associations between daily exposure to traffic-related air pollution and cardiovascular and cerebrovascular mortality — and certainly too few data to infer causality.

* These results do not appear in Table 4.3 or Figure 4.1 because there were no differences from those shown. Similar results were obtained when traffic noise was used as a continuous variable and for a variety of sensitivity analyses.

4.II.3 SUMMARY OF MORTALITY FINDINGS

Qualitatively, exposure to traffic-related ambient air pollutants is associated with an increase in all-cause and cardiovascular mortality. Despite some limitations, namely (1) that no one study addressed all relevant confounders and (2) that smoking was often treated as a confounder without evaluation as an effect modifier, the evidence from long-term-exposure studies provided "suggestive but not sufficient evidence to infer a causal relation" between long-term exposure to traffic-related air pollutants and mortality. The time-series and case–crossover studies addressed confounding by time and meteorologic factors; however, the small number of these studies did not provide as clear a picture of mortality effects of traffic-related exposure as did the studies of long-term exposure. The findings of these studies therefore led us to classify the evidence as "suggestive but not sufficient" to infer a causal relation.

Despite the conclusions offered above, several factors moderated our confidence that exposure to traffic-related air pollutants leads to premature mortality among exposed populations: (1) the heterogeneity of the populations studied; (2) the heterogeneity of the time periods studied, along with the attendant differences in the contributions of other pollutant sources to the exposure mixture; (3) the considerable uncertainty about the accuracy of the estimated traffic contribution to source-apportioned data; (4) the reliance on BC or BS as the sole marker for traffic in some of the studies; and (5) the limitations in the source-apportionment methods applied in other studies because of the difficulty of distinguishing the effects of sources that produced particles of similar chemical composition (especially when applied to measurements taken from a central site).

4.III. TRAFFIC EXPOSURE AND CARDIOVASCULAR MORBIDITY

As will be discussed in more detail in chapter 5, the consideration of possible cardiovascular effects of exposure to traffic-related air pollution has included both acute cardiac or vascular events and physiologic changes in the cardiovascular system. The studies that examined the associations of exposure to traffic-related pollution with these outcomes are summarized below.

4.III.1 PHYSIOLOGIC CHANGES

Alteration of cardiac physiologic responses consequent to exposure to traffic-related pollutants should in theory provide compelling evidence for a potential causal association between such exposures and adverse cardiac-health outcomes, conditional on adequate exposure assessment. Exposure to traffic-related pollutants has been associated with changes in cardiac function (measured by electrocardiogram), such as heart rate variability (HRV) and changes in ST-segment depression. HRV is a measure of the heart's beat-to-beat variability. As reported in Chapter 5, reduced HRV is associated with heart disease and is predictive of adverse cardiovascular events in patients with heart disease. However, the significance of transient changes in response to air-pollution exposure has not been established. HRV is assessed during controlled resting periods. Measures of HRV include high-frequency power (0.15–0.40 Hz), low-frequency power (0.04–0.15 Hz), and the low-frequency/high-frequency power ratio (LF/HF); the standard deviation of normal-to-normal sinus beat intervals (referred to as R-R interval)(SDNN); the root mean square of successive differences in normal-to-normal intervals (rMSSD); and the percentage of successive normal R-R-interval differences greater than 50 msec (PNN50) (Riediker et al. 2004a). Exercise-induced ST-segment depression is measured at 63 msec after J-point in the electrocardiogram and is considered to be an indicator of myocardial ischemia (Lanki et al. 2006).

Markers of inflammation have been associated with increased risk of cardiovascular morbidity and mortality along with alterations in HRV, which is primarily under the control of the parasympathetic nervous system (Jialal and Devaraj 2003; Brook et al. 2004).

Studies that measured these endpoints are difficult to summarize because of the wide variation in the subjects studied, endpoints, and units of exposure. Three studies evaluated cardiac changes in subjects who lived within short distances of fixed monitoring sites, data from which were used to generate surrogate measures of traffic-related pollutants exposures (see Table 4.6, at the end of the chapter) (Gold et al. 2005; Schwartz et al. 2005; Lanki et al. 2006). All of these studies involved subjects older than age 50, many with underlying cardiovascular disease. All three studies used standardized protocols, of which only one was based on exercise (Lanki et al. 2006). All controlled for meteorologic factors, smoking, and other factors using generally accepted statistical methods.

The study by Lanki and colleagues (2006) used source apportionment based on principal-components analyses to estimate source-specific $PM_{2.5}$ concentrations. They identified five major sources: a traffic source, a long-range transport source, and three other sources. Filter absorbance (BC), which was used as the indicator of traffic, was less correlated with the long-range transport than with the traffic source (0.46 compared with 0.74). The long-range transport

source showed smaller odds ratios (ORs) than the traffic source for the occurrence of ST-segment depression (generally attributed to transient cardiac ischemia) at lags of 1 day (OR = 1.00; 95% CI, 0.92–1.08 for long-range transport compared with OR = 1.22; 95% CI, 0.88–1.69 for traffic) and 2 days (OR = 1.11; 95% CI, 1.02–1.20 for long-range transport compared with OR = 1.53; 95% CI, 1.19–1.97 for traffic).The other two studies (Gold et al. 2005; Schwartz et al. 2005) also used BC as the primary traffic-exposure surrogate but used different exposure periods and outcomes than the study by Lanki and colleagues. Both studies showed adverse effects (ST-segment depression and reduced HRV, respectively) associated with BC. In the study by Schwartz and colleagues (2005), there was a suggestion that 12-hour exposures to BC concentrations had larger effects than 1-hour exposures, although the precision of the estimates precludes a more definitive statement. In the study by Gold and colleagues (2005), somewhat surprisingly, the associations with ST-segment depression during walking were not different from those when at rest. This, however, could have been caused by a relatively slow pace of walking in a group of largely older women (75% of the total group), who had a median age of 73 years.

A study by Adar and colleagues (2007) used a novel study design in which elderly subjects took standardized bus trips in groups, with a monitoring cart following the subjects. Concentrations of $PM_{2.5}$ and BC were measured continuously for 24 hours (starting before the trip). Analyses controlled for a wide variety of confounders, but the authors did not mention anything about possible confounding effects of the stress and noise related to the bus trips themselves compared with the quiet activities between the two trips (out and back) on a given day. A decrease in HRV was associated with increases in $PM_{2.5}$ and in BC. The effect for SDNN at a 5-minute lag on the bus was much larger than when off the bus for both pollutants. Results for the low-frequency/high-frequency power ratio were no different for on- and off-bus 5-minute lags for $PM_{2.5}$ but were highly significant for BC. The reason for the disparity was not clear from the data. How much could have been caused by, for example, differences in the measurement errors for the two pollutants was not discussed in the paper. Although the results are impressive with respect to exposure effects, the author's inability to separate out the effects of stress and noise related to the bus trip leaves open the possibility of some residual confounding of the estimates.

Two studies by Riediker and colleagues (2004a,b) were based on nine nonsmoking highway patrolmen, ages 23 to 30, who were exposed inside their vehicles to traffic-related pollution during 9-hour work shifts in North Carolina in the autumn of 2001. Both studies controlled for the potential influence of stress and used mixed linear models with random intercepts. One study focused on changes in HRV and vascular parameters in relation to in-vehicle monitoring of $PM_{2.5}$ over four consecutive days (Riediker et al. 2004a). The cardiovascular measures were taken during and after 9-hour work shifts. The data for SDNN, PNN50, and the low-frequency/high-frequency power ratio showed increases the morning after, but not immediately after, a work shift. There also were significant increases in premature ventricular contractions. Of note, C-reactive protein (a marker of vascular inflammation) increased as well, along with blood neutrophils. Effects were more consistent for estimates based on $PM_{2.5}$ derived from real-time light-scattering measurements than from gravimetric mass measurements. The authors noted that the findings of increased HRV suggested increased vagal activity and contrasted with other published findings cited in this chapter (as well as findings on air pollution not cited here), possibly because the authors had used younger and healthier subjects (see Chapter 5); the pathophysiologic relevance of the authors' findings is not known.

The second study by Riediker and colleagues (2004b) was based on a source apportionment from filter samples of in-vehicle $PM_{2.5}$. Of the four factors identified (see Table 4.6), HRV variables were significantly associated only with the "speed-changing traffic" factor (associated with aldehydes, sulfur, and copper), thought to be related to both brake-wear and gasoline-combustion products.* One analysis included von Willebrand factor and blood urea nitrogen as confounders, both associated with speed change. Because the authors demonstrated that exposure and the speed-change factor led to increases in these variables, their inclusion as confounders was probably inappropriate, because the factors were likely causal intermediates. This hypothesis is supported by the finding that, when the factors were included in the model, the association of the speed-change factor with HRV variables became attenuated and was no longer significant.

Overall, the studies discussed above provided evidence for a causal association between exposure to traffic-related pollutants and the dysregulation of autonomic control of HRV, an important marker of cardiac physiology. In general, the potential cofounders were addressed, although effect modification was not evaluated in the most important study where it could have been (i.e., Adar et al. 2007). This study based on pseudo-personal monitoring could

* Results for source factors, except speed-changing traffic, are only presented graphically, without exact numbers in the original text.

have been confounded by the effects of stress and noise in the buses, a problem that somewhat compromises the interpretation of the strength of the traffic-pollutant association in the study. Based on the criteria in Table 4.2a, we conclude that these studies meet the criteria for providing "suggestive but not sufficient evidence to infer a causal relation." Clearly, more studies in real-world settings are needed that control for these factors if a claim of "sufficient evidence" is to be made with any confidence.

4.III.2 HOSPITALIZATION AND OTHER MEASURES OF MORBIDITY

Four studies have evaluated the association between traffic-related air pollution and acute myocardial infarction, including survival, hospitalization, or a measure of coronary heart disease. They are shown in Figure 4.4 and in Table 4.7 (at the end of the chapter). It is difficult to compare the effect estimates because of the different outcomes measured.

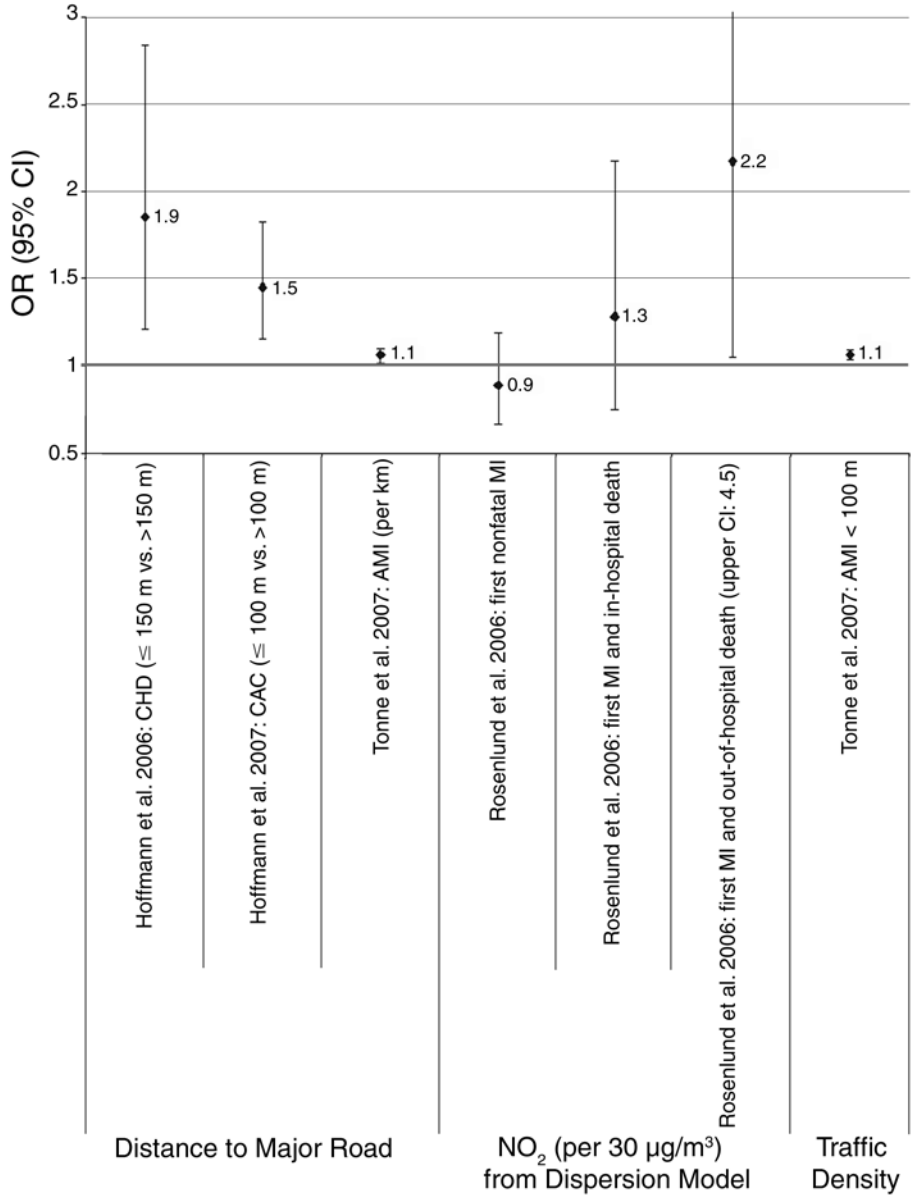

Figure 4.4. Studies of exposure to traffic pollution and cardiovascular morbidity (by exposure metric). See Table 4.7 for original data (data in figure have been rounded). Vertical lines indicate 95% confidence intervals. Abbreviations: CHD = coronary heart disease; CAC = coronary-artery calcification; and AMI = acute myocardial infarction.

Two well-executed studies reported on the association with myocardial infarction (Rosenlund et al. 2006; Tonne et al. 2007). Both controlled for important confounders and used appropriate statistical techniques. In each case, based on different traffic-exposure surrogates, statistically significant effects were observed for hospitalization for acute myocardial infarction or the prevalence of clinical coronary heart disease. The study by Rosenlund and colleagues performed an extensive evaluation for interactions. Although the study had low power to detect differences between groups, the group-specific point estimates were so similar that it is unlikely that any important interactions were missed. Only SES suggested such an interaction with traffic exposure. The study by Tonne and colleagues found that associations with traffic were largely confined to people less than 75 years of age; the group of people over 75 years of age very likely represented a survivor population that was likely to be less susceptible to exposure. Of note, the study observed an association with acute myocardial infarction in models that used traffic density within 100 m of the residence or distance to a major road alone as surrogates of exposure.

Hoffmann and colleagues (2006) measured the prevalence of coronary heart disease after long-term exposure to traffic-related air pollution, assessed as the distance of the residences from a major road, in a cohort of adults 45 to 75 years old, residing in one of two German cities. The analyses adjusted for SES and smoking. The OR for coronary heart disease was higher for long-time residents living in close proximity to major roads ($\leq$ 150 m) compared with those farther away (OR: 1.85; 95% CI, 1.21–2.84) in the full model.

In a subsequent study, Hoffmann and colleagues (2007) used their study subjects to evaluate the extent of coronary-artery calcification in relation to traffic exposure, based on a different distance metric from that used in their earlier study (2006) ($\leq$ 100 m rather than $\leq$ 150 m). Although the data were well analyzed, the 2007 study suffered from a participation frequency of only 55.8% of those eligible. Significant increases in coronary-artery calcification were observed for those with and without underlying clinical coronary heart disease in a model that adjusted for multiple individual and ecologic variables (some of which were likely to have been part of the causal pathway between traffic-related pollution and atherosclerosis). These data are consistent with those of Künzli and colleagues (2005), who demonstrated an increased risk for atherosclerosis related to more general exposure to air pollution.

Collectively, these four studies make a strong case for an association between exposure to traffic and acute and chronic atherosclerotic heart disease. Tonne and colleagues (2007) used traffic density together with distance from roadway in the same model along with group SES variables, a combination that would seem to provide good control for underlying SES differences related to residence that might have confounded their results. Based on the criteria in Tables 4.2a and 4.2b, these studies provide evidence for a causal association, but due to the heterogeneity of exposure metrics, populations, and outcomes a quantitative summary of effect estimates is not possible. Because of the small number of studies, we classify this evidence as "suggestive but not sufficient" to infer a causal relation.

No summary estimates are provided in the figure and the table for other studies that were considered, but did not meet the criteria for inclusion. A study by Grazuleviciene and colleagues (2004) in Lithuania, for example, provided association estimates without adequate control for factors such as spatial heterogeneity in sources of NO_2 (the traffic surrogate) and population characteristics that quite likely were major confounders in the authors' data. Similarly, a study by Peters and colleagues (2004, 2005) used only diary-based self-reporting of traffic exposure in a case–crossover study of acute myocardial infarction. No reliability data were provided. Subjects were recruited over an approximately 2.5-year period, and the authors' analyses did not control for seasonal or longer temporal confounding, nor did the authors consider the effects of stress and noise during the at-risk hours.

4.IV. TRAFFIC EXPOSURE, ASTHMA, RESPIRATORY SYMPTOMS, AND RELATED HEALTH-CARE UTILIZATION

Numerous studies have investigated the role of traffic-related pollution in respiratory health. The definitions of the respiratory-health outcomes and phenotypes have varied considerably across these studies. Although many studies used common labels for the outcomes, such as "asthma," "wheezing," or "COPD" (chronic obstructive pulmonary disease), a closer inspection reveals substantial inconsistencies across studies in the operational definitions of these outcomes. A few respiratory-health studies also reported on lung function and measures or markers of allergy that were used as the outcome of interest. More often, respiratory-health studies have investigated whether associations between traffic and respiratory health differ between atopic and non-atopic subjects without a discussion of the main associations with atopy itself.*

In addition to the problem of the inherent biologic diversity of asthma phenotypes, the diversity in outcome

* Atopic subjects are those with an increased tendency to develop immediate and localized reactions to allergens mediated by immunoglobulin E (IgE) or a history of eczema.

definitions posed some challenges for our review, particularly if one assumes that the etiologic factors, and hence the possible role of traffic-related air pollutants, potentially differed for different respiratory and allergic phenotypes. To address these issues, the following presentation is divided into three main sections: (1) the present section (4.IV), on asthma, respiratory symptoms, and asthma-related health problems; (2) section 4.V, on pulmonary function and objectively assessed COPD; and (3) section 4.VI, on allergy and allergic sensitization. Many of the studies included provide results related to more than one section. These studies are presented and discussed separately in the appropriate sections.

4.IV.1 DEFINITIONS OF ASTHMA-RELATED OUTCOMES AND STRUCTURE OF THE SECTION

Asthma is a complex inflammatory disease of the lung airways characterized by episodic obstruction of the airways that can lead to COPD (Eder et al. 2006). Clinicians diagnose asthma on the basis of medical history, a physical examination, assessment of the reversibility of airways obstruction, and the exclusion of other diseases with similar features. The definition of asthma used in epidemiologic research, however, is somewhat problematic, because there is no single, universally accepted set of criteria to identify asthma unambiguously. This is further complicated by the fact that various phenotypes of "asthma" may well exist. The occurrence of symptoms, reversible obstruction, or a doctor's previous diagnosis of asthma can all play a role in distinguishing a person with asthma from one without it. Some studies have characterized asthma as a "continuous trait," based on a score that integrates the occurrence of up to eight symptoms (Pekkanen et al. 2005).

Etiologic investigations of a disease as ill defined as asthma are a challenge, and this must be kept in mind in any review of the evidence for the role of traffic-related air pollutants in the etiology of the disease. One current, albeit debated, paradigm assumes that children are born without asthma but that some will develop the disease as a result of exogenous and endogenous factors. Once a person has developed asthma, he or she might suffer acute episodes of obstruction that lead to symptoms or severe asthma attacks requiring acute medication or a visit to a health-care provider or emergency room. In this paradigm, the causes of the development of asthma (i.e., the incidence of asthma) need to be distinguished from the factors that trigger acute episodes of bronchial reactivity or obstruction among people with asthma, because these causes and factors may well differ (Eder et al. 2006). In general, epidemiologic research into the role of air pollution in the occurrence of asthma follows this paradigm, distinguishing between risk factors for incidence and those for exacerbation. The present review follows this approach.

The paradigm outlined above is appealing biologically. However, its application in epidemiologic research comes with several issues that need to be taken into account when reviewing the literature.

First, having a history of asthma symptoms is often used in epidemiologic studies as part of both the definition of "asthma" onset and its prevalence and exacerbation. The occurrence of symptoms typically varies over time, reflects the expression of the acute nature of the disease, and can be triggered by air pollutants and other host and environmental factors. Many epidemiologic studies have assessed the occurrence of symptoms usually for some reference period (usually the last 12 months) and then characterized exposure to ambient pollution for the same time period. In cross-sectional and cohort studies, therefore, it is not unambiguously clear whether one is characterizing the contribution of air pollution to the acute, intermittent nature of asthma or to the onset of the disease among persons who had not previously been asthmatic.

Second, while repeated measurements of birth cohorts may be the most appropriate study design to investigate the causes of asthma incidence during childhood, the definition of "asthma onset" still may be based on the reporting of symptoms during the previous 12 months rather than doctor-diagnosed asthma or a more objective measure of the actual time of the first onset of the chronic disease. This results in the same inability to distinguish the role of a given risk factor (such as traffic exposure) in the development of the disease from its role in exacerbating the obstruction and other symptoms.

Third, despite the fundamental differences between cohort and cross-sectional studies, one may, under some plausible assumptions, expect similar results and conclusions from both the traffic-exposure studies that investigate asthma incidence (i.e., the cohort studies) and those that investigate asthma prevalence (i.e., the cross-sectional studies). In other words, if traffic-related pollution has a causal role in the development of childhood asthma, then associations between traffic-related pollution and asthma prevalence, assessed in cross-sectional surveys of, for example, elementary-school children, are likely to be similar to the associations between traffic-related pollution and asthma incidence derived from a birth cohort with follow-up into elementary-school age. The two approaches may reach similar conclusions only if the traffic-related exposure was well defined for the entire childhood period, which is indeed possible both retrospectively in cross-sectional studies and prospectively in cohorts. Moreover, the statement holds unless one presumes that asthma

in which traffic-related pollutants plays an etiologic role has a different natural history than asthma in which these pollutants play no role — a presumption that seems unlikely, given current knowledge of the natural history of asthma. In fact, when studies include a retrospective reconstruction of exposure to traffic-related pollution, they have features of cross-sectional cohort studies that under certain assumptions permit estimates of the incidence of, and incidence ratios for the occurrence of, asthma (Hudson et al. 2005).

Fourth, although wheezing is an important symptom in the expression and diagnosis of the disease, the presence of wheezing itself is not necessarily synonymous with the presence of "asthma." Some studies use "wheeze" in their definition of "asthma," either alone or in combination with "doctor-diagnosed asthma" and other symptoms or treatments. Studies that have utilized such combined definitions of asthma again preclude making a clear distinction between the onset of asthma and its exacerbation.

Fifth, childhood asthma and adult-onset asthma might be distinct phenotypes with different etiologic patterns. It is thus worth distinguishing between traffic studies conducted in children and those conducted in adults.

The five issues above were taken into account in structuring this review of respiratory health and in our interpretation of the studies. The first sections deal with studies conducted in children. Studies conducted in adults, of which there are far fewer, are discussed at the end.

In the evaluation of the evidence in children, we considered asthma onset and exacerbation separately. Data related to asthma onset are based on incidence and prevalence studies using "doctor-diagnosed asthma." These studies are summarized in Figure 4.5 and Table 4.8 (incidence; at the end of the chapter) and Figure 4.6 and Table 4.9 (prevalence; at the end of the chapter). Studies that reported on wheezing are discussed and summarized in Figures 4.7a and 4.7b and Table 4.10 (at the end of the chapter). Studies that included other respiratory symptoms among children both with and without asthma are discussed next and are summarized in Figures 4.8a and 4.8b and Table 4.11 (at the end of the chapter). In accordance with the Bates coherence criterion (1992), parallel increases in symptoms, medication, and health-care utilization would be expected if traffic exacerbated respiratory problems. These studies are discussed last and are summarized in Figure 4.9 and Table 4.12 (at the end of the chapter). Studies in adults are summarized in Figure 4.10 and Table 4.13 (at the end of the chapter).

4.IV.2 TRAFFIC EXPOSURE AND RESPIRATORY-HEALTH PROBLEMS IN CHILDREN

4.IV.2.A Onset of Asthma During Childhood

Seven cohort studies and one case–control study qualified for our assessment of traffic-related pollution as a potential cause of asthma incidence (see Figure 4.5 and Table 4.8). Data were obtained from two European birth cohorts that provided results at various ages (Brauer et al. 2002, 2007; Gehring et al. 2002; Morgen-stern et al. 2007, 2008), from a small sample of the Southern California Children's Health Study (Jerrett et al. 2008), from a cohort of children ages 6 to 9 years in the Chiba Prefecture of Japan (Shima et al. 2003), and a case–control study that covered children ages 4 to 14 years from five metropolitan areas in France (Zmirou et al. 2004).

The European studies utilized a Dutch cohort (the Prevention and Incidence of Asthma and Mite Allergy [PIAMA]) and two combined cohorts for the city of Munich (the German Infant Nutrition Intervention [GINI] cohort and the Influences of Lifestyle Related Factors on the Human Immune System and Development of Allergies in Children [LISA] cohort). These studies applied similar measurement-based exposure models (developed in the Traffic Related Air Pollution and Childhood Asthma [TRAPCA] study [Cyrys et al. 2005]) to characterize contrasts in traffic-related exposures for each subjects' home address at birth, with extensive adjustment for covariates. As summarized below, all the studies reported positive associations between traffic-related pollution and asthma onset, but some of the results did not reach statistical significance.

The two studies by Brauer and colleagues (2002, 2007) in the Dutch PIAMA cohort investigated the relationship between traffic-related air pollution and asthma symptoms and respiratory infections. Yearly average concentrations of three surrogates of traffic-related pollution — $PM_{2.5}$ soot, and NO_2, all of which were highly correlated ($r \geq 0.93$) — were estimated using a model combining air-pollution measurements with a geographic information system (GIS). The models included similar GIS variables for each pollutant, such as the number of heavy-traffic roads within 250 m of residences, the presence of a major road within a distance of 50 m, and the building density within a 300-m buffer. The models explained more than 80% of the variances in the measured annual average concentrations of soot and NO_2 and about 70% of the variance in $PM_{2.5}$.

The associations between pollution and the onset of doctor-diagnosed asthma were similar at ages 1, 2, and 4 and when cumulated over 2 and 4 years; but ORs reached statistical significance only for ages 0 to 12 months (Brauer et al. 2002) and when cumulated over 4 years, both for soot

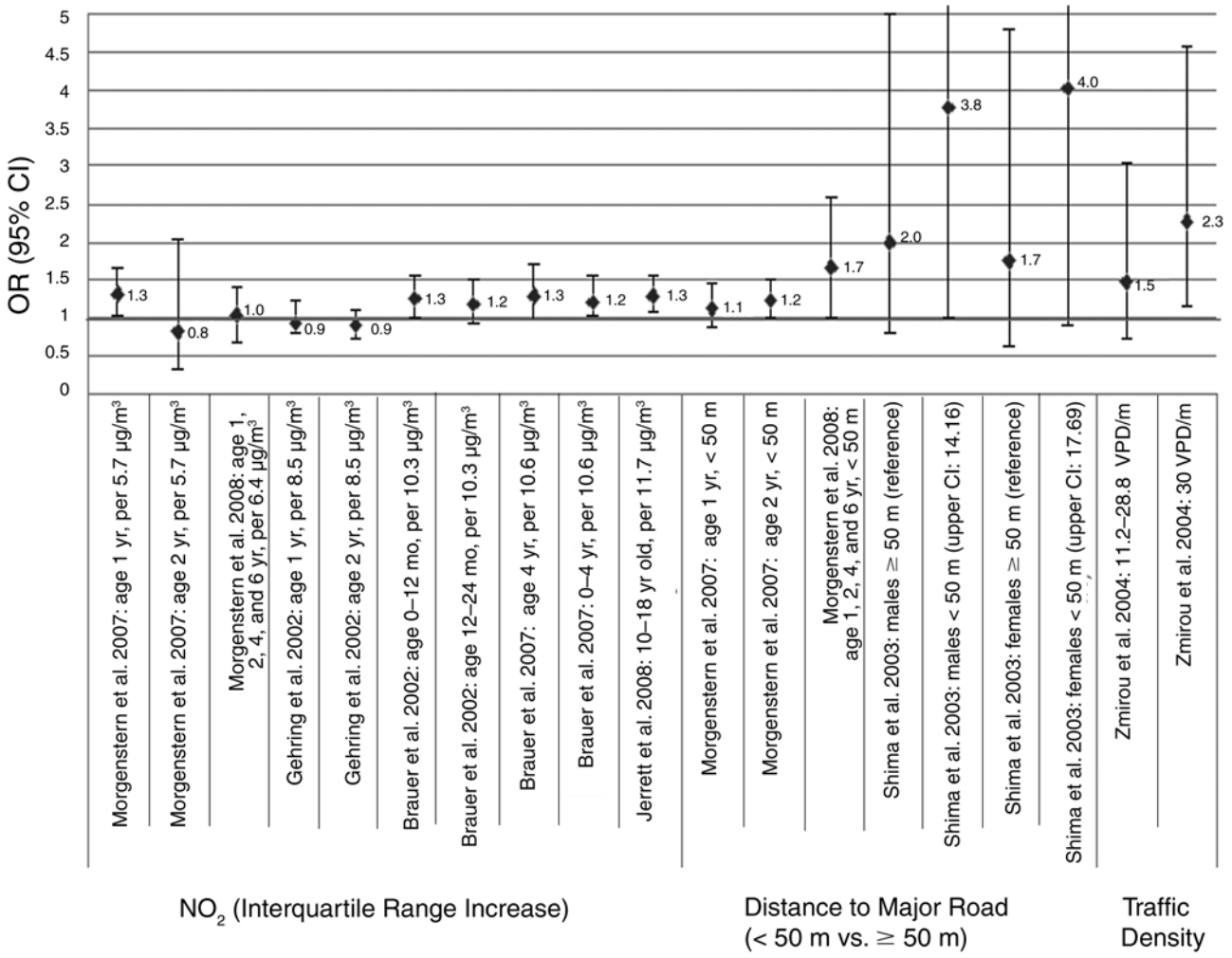

Figure 4.5. Studies of exposure to traffic pollution and incidence of doctor-diagnosed asthma in children (by exposure metric). See Table 4.8 for original data (data in figure have been rounded). Vertical lines indicate 95% confidence intervals. Abbreviation: VPD/m = vehicles per day per distance (m) to road.

and NO_2 (Brauer et al. 2007). Asthma-related symptoms gave results similar to those for doctor-diagnosed asthma. At age 4, approximately 4% of the children had doctor-diagnosed asthma, 12% had wheezing, and 21% had dry cough at night without cold. Cumulated over 4 years, the OR per IQR of soot was 1.26 (95% CI, 1.02–1.56) for doctor-diagnosed asthma (Brauer et al. 2007; Figure 4.5) and 1.18 (95% CI, 1.04 to 1.34) for "wheeze-ever" (Figure 4.7a). Stratification by allergen sensitivity revealed an association that was twice as strong among the 20% of children with food allergies; no associations were observed in those sensitized to other indoor or outdoor allergens (Brauer et al. 2007). In the German GINI and LISA cohorts, two sequential analyses of asthma and respiratory symptoms in children up to age 2 were conducted. The first focused on children living in Munich (Gehring et al. 2002), and the second extended the model to children living in the Munich metropolitan area (Morgenstern et al. 2007). A subsequent study examined the same groups of children at age 6 (Morgenstern et al. 2008). Exposure was assessed using a complex GIS model that predicted personal exposure to NO_2 and soot concentrations. In the first study, the model for soot and NO_2 explained 67% and 62% of the variances, respectively; in the second study, the model was less precise and explained 47% and 51% of the variances, respectively (Morgenstern et al. 2007); the specific coefficient for traffic and their partial R^2 were not reported. The concentrations and distributions of these two surrogates of personal exposure were rather similar in the Dutch and German studies.

Instead of "doctor-diagnosed asthma" (with a prevalence of < 1%), the analyses used diagnosed "obstructive/asthmoid bronchitis" as the outcome, possibly a reflection of the prevailing pattern found in Germany for the youngest patients (Gehring et al. 2002; Morgenstern et al. 2007). At 1 year of age, "obstructive/asthmoid bronchitis" was associated with traffic-related surrogates in the second, geographically extended study (Morgenstern et al. 2007) but not in the first (Gehring et al. 2002). In the larger sample, all surrogates of traffic (namely, $PM_{2.5}$ absorbance, NO_2, and living within 50 m of a main road) were associated with "asthmoid bronchitis" (e.g., an 8.5-μg/m^3 contrast in NO_2 was related to an OR of 1.30; 95% CI, 1.03–1.66). At 2 years of age, residential distance from roadways continued to be associated with the outcome (OR for living < 50 m from a roadway: 1.23; 95% CI, 1.00–1.51), but soot and NO_2 did not. Dry cough at 1 year of age increased significantly with all three markers of traffic in the first study (see Table 3 in Gehring et al. 2002 and Table 4.11 at the end of this chapter), with ORs of approximately 1.30 per IQR (e.g., for 8.5 μg/m^3 NO_2: 1.36 [95% CI, 1.07–1.74] at 1 year of age and 1.24 [95% CI, 1.02–1.51] at 2 years of age, respectively). All the models were adjusted for SES and other early-life factors. In most cases, the results for the second, geographically extended analysis became attenuated for both ages 1 and 2 years (see Table 5 in Morgenstern et al. 2007 and Table 4.11 at the end of this chapter). Results for NO_2 showed less attenuation (Morgenstern et al. 2007). The second study included "living within 50 m of a road" as a traffic-exposure metric. When data for ages 4 and 6 years were included, the asthma outcome was associated with soot (1.56 [95% CI, 1.03–2.37] per 0.2×10^{-5}/m) and distance (1.66 [95% CI, 1.01–2.59]) for living within 50 m of a busy road but not with NO_2 (Morgenstern et al. 2008).

In Japan, Shima and colleagues (2003) enrolled children ages 6 to 9 years and followed the ones who had lived at the same residence for three or more years (N = 2506). The children were recruited from 10 schools across eight Japanese communities. Six of the schools were located in zones with heavy traffic loads (63,000 to 76,000 vehicles per 12 hr); the others were in rural areas. NO_2 concentrations close to the schools ranged from 7 to 32 ppb and were < 20 ppb at all the rural schools. The urban residences were classified as those within 50 m of trunk roads, and the analyses compared outcomes across three categories (rural, > 50 m from trunk roads, and < 50 m of trunk roads). A variant of the usual questionnaire-based doctor-diagnosed asthma was used. Asthma was defined as including any of the following: recurrent wheezing, asthma attacks, or medication for asthma. The questionnaire was filled out by either parent annually for four years. The incidence of asthma among children who had no symptoms in the first survey was associated with the traffic marker in boys and girls but did not reach significance in the girls (P = 0.07). The 648 children lost to follow-up over the years of the study were more likely to have lived within 50 m of trunk roads and differed in several covariates used in the adjusted models. The impact of this loss and the relevance of SES were not discussed.

Jerrett and colleagues (2008) used a random small subsample of two Children's Health Study cohorts (recruited in 1993 and 1996) based on different levels of traffic exposure to investigate asthma incidence and traffic-related exposure. For all 217 subjects, free of asthma at baseline (age 10 years), home outdoor NO_2 measurements were taken with passive samplers that were deployed twice for two weeks in the year 2000 (in summer and in fall or winter). Both seasonal NO_2 and its mean ("annual mean") correlated significantly with new-onset asthma (between age 10 to 18 years). The models were not sensitive to adjustment for individual or contextual variables. Two-stage models with between- and within-community estimates and models with random effects for communities gave similar results. An IQR increase in home outdoor NO_2 of 6.2 ppb (11.7 μg/m^3) was associated with a 29% (95% CI, 7%–56%) increase in the risk of new-onset asthma. In their analyses, Jerrett and colleagues evaluated humidity as a potential confounder and reported that the associations with residential NO_2 were sensitive to the inclusion of humidity.

In France, Zmirou and colleagues (2004) chose a matched case–control design (N = 390) to investigate the association between traffic density (defined as the ratio of vehicles per day divided by the distance of the respective street to the home or school of the child) and recently diagnosed asthma. Participants' ages ranged from 4 to 14 years. Lifelong time-weighted exposure was not associated with asthma, but traffic density during the first three years of life showed a significant trend, with an OR of 1.30 (95% CI, 1.04–1.62) for a 1-unit increase in the log-transformed traffic-density measure, adjusted for SES, environmental tobacco smoke during pregnancy, and a range of other early-life factors. The tertile with the highest exposure had twice the prevalence of cases (i.e., subjects with a recent doctor's diagnosis of asthma) compared with the first tertile, which had the lowest exposure (2.28; 95% CI, 1.14–4.56). The upper tertile was defined as ≥ 30 vehicles/day per meter of distance to road, meaning that subjects exposed to 30,000 vehicles per day on a main road within 1 km of their home or school were considered to have had the same exposure as those exposed to 3000 vehicles per day within 100 m of the home or school. This measure does not really distinguish

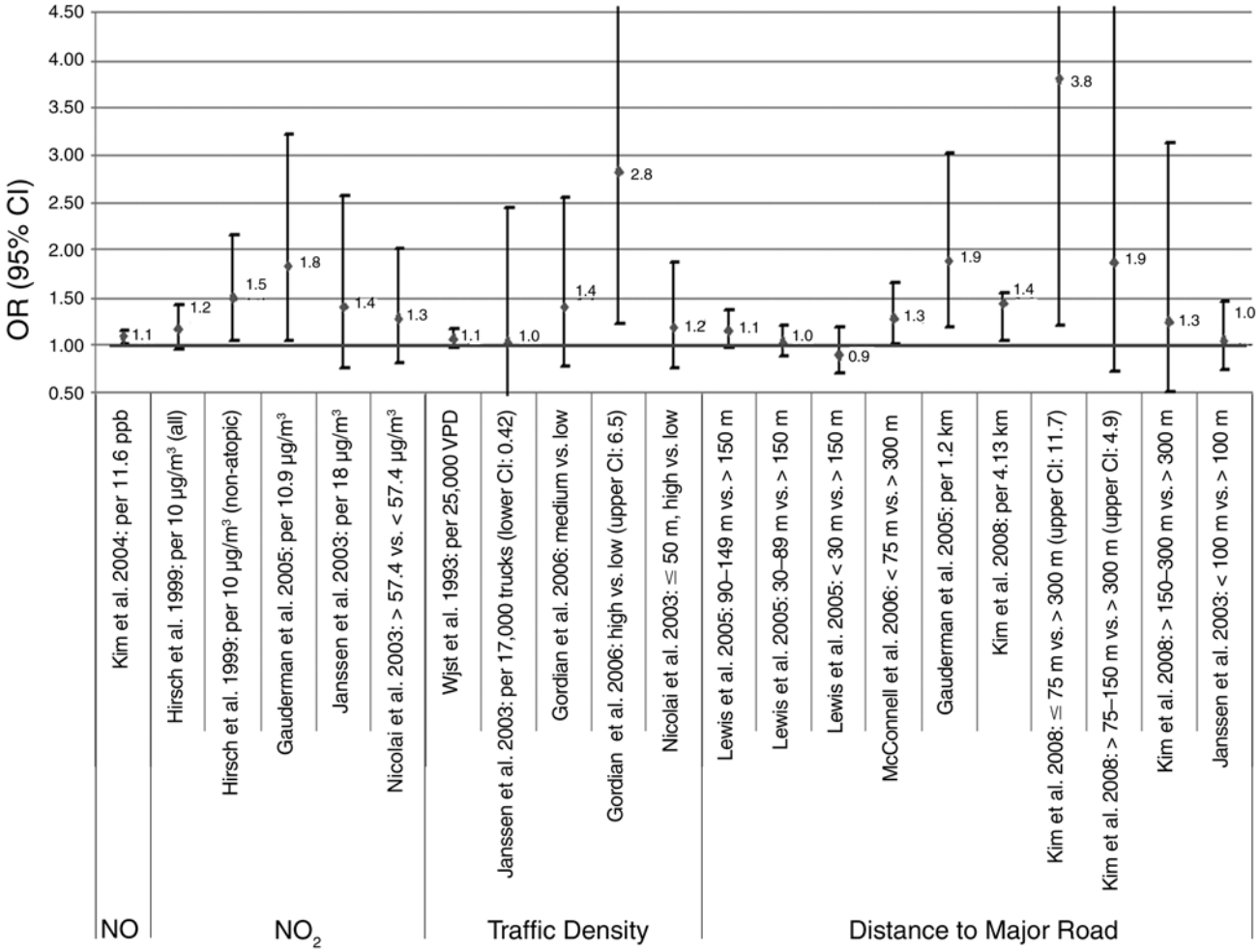

Figure 4.6. Studies of exposure to traffic pollution and prevalence of doctor-diagnosed asthma in children (by exposure metric). See Table 4.9 for original data (data in figure have been rounded). Vertical lines indicate 95% confidence intervals. Abbreviation: VPD = vehicles per day.

between intensity and distance effects on the observed association. Thus, although the results clearly indicated an effect of "traffic-related pollution," the uncertainties in the spatial scale of the marker have precluded a quantitative comparison of the estimates with those reported in other studies.

4.IV.2.B Prevalence of Doctor-Diagnosed Asthma

The 11 studies shown in Figure 4.6 and Table 4.9 report asthma prevalence among children in the age range of 4 to 12 years. These studies show mostly positive associations between various markers of traffic and asthma prevalence, but several do not reach statistical significance. The main studies are briefly described below prior to giving an integrated assessment.

Three studies were conducted in Germany and had proper control of relevant covariates. A study by Wjst and colleagues (1993) reported on doctor-diagnosed asthma prevalence and symptoms (and lung function; see section 4.V) in children 9 to 11 years old in relation to traffic density per increase of 25,000 cars/day passing through a school district in Munich. Traffic densities ranged from 7000 to 125,000 cars per day. The lifetime prevalence of doctor-diagnosed asthma was associated with traffic density, with an OR (per 25,000 vehicles per day) of 1.06 (95% CI, 0.97–1.16). A survey of 5421 children in Dresden, ages 5 to 7 and 9 to 11 years, by Hirsch and colleagues (1999) used the International Study of Asthma and Allergies in Children (ISAAC) questionnaire and air-pollution measurements on a 1 × 1-km grid (for CO, benzene, NO_2, SO_2,

and ozone) to investigate associations between pollution and the prevalence of doctor-diagnosed asthma (as well as symptoms and measures of lung function in the older age group). Pollutants were assigned individually as the distance-weighted mean of the four grid points closest to the child's residence and school (for the 9-to-11-year-olds only). The three surrogates of traffic-related pollution (benzene, CO, and NO_2) were all associated positively with asthma prevalence, although the estimates were statistically significant only among all children who were non-atopic. Nicolai and colleagues (2003) used traffic counts at the residential street as a surrogate of exposure in a study based on a subset (N = 3946) of the children in Munich enrolled in the ISAAC study. An emissions-based model also predicted soot, benzene, and NO_2 outdoors at home. The prevalence of doctor-diagnosed asthma increased across the tertile increases in traffic-count, soot, benzene, and NO_2 but did not reach statistical significance. Among those also exposed to environmental tobacco smoke, the OR for doctor-diagnosed asthma was 1.75 (95% CI, 0.98–3.12) in the "high exposure" group, with soot concentrations > 10.73 μg/m^3 (upper tertile) compared with 1.42 (95% CI, 0.92–2.2) for the rest of the children.

Two Dutch studies provided nonstatistically significant or negative results (van Vliet et al. 1997; Janssen et al. 2003). The study by Janssen and colleagues reported adjusted associations between traffic characteristics and respiratory symptoms in 2053 Dutch children sampled from 24 neighborhood schools located within 400 m of a motorway. Point estimates for ORs for associations between prevalence of asthma and distance of school (< 100 m) were 1.04 (95% CI, 0.74–1.45) and 1.36 (95% CI, 0.62–2.98) per IQR of soot. The study by van Vliet and colleagues examined the association between questionnaire-based doctor-diagnosed asthma and distance from freeways among 1068 children from 13 schools in southern Holland, where a large number of homes were located within 300 m of a freeway. The exposure metrics used were the distance of homes and schools from freeways, traffic density (especially truck density) on the freeways, and measures of BS and NO_2 in the schools. Doctor-diagnosed asthma was not associated with any of the markers. Point estimates for most ORs were less than 1, except for living within 100 m of a freeway, which had an OR of 1.68 (95% CI, 0.68–4.14).

All the studies in the United States reported statistically significant associations between asthma prevalence and markers of traffic-related pollution (Gauderman et al. 2005; Gordian et al. 2006; McConnell et al. 2006; Kim et al. 2008).

A subanalysis by Gauderman and colleagues (2005) of the Southern California Children's Health Study was based on 208 randomly selected fourth-graders (age 10 years) recruited in 1993 and 1996. Two 2-week periods of outdoor NO_2 measurements made at the subjects' homes were used to derive a long-term average for each child that was adjusted for seasonality. NO_2 was strongly and significantly associated with asthma prevalence; the estimates were robust to adjustment for various factors, including SES. The distance of the residence from freeways and the modeled freeway-related pollution (derived from a dispersion model) resulted in similar associations. Traffic volume within 150 m of the home and modeled pollution from other roads were positively, but not significantly, associated with asthma. Measures of the current state of asthma (recent wheezing, wheezing with exercise, and asthma medication) were all strongly associated with NO_2 as well. McConnell and colleagues (2006), the Children's Health Study researchers, recruited a cohort of 4762 children in 2003, ages 5 to 7 years, 55% of whom were of Hispanic origin, living in 13 communities in Southern California. Asthma prevalence was consistently associated with the distance of the home from major roads. Data were reported for four distance categories (< 75 m, 75–150 m, 150–300 m, and > 300 m from a major road), and associations usually reached statistical significance among the ~15% living within 75 m of a major road. This was the case both for the prevalence of "life-time asthma," defined as having "ever had doctor-diagnosed asthma," and "current asthma" in the last 12 months. The latter definition included wheezing and thus precludes making a clear distinction between acute symptoms and asthma onset. Associations were present only among children with no family history of asthma and were far stronger among children without allergic symptoms. Associations for lifetime asthma were observed only among the girls, and correlations with wheezing and with "current asthma" prevalence were stronger in the girls than in the boys.

Gordian and colleagues (2006) sampled 756 children ages 5 to 7 years from 13 schools in Anchorage, Alaska. Traffic exposure was based on traffic density within 100 m of the cross streets closest to the child's residence and was grouped into low-, medium-, and high-exposure categories. Asthma prevalence was associated with this traffic metric. The OR for the high-exposure group was 2.83 (95% CI, 1.23–6.51). Models were adjusted for sex, parental asthma, smokers in the household, and income as a proxy for SES. Interactions with these variables revealed much stronger and highly significant associations of traffic with asthma prevalence among children with no history of parental

asthma. The OR for the high-exposure group was 5.34 (95% CI, 2.08–13.74) in children with no history of parental asthma. In children with a history of parental asthma, traffic exposure was not associated with asthma prevalence.

Kim and colleagues (2004) reported positive associations between the prevalence of doctor-diagnosed asthma and traffic surrogates (NO_x, NO, and BC) characterized at 10 neighborhood schools in the Hayward–Oakland region of California's San Francisco Bay Area. Associations were strongest for NO_x and NO in girls and reached statistical significance among those who had lived at the same residence for more than one year. The associations were smaller and not significant in boys. A major determinant of the concentrations of NO_x and BC was location within 300 m downwind of busy roads. Markers of SES were not related to outcomes, and the schools had similar distributions of SES.

Later, Kim and colleagues (2008) reported a cross-sectional association between current asthma in children, in which "current" had been defined as an episode of asthma or wheezing during the last 12 months plus a doctor diagnosis at some time in the past ("Did you ever have asthma?"). As a consequence, the authors' results cannot be distinguished unambiguously from those of studies on acute effects on asthma symptoms. The fifth graders from the three schools studied by Kim and colleagues were of rather low SES. Traffic exposure at the residence was defined using several metrics: the maximum and closest average annual traffic density within 150 m of a freeway, traffic density within 150 m of a freeway, log distance to a freeway, distance to a freeway (75 m, 150 m, and 300 m), distance to a freeway upwind and downwind (300-m cutoff), and distance to principal arteries. A validation study demonstrated good agreement between NO_x concentrations and the distance metrics (especially within 150 m) for the source location, and the strong relevance of the downwind-versus-upwind location. Correlations of the distance metrics with measurements of NO_x, NO, and NO_2 were clearly higher than for traffic-density measures but explained less than 50% of the variability ($r = 0.69$ for NO and distance to a freeway). Associations with asthma were also largest for distance metrics, for example, ORs were 3.80 (95% CI, 1.20–11.71) for living within 75 m of a freeway or highway and 1.43 (95% CI, 1.04–1.54) for log distance of 939 m). Potential effect modifiers (sex, atopy, or non-movers) were not significant. Those with no history of maternal asthma appeared to have larger effects of proximity.

In a large, random sample of 11,562 children ages 4 to 6 years from two regions in the United Kingdom, Lewis and colleagues (2005) observed no associations between reported doctor-diagnosed asthma prevalence (or wheezing and asthma medication) and distances of homes from a main road. ORs adjusted for age, sex, area, smokers at home, diet, and neighborhood socioeconomic status were not significant, and rates among those closest to the roads (< 30 m) were not elevated in comparison with those farther away (> 150 m). No information was provided about the objective concentrations of pollutants in these areas of the United Kingdom across the four distance categories (< 30, 30–89, 90–149, and > 150 m).

Shima and colleagues (2003), discussed earlier in connection with asthma incidence, also evaluated asthma prevalence in relation to distance from roads in a cohort of Japanese children. The findings suggested increased prevalence in girls but no changes for boys. The limitation in the study design and the lack of control for confounders make this study hard to interpret. A study by Yang and colleagues (2003), who measured the prevalence of asthma in two groups of children attending two schools at different distances from a highway (150 m and > 1500 m), was also hard to interpret, because of limitations in the study design. There was no difference in asthma prevalence between the two groups. These studies are not included in Table 4.9.

4.IV.2.C Evaluation of the Role of Traffic in Asthma Development

Based on the studies presented in Tables 4.9 and 4.10, we conclude that living close to busy roads is an independent risk factor for the onset of childhood asthma. As discussed below, whether the evidence for a causal relation is considered "sufficient" or "suggestive but not sufficient" is not clear-cut but in a gray zone in our four-category evidentiary scheme (Tables 4.2a and 4.2b). Although socioeconomic factors, race, and other factors might be confounders associated with both the disease and the exposure, the various study findings cannot be explained by confounding alone. Results from modeled soot or NO_2 and proximity as well as the use of simpler exposure metrics (Zmirou et al. 2004) all led to similar inferences. The findings on asthma incidence also were rather consistent with the findings of the prevalence studies, although the latter were more heterogeneous. All but one of the studies with measured or modeled individually assigned NO_2 or soot concentrations reported positive associations between the prevalence of doctor-diagnosed asthma and these traffic metrics (Hirsch et al. 1999; Janssen et al. 2003; Nicolai et al. 2003; Kim et al. 2004). The null findings published by van Vliet and colleagues (1997) used measurements of pollutants (NO_2 and soot) made at schools to

characterize exposure. In the same study, living within 100 m of a freeway was positively, but not statistically significantly, associated with asthma prevalence. Other studies with both pollutants and distance-based or traffic-density measures observed more consistent results across these metrics, although a number of the studies provided somewhat imprecise estimates. The study by Shima and colleagues (2003) did not qualify in our assessment, because the definition of doctor-diagnosed asthma included the acute expression of the diseases (wheezing and asthma medication) and prevalence estimates were not adjusted for confounders.

Most cross-sectional studies using distance-based or traffic-density measures reported positive associations with asthma prevalence as well, but only the findings from three of these studies — all from the United States — reached statistical significance (Gauderman et al. 2005; Gordian et al. 2006; McConnell et al. 2006). The studies by Gauderman and colleagues and McConnell and colleagues examined children who were enrolled in the Southern California Children's Health Study. A large study by Lewis and colleagues (2005) in the United Kingdom was notable for not finding any indication of an association between asthma prevalence and distance of residences from main roads, although the latter had been defined at an appropriately small spatial scale (down to 30 m). In this study, crude associations were not affected by adjustment for a neighborhood deprivation index, arguably a potential proxy for poor air quality. The concentrations and contrasts of pollution related to proximity in the study areas are not known nor is the correlation between proximity and traffic density. It is thus difficult to evaluate whether the null findings were related to methodologic issues or reflected there being actually no effect of traffic-related pollution on asthma in England.

A recent review (Salam et al. 2008) suggested that there is consistent evidence that living near busy roads was associated with higher asthma incidence. However, the review did not apply our formal scheme of evidence assessment (see Tables 4.2a and 4.2b). The attempt to put the asthma literature in this evidentiary scheme highlights the literature's limitations and leads us to assign the studies to a gray zone between "sufficient evidence" and "suggestive but not sufficient evidence" to support the hypothesis that the traffic-derived pollutants encountered in very high concentrations along busy roads are a causal component in the development of asthma. One can make an argument for either classification, but the final decision depends on the valuation of chance in light of the numerous positive but not necessarily statistically significant findings. Although it is impossible to dismiss chance fully as an explanation, the results observed across the studies followed a pattern supporting the plausible assumption that the pollutants were indeed causally related with asthma development, though only among a subset of children with some joint pattern of exogenous or endogenous susceptibility factors. Several of the studies clearly supported the notion of heterogeneity of effects, with several significant results in various subgroups (defined by such factors as sex, atopy, or parental asthma), but the assessment of the factors had not been made in a standardized manner. Moreover, statistical power to detect a "significant interaction" was usually limited; one is thus left with many statistically significant subgroup findings but uncertainties about the overall significance of the interactions.

Based on these diverse approaches to investigating susceptibility, the conditions that underlie an increased risk for asthma development among children exposed to traffic-related pollutants are not known with certainty, and the results across studies that addressed these conditions are in some cases not consistent and in other cases not comparable. Some studies suggest greater risks in girls, although the evidence for this interaction was not assessed consistently across the studies. Children who were non-atopic or who had no parental history of asthma appeared to be at higher risk as a result of traffic exposure, based on studies in Southern California (McConnell et al. 2006), Germany (Hirsch et al. 1999), and Alaska (Gordian et al. 2006). The finding in the Dutch PIAMA cohort about the relevance of sensitization to food allergen as a risk modifier, but not of any other allergic sensitization, is intriguing (Brauer et al. 2007). Interactions with food allergens, however, have not been tested in other studies, and interactions with sensitization to outdoor allergens have been found in other studies (Janssen et al. 2003) but not in Brauer and colleagues (2007) (see section 4.VI). Inconsistencies across studies, in fact, might be driven by different distributions across populations of various factors, including sex, race, age, sensitization, antioxidant intake, SES, genetic background, and geography, to name a few. As indicated in the study by McConnell and colleagues (2006), the age at which the exposure occurs might matter; the study suggested that only early-life exposure to traffic-related pollutants played a role in asthma onset. The recent analysis of the Southern California Children's Health Study by Jerrett and colleagues (2008) highlighted the relevance of ambient cofactors such as humidity, a factor that might play a modifying role on the physical, biologic, and toxicologic properties of traffic-related particulates. Humidity has not been controlled or much discussed in other asthma studies. More

data are needed on the factors and developmental time period that might underlie susceptibility to traffic-generated pollutants with respect to childhood asthma.

It is not known, and it cannot be inferred from the available data, whether children who develop asthma because of traffic-related pollutant exposure would develop asthma later in life had they not been exposed. In complex, chronic diseases with multiple phenotypes such as asthma, interactions between a range of competing causal factors are likely. Understanding the changes in the course or frequency of complex diseases that would occur in a population after the removal or addition of an etiologic factor (such as traffic-related pollution) is a major research challenge. Its clarification is of particular relevance in the evaluation of the public-health risks one would attribute to the respective etiologic factors. As shown in a recent analysis by Künzli and colleagues (2008), if traffic-related pollution causally contributes to the incidence of childhood asthma and if children with traffic-related asthma would not have developed asthma in the absence of this pollution, then the burden of asthma-related morbidities attributable to pollution would be substantially larger than previously thought.

4.IV.2.D Exacerbations of Symptoms in Children with and without Asthma

This section evaluates the studies that examined the association between exposure to traffic-related pollution and the occurrence of wheezing and other respiratory symptoms. With very few exceptions, these studies were either cohort or cross-sectional studies in which parents reported the occurrence of symptoms during a period of time prior to an interview. Given the important role of wheezing in the epidemiologic definition of asthma, the related figures and tables distinguish between wheezing (Figures 4.7a and 4.7b and Table 4.10) and all other respiratory symptoms (Figures 4.8a and 4.8b and Table 4.11). Many studies appear in both tables and figures. This section describes studies that measured both wheezing and other respiratory symptoms. The subsequent section will describe the studies that examined the associations of exposure to traffic-related pollution and health-care utilization. An integrated discussion follows thereafter.

The cohort studies discussed in the earlier sections on asthma incidence and prevalence also reported results for wheezing based on questionnaires that asked about wheezing and dry cough occurring in the previous six or 12 months, depending on the age of the child. Brauer and colleagues (2002, 2007) reported associations between elevated modeled concentrations of NO_2 and soot at children's homes and increased risk of wheezing in children in the Dutch PIAMA cohort. The associations reached significance only for the first 4 years of life, a result that was very similar to that for doctor-diagnosed asthma. During the first 4 years of life, the OR for elevated wheezing was 1.18 (95% CI, 1.04–1.34) for soot and 1.19 (95% CI, 1.05–1.34) for NO_2 (see Figure 4.7b). The largest associations were among children with food allergies (see Table 4.10) (Brauer et al. 2007).

Symptom results were presented in two separate analyses of the GINI and LISA cohort study in Munich (Gehring et al. 2002; Morgenstern et al. 2007). Estimates for wheezing at age 2 were slightly higher in girls; dry cough at night had a greater association with traffic-related pollution in boys at ages 1 and 2 years. The association with dry cough became attenuated at age 2 years; ORs were 1.24 (CI, 1.02–1.51) in the study by Gehring and colleagues and 1.16 (CI, 0.92–1.47) in the study by Morgenstern and colleagues (see Figure 4.7b for wheezing and Figure 4.8b for dry cough). Adjustments were made in all models for SES and other early-life factors. However, there was no association between exposure to traffic-related pollution (modeled NO_2 or "soot" concentrations at the home addresses) and wheezing in either study's analyses. In a subsequent study by Morgenstern and colleagues (2008) in children ages 4 and 6 years based on distances from a busy street (50 m, 250 m, 1000 m, or > 1000 m) in Munich revealed associations between distance and symptoms of asthma, hay fever, and eczema (not shown in Table 4.11). The 50-m-distance category reached statistical significance for asthma symptoms (OR = 1.24; 95% CI, 1.01–1.52), but not for the other symptoms.

In the Japanese children studied by Shima and colleagues (2003), discussed earlier in connection with asthma onset, living within 50 m of a major road was not significantly associated with wheezing, although estimates were positive in boys but not in girls (see Table 4.10).

A recent study by Nordling and colleagues (2008) used the Swedish Birth Cohort, recruited between 1994 and 1996, to assess the association between traffic exposure during the first year of life and wheezing up to age 4 years. Exposure metrics were derived from source-specific emissions inventories (by vehicle type) using a dispersion model, in which both PM_{10} and NO_x (used as surrogates for traffic) were estimated above background at the home addresses. Persistent wheezing (i.e., episodes both earlier and more recently) was associated with traffic-related PM_{10} (OR = 1.64; 95% CI, 0.9–3.00) and traffic-related NO_x (OR = 1.60; 95% CI, 1.09–2.36) (Figure 4.7b), with higher estimates in girls (ORs = 2.32 and 1.94, respectively) than in boys (ORs = 1.52 and 1.55, respectively). However, the association with persistent wheezing was observed largely

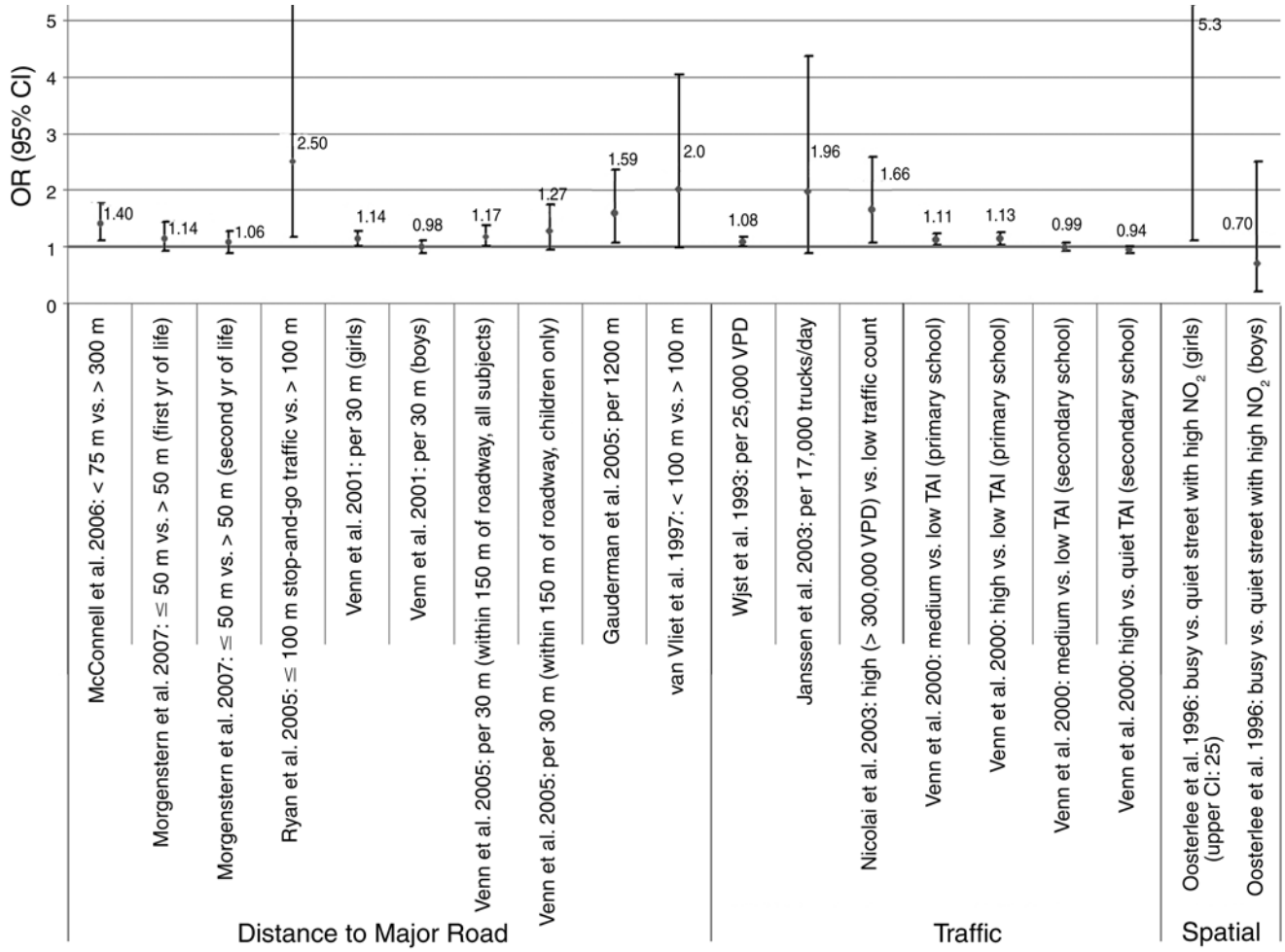

Figure 4.7a. Studies of exposure to traffic pollution (traffic distance and density) and wheeze in children (by exposure metric). See Table 4.10 for data. Vertical lines indicate 95% confidence intervals. Abbreviations: VPD = vehicles per day and TAI = traffic activity index.

in non-atopic subjects (OR = 1.46; 95% CI, 1.00–2.13); associations were not significant among atopic subjects with wheezing (OR = 1.11; 95% CI, 0.55–2.22).

Nicolai and colleagues (2003) reported associations in Munich between traffic counts and "current asthma," characterized as asthma symptoms (including wheeze and cough) during the last 12 months. The prevalence of reported "current asthma" increased across the traffic-count tertiles. Results were similar for current wheezing (Figures 4.7a and 4.7b) and cough (Figures 4.8a and 4.8b). Modeled soot, benzene, and NO_2 were all associated positively with current asthma, current wheezing, and cough. When stratified by exposure to secondhand smoke, stronger associations were seen among those also exposed to secondhand smoke.

Results for wheezing were also consistent with those for asthma prevalence reported above in the Southern California Children's Health Study analyses and showed an association between recent wheezing with exposure measured either as NO_2 concentrations outside children's homes or as the distance from a major road (see Figure 4.7a). An association was also observed with asthma-medication use (see Figure 4.9) (Gauderman et al. 2005). McConnell and colleagues (2006) reported similar results in new cohort of the Southern California Children's Health Study of school children. In this study, current wheezing increased among children living within 75 m of a major road (see Figure 4.7a).

Ryan and colleagues (2005) enrolled 633 families from the Cincinnati region of Ohio to investigate wheezing without a cold in relation to traffic pollution among children

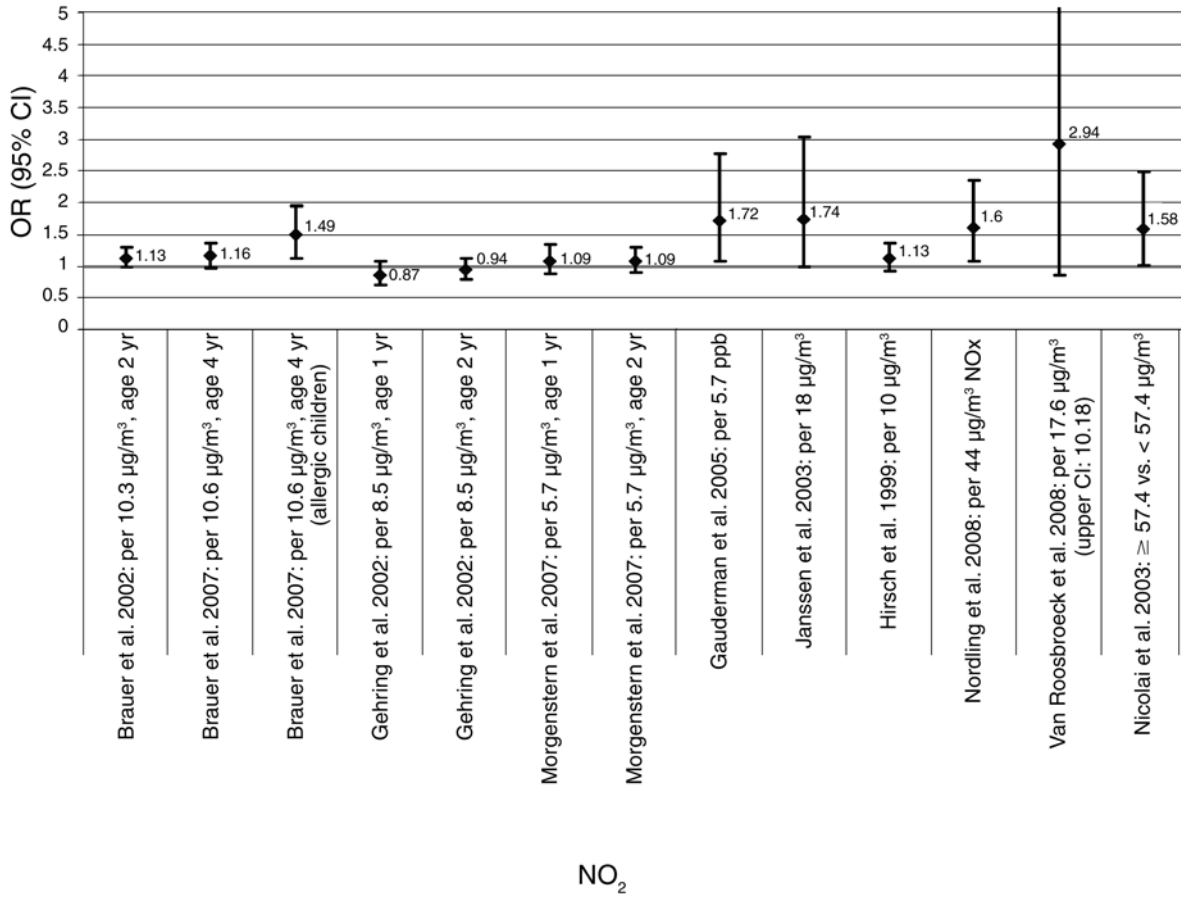

Figure 4.7b. Studies of exposure to traffic pollution (per unit increment in NO_2 concentration) and wheeze in children. See Table 4.10 for data. Vertical lines indicate 95% confidence intervals.

6 months old. At least 1 month of symptom diaries was available for each child; wheezing was reported for 8% of the children. Among those living in proximity (50 m) to a state or bus route with stop-and-go traffic (< 50 miles/hr), the OR of wheezing was three times higher than among the unexposed. The OR for those within 100 m was 2.50 (95% CI, 1.15–5.42) relative to the unexposed (Figure 4.7a). The unexposed were those who lived more than 100 m from stop-and-go traffic and more than 400 m from an interstate road with moving traffic (> 50 miles/hr and > 1000 trucks daily). In contrast to stop-and-go-traffic, the density of moving traffic was not associated with wheezing. However, the average distance (~250 m) to what was considered "high moving traffic" was rather large — possibly too far, in other words, to result in substantial exposure contrasts. In contrast, the median distance of subjects' residences to what was defined as "high stop-and-go traffic" was only 45 m and was thus close enough to result in peak concentrations near these residences.

Several studies conducted in the Netherlands reported associations between traffic-related pollution and asthma symptoms. Oosterlee and colleagues (1996) sampled children and adults from areas that had been selected based on modeled NO_2 concentrations. One group lived along busy streets, the other on streets with little traffic. Models were adjusted for SES, secondhand smoke, pets, humidity, and other relevant covariates. In children, symptom frequencies were higher in those living in the heavy-traffic areas. Stratification by sex revealed significant associations with living in a heavy-traffic area among girls but less so in boys. For girls, all seven symptoms were more frequent in those living in the heavy-traffic area, and five symptoms reached statistical significance ("wheeze ever," "wheeze in past year," "attacks of dyspnea with wheeze ever and in

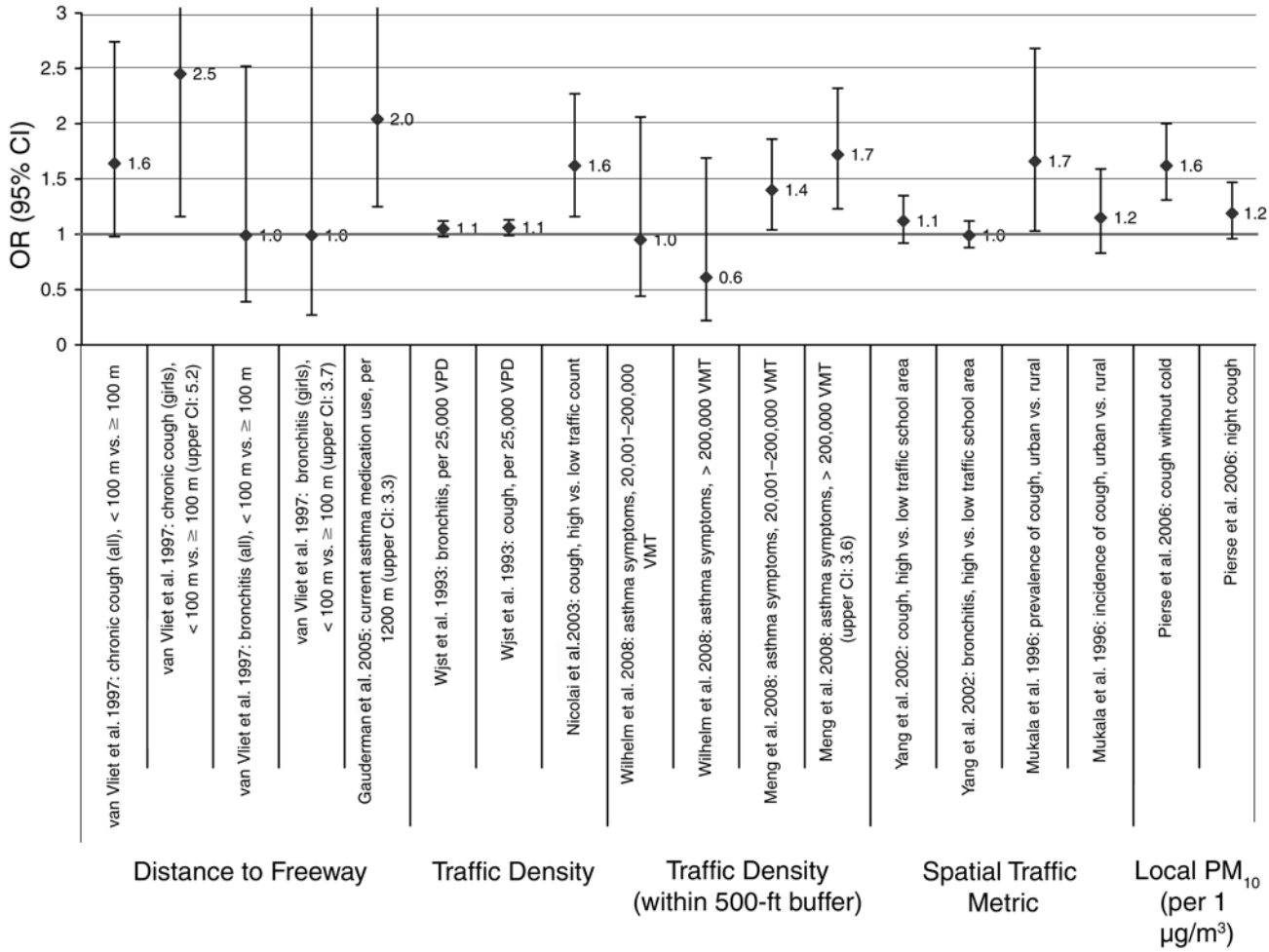

Figure 4.8a. Studies of exposure to traffic pollution (traffic distance and density, area differences, PM_{10}) and other respiratory symptoms in children (by exposure metric). See Table 4.11 for original data (data in figure have been rounded). Vertical lines indicate 95% confidence intervals. Abbreviation: VMT = vehicle miles traveled.

past year," and "respiratory medication"). Results for wheezing in the past year are shown in Figure 4.7a.

A previously cited study of 1068 Dutch children by van Vliet and colleagues (1997) also reported associations between traffic surrogates and wheezing, asthma attacks, doctor-diagnosed bronchitis, bronchitis during the past year (and rhinitis and atopy; see below), and chronic cough. The children were all living in proximity to freeways with heavy traffic loads (80,000 to 150,000 vehicles per day). Among children living in a home within 100 m of a freeway, traffic density, BS, and NO_2 outside the school were all associated with these symptoms, except for asthma attacks (see Figure 4.7a for results on wheeze for children living within 100 m of a freeway and Figure 4.8a for bronchitis and chronic cough). Stratification by sex revealed stronger and significant results in girls; no associations were revealed in boys. Asthma attacks in girls, but not boys, were associated with truck density (OR: 4.34; 95% CI, 1.12–16.8) and BS (OR: 1.96; 95% CI, 0.3–12.7) (see Table 5 in van Vliet et al. 1997).

A previously cited study by Janssen and colleagues (2003) also reported adjusted associations between traffic characteristics and respiratory symptoms in 2071 Dutch children from 24 schools within 400 m of a motorway. Point estimates of ORs for associations between measures of traffic and pollutants were > 1 for current wheeze (see Table 4.10 and Figure 4.7a), current phlegm, and bronchitis (see Table 4.11). Associations were estimated most precisely only among subgroups with bronchial hyperreactivity or positive skin-prick tests to outdoor allergens. Van Roosbroeck and colleagues (2008) analyzed a subsample of the same data and used validation studies to correct

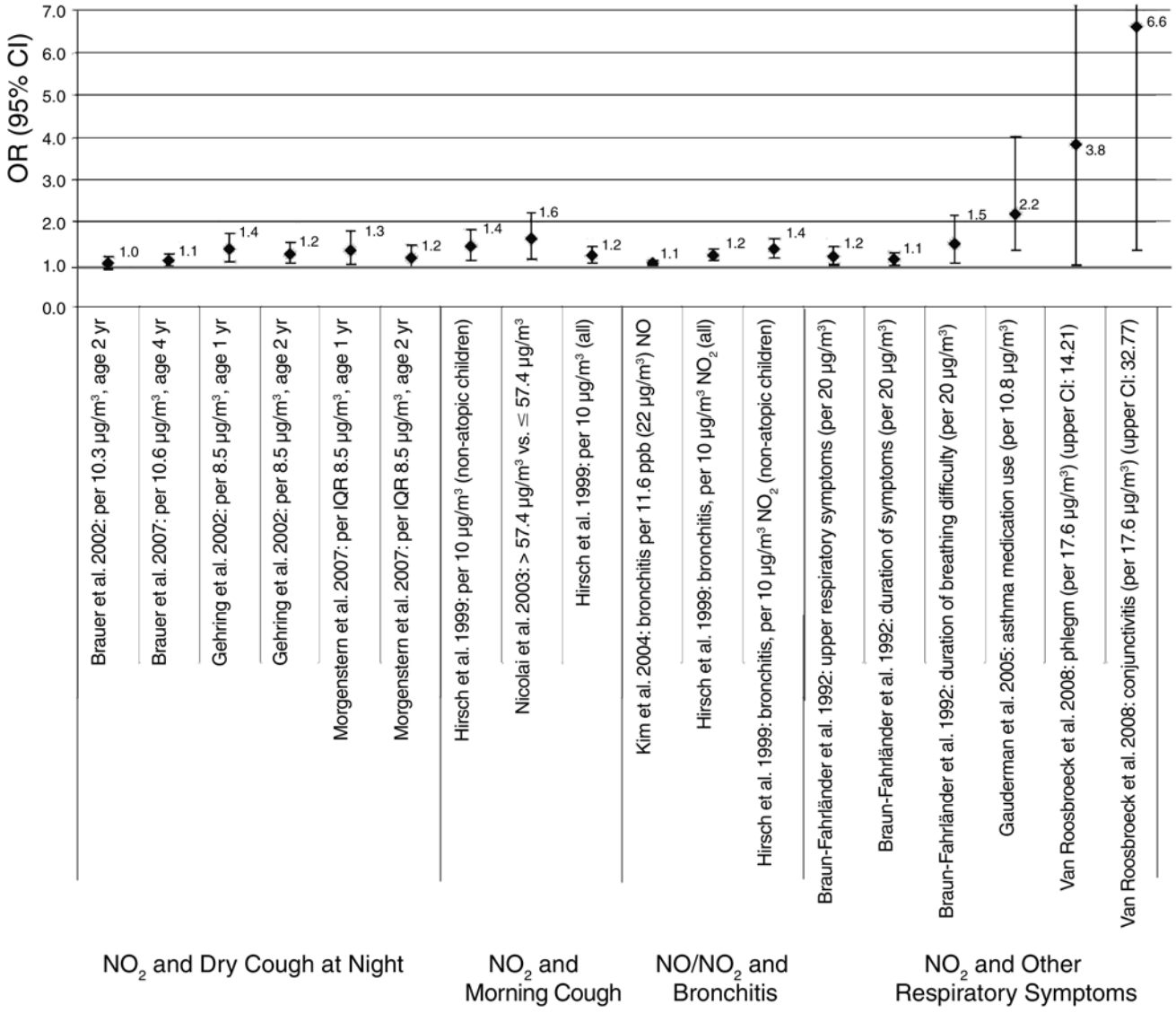

Figure 4.8b. Studies of exposure to traffic pollution (per unit increment in NO and NO_2 concentrations) and other respiratory symptoms in children. See Table 4.11 for original data (data in figure have been rounded). Vertical lines indicate 95% confidence intervals.

for exposure-measurement errors. This revealed substantial underestimations of the original risk estimates for "current phlegm" and "current conjunctivitis" as well as for "current wheezing." However, estimates for the latter did not reach statistical significance (ORs = 2.15 [95% CI, 0.59–7.74] per 9.3 µg/m^3 soot and 2.94 [95% CI, 0.85–10.18] per 17.6 µg/m^3 NO_2) (Figure 4.7b). Prevalence ORs were more than twice the size after adjusting for measurement error for phlegm (2.24 increased to 5.29 for soot, and 1.76 increased to 3.82 for NO_2) (Figure 4.8a).

A previously cited study by Wjst and colleagues (1993) reported results for symptoms for each increase of 25,000 cars per day that passed through a Munich school district. Wheezing, dyspnea, common cold, cough, and recurrent bronchitis were all associated positively with traffic density, adjusted for SES and a range of covariates. ORs were 1.08 (95% CI, 1.01–1.16) for wheezing (Figure 4.7a), 1.10 (95% CI, 1.00–1.20) for dyspnea, 1.20 (95% CI, 1.08–1.34) for colds, and 1.09 (95% CI, 1.00–1.18) for croup. ORs for bronchitis and cough are shown in Figure 4.8a.

Hirsch and colleagues (1999), who studied children living in Dresden, reported mostly significant associations between individually assigned distance-weighed mean benzene, NO_2, and CO and wheezing, bronchitis, and

cough in the last 12 months (Hirsch et al. 1999) (Figure 4.7b for wheezing and Figure 4.8b for bronchitis and cough). The model adjusted for SES, maternal smoking, pets, dampness, and other covariates. All three symptoms were associated positively with the three surrogates of traffic-related pollution although for wheezing the increase was not significant. As was the case for asthma prevalence cited previously, these associations were observed only in children who were non-atopic. As noted previously, it is not clear to what extent the 1 × 1-km monitoring grid used in the study captured local exposure characteristics along busy roads.

Venn and colleagues (2000) investigated the association between reported wheezing and local traffic activity in 22,968 primary- and secondary-school children in Nottingham, United Kingdom. The study underscored the need to capture "traffic exposure" within a rather narrow buffer around traffic arteries. Traffic flow was measured at schools to derive a traffic-density index for the 1 × 1-km grid that contained the school. Findings were largely null. The limitation of the large 1 × 1-km grid was addressed in a reanalysis (Venn et al. 2001) that was restricted to children living within 150 m of a main road. Within this buffer, the occurrence of wheezing was associated significantly with distance from the roads. For each 30 m change, wheezing prevalence increased. Stratification by sex revealed that the associations were present in girls only (OR = 1.14; 95% CI, 1.01–1.28) (see Figure 4.7a).

A later study by Venn and colleagues (2005) used a sample population that included 1413 children under age 16 and 2179 adults in Ethiopia. As in the earlier study by Venn and colleagues (2000) in Nottingham, wheezing prevalence was similar for those living within and outside 150-m buffers. Among the subjects within the 150-m buffer, however, distance to traffic was associated significantly with wheezing prevalence, showing an increase of 1.17 (95% CI, 1.01–1.36) per 30-m change in proximity to a main road (Figure 4.7a). Adjustment was made for age, sex, SES, and kerosene use. In general, traffic density was low, and traffic was usually restricted to a few arteries.

Pierse and colleagues (2006) investigated a random sample of children recruited from Leicestershire, United Kingdom, on two occasions (in 1998 and in 2001) to examine the associations between symptoms (wheezing, cough without cold, and nighttime cough) and exposure to traffic-related pollution. The pollution was characterized using a small-scale PM_{10}-dispersion model that accounted for locally generated PM_{10} (on a 50 × 50-m grid), traffic flow, and wind directions. Modeled estimates of local PM_{10} concentrations were assigned individually to each residence. The data for wheeze are presented in Table 4.10; the data for cough are presented in Figure 4.8a and Table 4.11. The incidence of wheeze and cough symptoms was associated with increased exposure to traffic PM_{10}; in both the 1998 and 2001 surveys several estimates reached statistical significance. The data showed that, among those free of symptoms in 1998, the reporting of symptoms at follow-up was associated significantly with local PM_{10} concentrations for all three symptoms.

A study by Krämer and colleagues (2000) focused on allergy-related symptoms in 317 children, age 9 years, who were living close to busy roads in Düsseldorf. Concentrations of home outdoor (interpolated from measurements of multiple sampling points) personal NO_2 concentrations were used as markers for traffic-related pollution. The home outdoor concentrations, but not the personal concentrations, were associated with wheezing after adjustment for sex, socioeconomic status, and older siblings. Results were significant in girls and in an urban subsample.

Pikhart and colleagues (1997) used survey data from the Small Area Variations in Air pollution and Health Project (SAVIAH) on 3680 children, ages 7 to 10 years, from the Prague region. NO_2 exposure was estimated using a linear regression model (that included measurements taken at 80 locations during four 2-week periods, traffic volume, altitude, and land cover) and kriging. Individual assignments of exposure were based on the location of homes and schools. Models were adjusted for age, sex, traffic noise, SES, and other covariates. Both home and school NO_2 was associated with wheezing or whistling during the last 12 months in unadjusted models but reached statistical significance only for the schools. Unfortunately, interpretation of these results is difficult, because the models contained home and school NO_2 as well as traffic-related noise, all of which were correlated. Yang and colleagues (2002) compared symptoms for > 6000 children sampled from two schools, one with high and one with low traffic density, in Taiwan. The authors' results are difficult to interpret, because the higher prevalence of cough, wheeze, dyspnea, bronchitis, upper respiratory symptoms, and asthma in the highly exposed school could be explained by other local factors.

The next group of studies reported only on the association between exposure to traffic-related pollution and various respiratory symptoms. The results are shown in Figures 4.8a and 4.8b and Table 4.11.

Braun-Fahrländer and colleagues (1992) conducted a panel study with 625 children living in two Swiss cities. NO_2 as a surrogate of traffic-related pollution was measured inside and outside homes during a 6-week period. The 6-week incidence of cough was not associated with the outdoor NO_2. An increase of 20 $\mu g/m^3$ in outdoor NO_2

was associated with the incidence of upper respiratory symptoms (OR = 1.19; 95% CI, 0.99–1.42) (Figure 4.8b), which decreased somewhat in a model that included background pollution based on total suspended particulates measured at a central monitor (OR = 1.14; 95% CI, 0.93–1.40). The duration of any episode of symptoms was associated significantly with NO_2 (OR = 1.13; 95% CI, 1.01–1.27) as was duration of breathing difficulties (OR = 1.50; 95% CI, 1.04–2.16) (Figure 4.8b).

In a study by Kim and colleagues (2004) of children in the San Francisco Bay Area, discussed earlier in connection with asthma prevalence, bronchitis symptoms were associated with NO_x, NO_2, NO, and black carbon (measured at schools) in a sample of approximately 1100 children (see Figure 4.8b). Again, results were stronger in girls, and the authors stated that the association was driven by children with a history of asthma. In their subsequent analyses of the same children, Kim and colleagues (2008) reported an association between bronchitis symptoms and GIS-derived exposure estimates based on proximity to traffic to children's homes (expressed as traffic density at different distance to the residence or as distance from the residence to a freeway). The results were similar to those noted for "current asthma," showing clearer associations with distance than with traffic density. Most of the associations were not significant, however, except for the OR for the log distance to freeways or highways (OR = 1.47; 95% CI, 1.11–1.96) (not shown in Figure 4.8).

Two recent cross-sectional studies that used the 2005 California Health Interview Survey also reported on the prevalence of symptoms (Meng et al. 2008; Wilhelm et al. 2008). The California Health Interview Survey is a geographically stratified random-digit-dialed sample of California households. In the study by Wilhelm and colleagues (2008), daily and weekly symptoms were not associated with traffic density (Figure 4.8a); emergency-department visits among those with doctor-diagnosed asthma ("asthma ever") were associated (see section 4.IV.2.E). Meng and colleagues (2008) reported a significant association between "frequent" (daily or weekly) asthma symptoms and traffic density in a 500-ft buffer (OR = 1.72 [95% CI, 1.23–2.32] for > 200,000 versus ≤ 20,000 vehicle miles traveled per square mile) (Figure 4.8a); the association was strongest among those below the federal poverty level (OR = 2.80; 95% CI, 1.04–4.91).

Mukala and colleagues (1996) studied respiratory symptoms in a panel of 172 preschool children, ages 3 to 6 years, in Helsinki during seven weeks in winter and eight weeks in spring 1991. Personal NO_2 was measured weekly on each child using Palmes-tube passive samplers. NO_2 concentrations were higher for children living in a central area (27.4 μg/m^3) than in a suburban area (18.2 μg/m^3), where traffic density was noted to be lower. Although stuffed nose and cough were reported significantly more frequently in the central area, personal NO_2 was not significantly associated with symptom prevalence or incidence; the trends were, however, suggestive for cough (Figure 4.8a). Models were adjusted for area, stove type, socioeconomic status, and smoking.

Murakami and colleagues (1990) reported crude prevalences among children, fathers, and mothers from 1100 families living within 20 m, 20 to 50 m, and 50 to 150 m from a road in Japan. Various symptoms were significantly more frequent in the group closest to the road (including asthma-like symptoms, wheezing, severe cold with phlegm in the children; and persistent cough and chronic bronchitis in the parents), but lack of adjustment for confounders precludes further interpretation of the study, which is not included in Table 4.11. Findings from a panel study by Chauhan and colleagues (2003) are also difficult to interpret. The study involved 114 children, ages 8 to 14 years, in Southampton, U.K., with a history of wheezing (in the last 12 months). Based on a diary report of upper and lower respiratory symptoms, a score of ≥ 4 triggered a doctor visit within 48 hours to test nasal aspirates for viral infections. Each child wore Palmes tubes that were changed every seven days. Personal NO_2 before the start of a picornavirus infection was significantly associated with the lower-respiratory-tract-symptoms score and a reduction in the peak expiratory flow (PEF). Although personal NO_2 appeared to be a relevant surrogate for adverse effects, interpreting the results from a traffic perspective is difficult, as the source-specific contributions to NO_2 exposure were not formally investigated; thus, whether NO_2 was mostly a surrogate of gas cooking (as it was considered to be by the authors) or traffic pollution cannot be judged conclusively. Thus the results are not presented in Table 4.11. In addition, comparison of the symptom scores with the findings from other symptom-based studies is not possible.

4.IV.2.E Health-Care Utilization for Respiratory Problems in Children

The assessment of associations between traffic-related pollution and health-care utilization comes with challenges that are, in some respects, inherently different from those of the other outcomes discussed above. Health-care utilization occurs further "downstream" in terms of causation than those outcomes do and depends on various factors that affect the link between health problems and health-care utilization, in addition to any effect of traffic exposure. These factors (such as access to health care, asthma management, treatment, adherence to treatments,

and support in asthma management by parents or the school) may well be associated with socioeconomic factors that may or may not be associated with exposure. None of the following studies was able to control for these factors. Moreover, a common feature of all but two of the studies discussed below (Pershagen et al. 1995; Wilhelm et al. 2008) is the use of registry data with very limited individual-level data (usually only sex and age). Our evaluation is thus based on aggregate data. Although lack of control for individual-level covariates could likely result in a bias toward the null, bias away from the null is also possible. Selected studies' results are presented in Figure 4.9 and Table 4.12.

A case–control study by Pershagen and colleagues (1995) defined cases as children ages 4 months to 4 years living in Stockholm who were admitted to a hospital for the first time with wheezing bronchitis. Concentrations of NO_2 were estimated with a spatial model that included cars per day, velocity, street width, distance from house front to street, type of street, risk of traffic congestion, distance to street crossing. Values were assigned to all lifetime residences and day-care-center addresses of each child. Among girls admitted with wheezing bronchitis, time-weighted, individually assigned NO_2 concentrations were higher than among the controls, who were selected from a population registry. No association was observed in boys (see Table 1 and 3 in Pershagen et al. 1995 and Table 4.12 in this report).

Wilhelm and colleagues (2008) used data from the 2005 California Health Interview Survey on children up to 17 years old. Emergency-department visits among those with doctor-diagnosed asthma ("asthma ever") were significantly associated with traffic density (in three categories), showing a clear trend across the categories and a significant association in the high-traffic-density group, which had more than 200,000 vehicle miles traveled per square mile within a 500-foot buffer around residences (OR = 3.27 [95% CI, 1.08–9.89], adjusted for race, ethnicity, and poverty level [based on income]).

English and colleagues (1999) compared the exposure history of doctor-diagnosed asthma cases and controls among children (≤ 14 years of age) living in a low-income area of San Diego, California, whose exposure was based on traffic density on the nearest street within 550-foot buffer around the residences or the traffic density on the street with the highest density within the buffer. Cases were defined as the first paid claim in the Medical Care Statistics Program of California that appeared with a diagnosis of asthma in the 1993 records. Ages ranged from < 1 year to 14 years. None of the traffic-density measures was associated with paid-claim records related to asthma. However, having two or more medical-care visits on record for children with asthma was associated with traffic volume (measured on the nearest street within the 550-foot buffer). This pattern was not apparent across the traffic-flow quintiles; it emerged only in the top decile, with traffic densities on the nearest street of > 27,500 (90th percentile), > 41,000 (95th), and > 161,000 (99th) cars per day and race-adjusted ORs of 1.86 (95% CI, 0.82–4.18), 2.91 (95% CI, 1.23–6.91), and 3.58 (95% CI, 0.78–16.44), respectively. Although the top decile of traffic density might have captured increases in traffic-related pollution beyond the "background neighborhood" level, the positive result might also have been an artifact or chance finding in the small subset of cases with multiple medical-care visits. Other measures of exposure, such as distance to the nearest road or street with the highest traffic flow, were not correlated with health-care use.

Lin and colleagues (2002) compared the traffic exposure of 417 children admitted to hospitals for asthma with that of children admitted for gastroenteritis or non-traffic accidents (as controls) in Erie County in New York. Three traffic-exposure variables were used: (1) distance from residence to a major state route, (2) proportion of heavy trucks on the state route passing within 200-m and 500-m buffer zones of the residence, and (3) traffic density as vehicle miles traveled on the state routes within these buffers. Similar to other studies, traffic within the larger buffer (≤ 500 m) and overall distances to roads were not associated with hospital admissions, while traffic within 200 m was associated with admissions. The OR for heavy trucks passing within 200 m, for example, was 1.43 (95% CI, 1.03–1.99), and the OR for heavy trucks within 500 m was 0.99 (95% CI, 0.72–1.35). In addition, children admitted for asthma were more likely to live in a residence in the highest tertile of vehicle miles traveled within 200 m (OR = 1.93, 95% CI, 1.13–3.29); but there were no effects for children in the highest tertile of vehicles miles traveled within 500 m. Adjustments were made for age, sex, education, and poverty level (based on income and characterized at the neighborhood level).

Edwards and colleagues (1994) examined the risk of hospital admission for asthma in young children (< 5 years of age) in Birmingham, U.K. Residential locations of admitted asthma cases were compared with a random sample of comparable young children admitted for other causes. Analyses were unadjusted. The children admitted for asthma were significantly more likely to live in areas with heavy traffic flow, to have high traffic along the nearest adjacent street, or to live less than 200 m from a main road. Among those living within 500 m of major roads, traffic flow was associated with hospitalization. SES was

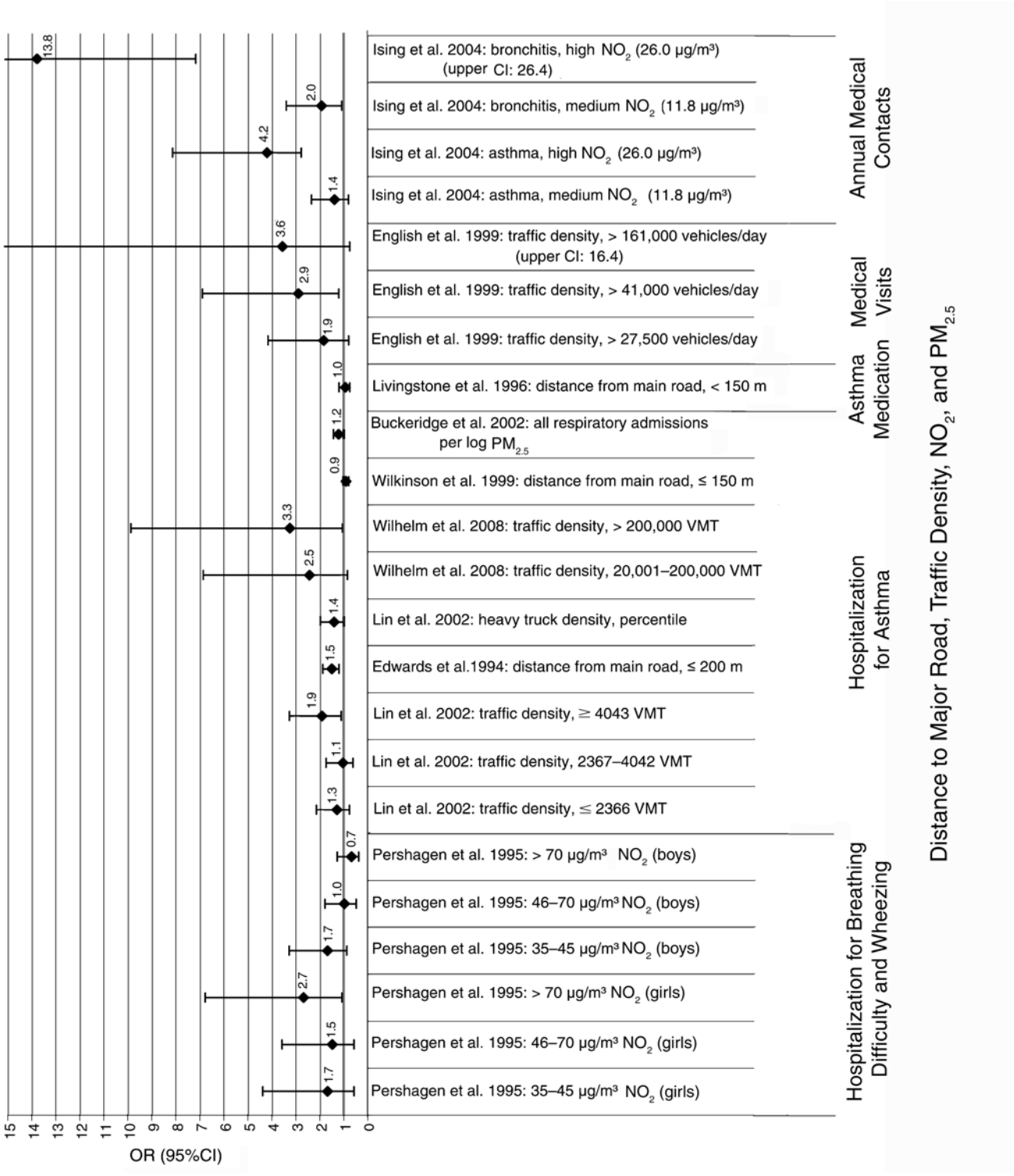

Figure 4.9. Studies of exposure to traffic pollution and health-care utilization in children (by outcome). See Table 4.12 for original data (data in figure have been rounded). Vertical lines indicate 95% confidence intervals. Abbreviations: VMT = vehicle miles traveled.

not controlled. In general, the study observed higher hospitalization rates (for all causes) among children living within 200 m of main roads. Lack of adjustment for SES makes it very difficult to evaluate the actual contribution of traffic to the increase in hospitalization rates.

Livingstone and colleagues (1996), cited earlier, did not find an association between asthma-drug prescriptions and proximity (≤ 150 m) to busy roads in children (ages 2 to 15 years) in London.

Buckeridge and colleagues (2002) analyzed the ecologic association between hospitalization rates in census areas of Toronto and traffic-related modeled $PM_{2.5}$. The model integrated emissions and dispersion and considered 10-m buffers around streets (based on the observation reported by others that $PM_{2.5}$ concentrations declined to 50% within 10 m of a traffic source). A subset of respiratory hospital-discharge diagnoses was associated with $PM_{2.5}$; genitourinary diagnoses used as controls were not. Crude associations and those adjusted for area-level SES were similar.

Wilkinson and colleagues (1999) found no differences in emergency-admissions rates for asthma between 1992 and 1993 in London compared with other causes (except accidents) in relation to residential proximity to traffic. Rates in children ages 5 to 14 years were not higher among those living within 150 m of a main road than for those farther away. Traffic volumes among those living within 150 m were also not associated with emergency admissions. This ecologic analysis adjusted for age, sex, hospital, and a neighborhood deprivation score (based on census variables of overcrowding, social class, unemployment, and access to car). It is not clear to what extent the latter was associated with exposure. The study did not further partition the 150-m buffer to evaluate associations within buffers of smaller radii, as had been shown to be relevant in other studies in the United Kingdom (Venn et al. 2001).

Ising and colleagues (2004) recruited 371 children from two pediatric offices in Germany. The children were divided into three groups, for low, medium, and high exposure to traffic-related noise and air pollution (based on NO_2 concentrations). The authors determined the contact rates for asthma, bronchitis, and neurodermatitis in the prior 5 years. Although frequent doctor contact because of bronchitis was associated with NO_2, further interpretation of the data is difficult because the authors' analytic approach precluded a clear understanding of the contribution of the traffic-related noise to that of the traffic-related air pollution.

Several studies have made only limited contributions to the evidence base because of methodologic limitations and were not plotted in the figure, listed in the table, or considered in the evaluation of the evidence. Lee and colleagues (2007) compared asthma-related hospital admissions during the 2002 Summer Asian Games in Busan, South Korea, with those of the year before and after (Lee et al. 2007). Regulations were implemented during the games, including restrictions not only on driving but also on industries. As a result, a clear assignment of the reduced hospital admissions to reduced traffic cannot be made. Oyana and Lwebuga-Mukasa (2004) analyzed spatial patterns in asthma-related health-care utilization based on emergency-room visits and hospital registries in the greater Buffalo, N.Y., area. Although asthma-related health-care utilization showed substantial spatial clustering and higher rates in areas closer to main roads, the authors' analyses did not adjust for individual factors and the associations were not quantified. Lwebuga-Mukasa and colleagues (2004) analyzed the ecologic association between the steady increase in truck traffic across the U.S.–Canadian border since 1991 (as a consequence of the North American Free Trade Agreement [NAFTA]) and asthma-related health-care utilization. Increases in health-care utilization were observed in areas with increased commercial-traffic volume (identified by postal code).These positive associations reached statistical significance in 12 postal codes. A post-NAFTA increase in commercial traffic of 24% over pre-NAFTA levels in the postal code closest to a traffic corridor, for example, was associated with a 70% increase in health-care use for asthma. The study lacked information for a quantitative summary of the pre- and post-NAFTA comparisons.

4.IV.2.F Evaluation of the Role of Traffic in the Exacerbation of Respiratory Problems

Among the more than 20 studies that have examined the association between traffic and wheezing, there has been a rather high consistency in the reporting of positive associations; many of the associations have reached statistical significance. This was true particularly for the studies that assigned model-based local concentrations of pollutants, such as NO_2 or soot, to the residence locations of the participants (Pershagen et al. 1995; Oosterlee et al. 1996; Hirsch et al. 1999; Krämer et al. 2000; Brauer et al. 2002, 2007; Janssen et al. 2003; Nicolai et al. 2003; Gauderman et al. 2005; Pierse et al. 2006; Morgenstern et al. 2007; Nordlung et al. 2008) (shown in Figures 4.7a. 4.7b, 4.8, and 4.9). The main exception among the studies was the first German TRAPCA study by Gehring (2002), which found no associations in a small sample of children. However, a subsequent study did find positive, albeit not statistically significant, associations in an analysis using a larger sample but a less valid exposure model (Morgenstern et al.

2007). Of note were results from four studies that indicated larger effects in girls and smaller or null effects in boys (Pershagen et al. 1995; Oosterlee et al. 1996; van Vliet et al. 1997; Venn et al. 2001). However, the evidence for the identification of susceptibility factors was not conclusive.

Studies based on proximity or traffic density have also indicated a role for exposure to traffic in asthma exacerbation and wheezing. Two studies in the United Kingdom by Venn and colleagues (Venn et al. 2000, 2001) made an important observation with respect to the spatial scale of "proximity," demonstrating that associations were very sensitive to the spatial scale over which exposure to traffic is assessed. Consistent with the notion that, depending on the urban structure, traffic-related pollutants may reach urban background concentrations already within some 50 to 100 m from busy roads, health problems steadily decreased in each 30-m buffer reaching baseline levels after 90 m. The small spatial scale appeared to be particularly important in the association between exposure to traffic and the onset of asthma. However, more data are needed to understand the relevant spatial scale of the various pollutants and their related health outcomes.

Exacerbations of cough or dry cough were also associated with traffic-related pollution, with rather consistent findings across various metrics of exposure. Although most studies were not restricted to subjects with asthma, the prevalence of these symptoms is higher among such subjects, and it is very likely — as was remarked upon in one of the studies (Kim et al. 2004) — that the observed associations were also driven by exacerbations of asthma.

We therefore conclude that the evidence is "sufficient" to infer a causal association between exposure to traffic-related pollution and exacerbation of asthma symptoms in children with asthma but the evidence is "inadequate and insufficient" to infer a causal association between exposure and symptoms in children without asthma.

The question thus arises whether the evidence of a role for traffic in the exacerbation of asthma and symptoms in general can be corroborated by the health-care-utilization studies. As shown in Table 4.12, these studies are more heterogeneous than those discussed earlier. Although most studies reported positive associations between traffic exposure and hospital-admission rates, the majority of the studies had somewhat unique methodologic problems. In particular, only two studies used modeled traffic-related pollutants: In one of these studies, hospital admissions were associated significantly with exposure to $PM_{2.5}$ (Buckeridge et al. 2002). In the other, hospital admissions were elevated only among girls for exposure to NO_2 (Pershagen et al. 1995). Moreover, apart from the study by Pershagen and colleagues (1995), these studies were ecologic in nature, and adjustments were limited to sex, age, and sociodemographic factors characterized at the neighborhood level. With regard to the null results reported for asthma-related prescriptions in a study by Livingstone and colleagues (1996) in the United Kingdom, one should bear in mind that filling prescriptions for medications is only a crude surrogate for health problems and that therefore the lack of an ecologic association between prescriptions and traffic exposure does not preclude the possibility that traffic-related pollutants might have caused the health problems. The inconsistent findings of English and colleagues (1999), too, might point in this direction: their null results for payment claims in California contrasted with strong associations for "two or more medical care visits" in the top decile of their study's traffic-density distribution. The findings of Venn and colleagues (Venn et al. 2000, 2001) in the United Kingdom suggested that contrasts in traffic-related pollution probably occurred only within 150 m of the source and then reached background concentrations beyond this distance. This might in part explain the null results observed in the study by Wilkinson and colleagues (1999) for emergency-room visits in the United Kingdom, in which "exposure" was defined simply as being "within 150 m of a main road"; no further distinctions were made within this buffer. Future studies need to evaluate contrasts in pollutants and health problems within the most proximal scale along busy roads. Several studies discussed in this chapter strongly supported the importance of using very local spatial scales (van Vliet et al. 1997; Venn et al. 2000, 2001; Lin et al. 2002). These observations raise questions about the validity of results from studies based on larger distance scales.

In summary, the evidence for the effects of traffic-related pollution on health-care utilization is heterogeneous and "inadequate and insufficient" to infer the presence or absence of a causal relation. However, the non-significant results should not be taken as evidence for a lack of coherence with the other results discussed in earlier in this section, and the positive results do not give much support to the "coherence criterion." Instead, one must acknowledge the inherent methodologic limitations in these studies for making causal inferences.

4.IV.3 TRAFFIC EXPOSURE AND RESPIRATORY-HEALTH PROBLEMS IN ADULTS

There are several few studies on traffic-pollution exposure and health problems related to asthma or other respiratory diseases in adults. Selected results of the studies reviewed (such as respiratory symptoms and health-care utilizations) are shown in Figure 4.10 and Table 4.13.

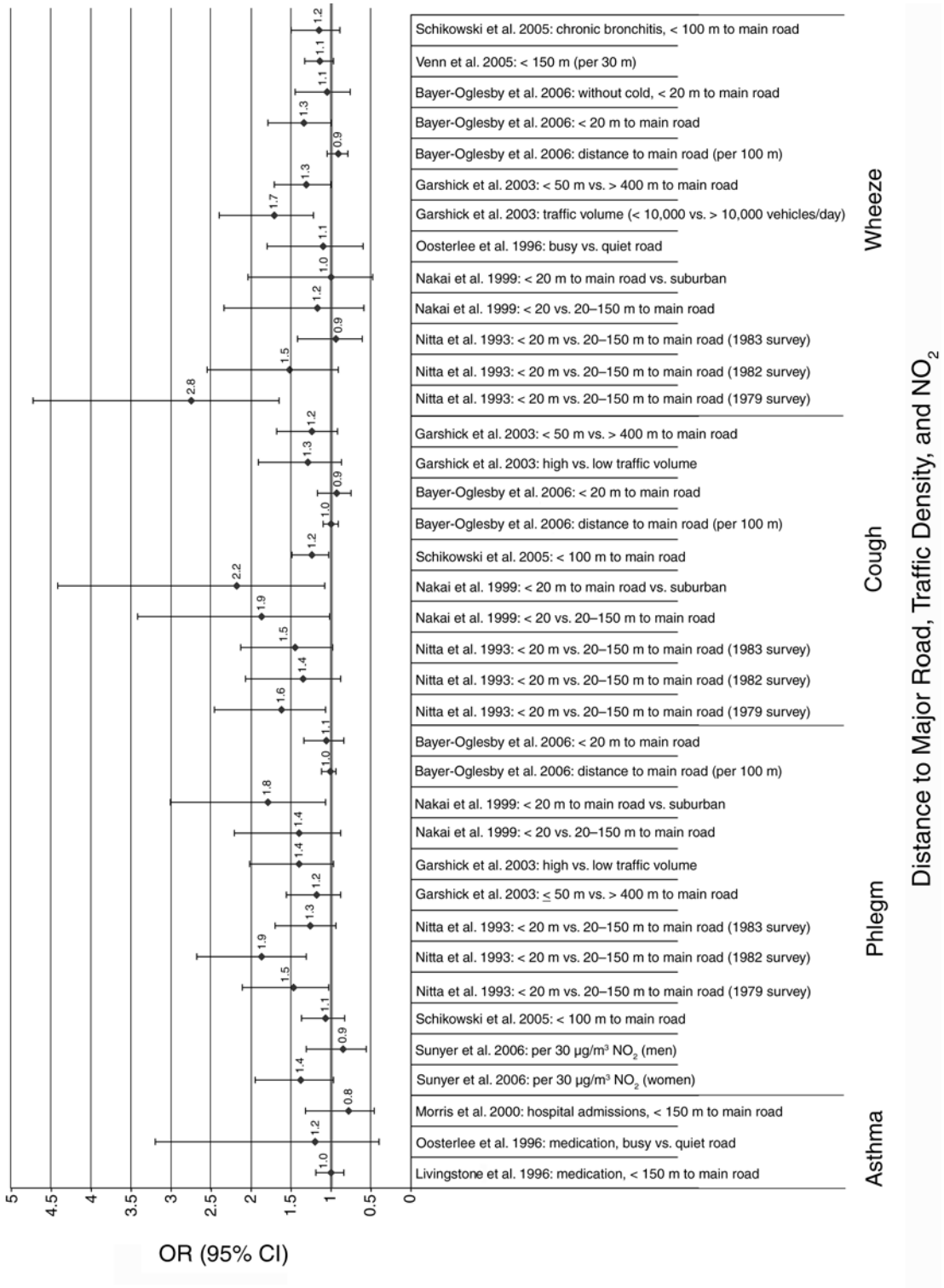

Figure 4.10. Studies of exposure to traffic pollution and asthma or respiratory symptoms in adults (by type of symptoms). See Table 4.13 for original data (data in figure have been rounded). Vertical lines indicate 95% confidence intervals.

4.IV.3.A Asthma Onset During Adulthood

As with the studies of children, it is difficult to distinguish clearly between the onset of asthma and the exacerbation of preexisting asthma in studies based on symptoms or medication use during the previous 12 months. This is particularly difficult in adults, because the apparent onset of asthma in adults could have been a recurrence of childhood asthma, the latter having been underreported in follow-up evaluations until the recurrence in later life. To date, the study by Modig and colleagues (2006) is the only published work that can be interpreted as a study investigating the contribution of traffic-related pollution exposure to adult-onset asthma. In the study, traffic was characterized by measurements of outdoor NO_2 and traffic flow at the subjects' residences. There were 203 incident cases of asthma among all people 20 to 60 years old living in a Swedish town. The cases were age- and sex-matched with 203 control subjects without asthma selected from the Swedish population registry. The "asthma" diagnosis was based on a standardized clinical examination. The subjects with asthma had a tendency to have higher residential exposure to traffic flows and NO_2 concentrations compared with the controls; however, the association between exposure and asthma hospitalization did not reach statistical significance and was only borderline significant for the 67 cases with positive skin tests.

4.IV.3.B Respiratory Symptoms in Adults

Sunyer and colleagues (2006) examined the association between home outdoor measurements of NO_2 and prevalence of symptoms of chronic phlegm reported by participants in a random sample of the European Community Respiratory Health Survey (ECRHS) II (from 21 cities) followed up from 2000 to 2002. NO_2 measurements were conducted up to two times during a 14-day period, and annual means were estimated with adjustment for seasonal variation based on data from a central monitor. Chronic phlegm was associated positively and significantly with NO_2 among 886 women but not in 734 men. ORs (per 30 $\mu g/m^3$ increase in NO_2) were largest in women with > 16 years of education (OR: 1.90; 95% CI, 1.23–2.93) and never-smokers (1.49; 95% CI, 0.77–2.91) compared with an OR = 1.38 (95% CI, 0.97–1.95) for all women. Multi-level models with 20 European cities focused on within-city associations; there was no evidence of heterogeneity of effects across the 20 cities, but statistical power to assess heterogeneity was limited.

Bayer-Oglesby and colleagues (2006) used the previous 12 month's prevalence of respiratory symptoms from the 1991 baseline Swiss Study on Air Pollution and Lung Disease in Adults (SAPALDIA) and the 2002 SAPALDIA follow-up study to investigate associations with traffic exposure. The three traffic metrics used were the distance to the closest main road (per 100 m), the length of main road segments within 200 m (per 500-m increments), and living (or not) within 20 m of a main street. The symptoms evaluated were wheezing with breathing problems, attacks of breathlessness, and wheezing without cold, cough, and phlegm. In most cases, the associations were somewhat stronger in the subsample of never-smokers. In this subgroup, the prevailing pattern across all models was an adverse association between all three measures of traffic and attacks of breathlessness, wheezing, and phlegm; several results reached statistical significance. For regular cough, results were less consistent. Differences in the 1991 and 2002 estimates were reported: The length of main streets within 200 m of residences became less relevant in 2002, and the effects of living within 20 m of a main street on wheezing became stronger. These changes were interpreted to result from changes in the car fleet, fuel formulation, and other factors that might have modified the toxicity of or exposure to traffic-related pollutants. Other explanations that were not considered included chance, changes in population susceptibility, and model misspecifications.

Schikowski and colleagues (2005) investigated the association between traffic and respiratory health among 4757 adult women 55 years of age at examination (between 1985 and 1994) who were living in the Rhine-Ruhr Basin of Germany. Concentrations of PM_{10} and NO_2 were used to characterize background concentrations; distance (with a 100 m cut-off) of the subjects' residences from the nearest road was used as the surrogate of traffic exposure. Doctor-diagnosed chronic bronchitis, chronic cough with phlegm, and frequent cough were all associated with proximity to roads, but only the latter symptom reached statistical significance after adjusting for SES and other covariates. A subsequent study by Schikowski and colleagues (2008) of a subsample with a focus on the contribution of exposure to traffic-related pollution to social differences in respiratory health showed positive association as well, albeit not statistically significant.

Garshick and colleagues (2003) investigated a population sample of 2985 U.S. veterans. Residence within 50 m versus > 400 m of a major roadway was associated with persistent wheeze (OR = 1.31; 95% CI, 1.00–1.71) and less so with chronic cough (OR = 1.24, 95% CI, 0.92–1.68) and chronic phlegm (OR = 1.18; 95% CI, 0.88–1.56). Among subjects living within 50 m of a major roadway, average traffic counts ($\geq$ 10,000 versus < 10,000 vehicles per day) were associated with persistent wheeze (OR = 1.71; 95% CI, 1.22–2.40). Results were stronger among never-smokers. Adjustment for having asthma or COPD did not affect the

results; the effects were similar among those with and without chronic respiratory diseases.

Burr and colleagues (2004) investigated the effect on symptoms of a change in traffic load caused by the opening of a new bypass (see also the children's studies above). A total of 448 adults out of 811 participants provided data both before (1996) and after (1999) the opening of the bypass. Subjects were sampled initially from both a congested and an uncongested area. The opening of the new bypass resulted in substantial decreases in traffic, and air quality improved in both the congested and uncongested areas. Symptoms tended to improve in both areas but more so in the uncongested area after the opening of the bypass. None of the associations were statistically significant. The results are difficult to interpret, because the populations might have changed as the bypass was built, and the air quality improved in both areas (not shown in Figure 4.10).

Nitta and colleagues (1993) reported results from three cross-sectional surveys (1979, 1928, and 1983) of women living within 150 m of heavily trafficked roads in the suburbs of Tokyo. Each survey focused on different suburbs. The prevalence of symptoms was compared across two groups, those living within 20 m and those living between 20 and 150 m of the roads in the first and third surveys and those living within 20 m and those living 50 to 150 m from roads in the second survey. NO_2 concentrations differed between these zones and were highest within 20 m of the road. Adjusted ORs were similar across the three surveys. Data were not pooled. The major inconsistency was observed for wheezing, which showed a strong association for those living within 20 m versus those living between 20 and 150 m of the roads (OR: 2.75; CI, 1.65–4.73) in the 1979 survey (N = 1173), a non-significant association (OR: 1.52; CI, 0.91–2.55) in the 1982 survey (N = 2015), and no association (OR: 0.94; CI, 0.61–1.42) in the 1983 survey (N = 2023). The authors speculated that these results could be explained by changes over time in the region's air pollution. Chronic cough, chronic phlegm, and shortness of breath were positively associated with living ≤ 20 m of the road.

Nakai and colleagues (1999) compared symptom rates among women ages 30 to 59 years living in three zones in Tokyo, i.e., within 20 m of heavy traffic (zone A), 20 to 150 m from heavy traffic (zone B), and in a suburb with light traffic (zone C). Measured and modeled pollutants (NO_x) revealed substantially higher concentrations in zone A; the lowest concentrations were observed in zone C. Chronic cough and phlegm were higher in zone A as compared with both zones B and C. Breathlessness and persistent wheezing were not associated with exposure to traffic.

An Ethiopian study by Venn and colleagues (2005) discussed previously also included adults in its household survey. As mentioned, wheezing increased monotonically per 30-m proximity among those living within a 150-m buffer of traffic arteries, although the arteries had far less traffic than those of the European studies; and again, a comparison between results for those living at distances of < 150 m versus ≥ 150 m showed no association with wheezing.

Oosterlee and colleagues (1996) also sampled adults (see earlier section on children's asthma). One group lived on busy streets with 10,000 to 30,000 vehicles per day; the others lived on quiet streets with little traffic, in the same neighborhoods that had the busy streets. Associations between symptoms or "asthma ever" and traffic were weak or absent (see Table 4 in the original publication).

Murakami and colleagues (1990), cited previously, reported crude associations between the distance to main roads and the prevalence of respiratory symptoms in fathers and mothers from 1100 families in Japan. However, the data were not adjusted for potential confounders and are not considered further here. Lwebuga-Mukasa and colleagues (2004) conducted a survey among 1608 randomly selected households in the Buffalo area. Ultrafine particles were monitored with a P-Trak portable sampling device at 16 locations in two zip codes. The distribution of asthma prevalences followed the estimated distribution of ultrafine particles downwind of the principal truck-traffic corridor that connects the U.S. with Canada. However, the data were not adjusted for individual-level covariates and are not considered further here. Neither study is included in Table 4.13.

4.IV.3.C Health-Care Utilization for Respiratory Problems in Adults

The main results of some of the studies reviewed in this section are shown in Figure 4.10. All studies are included in Table 4.13. Smargiassi and colleagues (2006) compared case hospitalizations (N = 5805) for respiratory diagnoses (ICD-9 codes 460–519) with hospitalizations for three groups of controls (all non-respiratory diagnoses [except trauma and cardiovascular or cancer diagnoses], gastrointestinal diagnoses, and genitourinary diagnoses) among residents ages 60 years and older in Montreal. Data on morning peak traffic volume on the closest segment of road to the residence of the cases and controls were used as the exposure indicator. Respiratory admissions, adjusted for neighborhood SES, were significantly related to traffic density in comparison with all three control groups. Those living in high-traffic locations (with > 3160 vehicles/3-hr morning peak) had an 18% higher admission rate for respiratory problems (OR 1.18; 95% CI, 1.06–1.31) compared with those living off the road network (i.e., not in proximity to the Montreal road network). The OR for those in the intermediate traffic-exposure locations (with

1–3160 vehicles/3-hr morning peak on the nearest road segment) was 1.05 (95% CI, 0.98–1.12) (not shown in Table 4.13). Further adjustment for SES by census dissemination area (the smallest area for which data on SES are available in Canada) strengthened the associations, resulting in significant associations for both the high- (OR 1.24; 95% CI, 1.12–1.38) and intermediate- (OR 1.08, 95% CI, 1.12–1.38) exposure groups, when compared with those for all other diagnoses. Results were particularly strong when respiratory admissions were compared with genitourinary causes of admissions. The potential misclassification of respiratory-discharge diagnoses compared with that of cardiovascular diagnoses was not discussed.

Morris and colleagues (2000) repeated a case–control study to investigate associations between hospital admission rates in eastern London and proximity to traffic (see Figure 4.10). In this area of London, hospital admissions for asthma were 80% above the national average. The cases were subjects ages 15 to 90 years old who were admitted in 1991 and 1992 with a diagnosis of asthma or COPD. The controls were subjects with non–chest-related admissions (except surgical and trauma admissions) and were matched individually on sex, year of admission, and consultant team. Distance to major roads (≤ 150 m) was not associated with respiratory admissions. The analysis adjusted for age, sex, ethnicity, and a socioeconomic deprivation index. Smoking data were not available. The inclusion of cardiovascular causes of admission (such as for stroke) — which are possibly associated with traffic-related pollution — in the control group might have attenuated these associations. A further subdivision of the 150-m buffer was not discussed.

Livingstone and colleagues (1996), cited earlier, did not find an association between asthma-drug prescriptions and proximity (≤ 150 m) to busy roads in adults (ages 16 to 64 years) (see Figure 4.10).

4.IV.3.D Evaluation of the Role of Traffic in Respiratory Health in Adults

The role of traffic-related pollution in adult-onset asthma is not established; indeed it has been investigated in only one study (Modig et al. 2006). The evidence is thus "inadequate and insufficient" to infer a causal role. Further studies are needed, and these might need to be substantially larger. In fact, a recent study (Jacquemin et al. 2009) based on European Community Respiratory Health Survey data (on 4185 subjects) appeared to confirm the findings of Modig and colleagues (2006) (on 406 subjects) but did not have sufficient power to investigate the presence of susceptible subgroups.

With one exception (Sunyer et al. 2006), all symptom-based studies have relied on proximity or density measures rather than traffic-specific pollutant measurements or models. The model-based findings of Sunyer and colleagues (2006) were positive only in women, and the 1 × 1-km NO_2 model used in the ECRHS data on which the authors' study was based might not necessarily have reflected "traffic" on the small spatial scale that is the focus of this review. All proximity-based studies reported clearly positive and mostly statistically significant findings for wheezing, cough, or phlegm. As with the other studies reviewed here, however, meta-analytic pooling of the estimates is not warranted, because the same "proximity" might stand for different kinds and concentrations of traffic-related pollution and different kinds of exposed populations. Figure 4.10, a graphic presentation of the study findings, suggests consistently positive associations between symptoms and exposure to traffic-related pollution. Overall, in our view, these findings are "suggestive but not sufficient" to infer a causal role for traffic in the exacerbation of respiratory symptoms among adults.

The few studies in adults that are available did not provide much detail about effect modification. It is therefore not possible at this time to identify susceptibility factors with any precision. Findings for men and women appear to differ, but there are not enough data to draw firm conclusions.

The evidence on associations between traffic-related pollution and hospital admissions for respiratory problems was not consistent. The study in Montreal (Smargiassi et al. 2006) provided strong evidence that those hospitalized for respiratory conditions were more likely to live near traffic hot spots than those hospitalized for genitourinary diseases. In contrast, the two studies in the United Kingdom (Livingstone et al. 1996; Morris et al. 2000) presented what amounted to null findings. Both the lack of further partitioning of the 150-m buffer and the inclusion by Morris and colleagues of cardiovascular causes of admissions in the control group further hampered interpretation of the data.

4.IV.4. SUMMARY

For children there is "sufficient evidence" to infer a causal role for traffic-related pollution in the exacerbation of asthma and "suggestive but not sufficient evidence" to infer a causal role for traffic in the onset of asthma. There is "suggestive but not sufficient evidence" to infer a causal role for traffic in the exacerbation of symptoms in adults.

More data are needed to understand the contribution of exposure to traffic-related air pollution to the onset of adult asthma and potential interactions between asthma

treatment and health-care utilization. The evidence is not sufficient to unambiguously characterize the subgroups of children or adults who might be at higher risk from exposure.

4.V. TRAFFIC EXPOSURE, LUNG FUNCTION, AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

4.V.1 INTRODUCTION

Standardized spirometry can provide a range of functional measurements that are related to respiratory health (American Thoracic Society 1979). Volumetric measures, such as forced vital capacity (FVC) or forced expiratory volume exhaled during the first second of a spirometric test (FEV_1), are used widely to monitor health. FEV_1 and the ratio FVC/ FEV_1 are used to classify the degree of airway obstruction in cases of asthma and COPD. Spirometry can also provide measures of air flow at various points in time during exhalation, such as the maximum achieved flow (peak expiratory flow [PEF]) or the flows at 25%, 50%, or 75% of the exhaled volume, known variously as the maximum expiratory flows (MEF_{25}, MEF_{50}, and MEF_{75}) or forced expiratory flows (FEF_{25}, FEF_{50}, and FEF_{75}). Another often-used measure is the integrated mean flow during exhalation from 25% to 75% of the total volume ($MEF_{25–75}$ or $FEF_{25–75}$). The latter flows and the flows at low lung volumes (e.g., FEF_{75}) are correlated and have been shown, particularly for FEF_{75}, to reflect the status of small airways, which are the principal sites of chronic obstruction in asthma and COPD. FEV_1 or PEF are more affected by the functional properties of the larger airways (Bates 1989).

Modern spirometers are able to provide multiple measures of lung function, particularly those related to small airways. Many studies, however, have not reported associations between exposure to air pollution and the full range of modern spirometric measures. At the population level, fortunately, these measures tend to be highly correlated, and associations with risk factors thus tend to be similar (with the possible exception of FVC, an indicator of lung size). Because FVC and FEV_1 have the smallest within-subject measurement error and have been used in epidemiologic studies for many decades, they are reported most frequently. Alteration of small-airway function is considered an early preclinical marker of pathologies that are associated with exogenous risk factors, such as smoking, and is thus of particular importance and is now being reported more frequently in studies of health effects associated with air pollution.

This review will not discuss associations between traffic-related air pollution and every measure of lung function. Instead, we refer to "lung function" and present the markers used in the various studies — primarily FVC and FEV_1 and, less frequently, measures of small-airway function. However, two points need to be emphasized: First, PEF, a measure of large-airway obstruction, shows substantial within-subject variation over time; for this reason it is widely used in the short-term monitoring of asthma to assess short-term variations in obstruction, a hallmark of asthma. In this sense, then, PEF is a proxy for the state of asthma and as such is an outcome comparable to the occurrence of symptoms or the use of medication among people with asthma. For these reasons, PEF will not be highlighted in this section; and in fact only two studies provided results for PEF (Chauhan et al. 2003; Burr et al. 2004). Second, the ratio of FEV_1/FVC presents two problems — in its combined use of two functional measures (which has implications for modeling and interpretation) and in its role in defining and assessing the stages of COPD (Vollmer et al. 1987; Halbert et al. 2006). In fact, because stage I COPD is based on a statistical cut-point for this ratio, questions are raised about its specificity for the diagnosis of early COPD.

Measures of lung function such as FVC and FEV_1 are valid markers of health that reflect cumulated exposure to exogenous and endogenous factors that might have adverse health consequences. Within populations, lower levels of lung function are associated strongly with future morbidities and are a strong, well-known predictor of life expectancy (Hole et al. 1996). Although lung function varies in the short term, age-related changes and between-subject variability play a dominant role in a person's measured lung function at any given point in time. Accordingly, cross-sectional studies primarily reflect lung function as a result of long-term histories of exposure to relevant factors superimposed on short-term variations in function caused by recent exposures or physiologic factors (such as diurnal variation). If air pollution also affects the growth or decline of lung function over time, cross-sectional studies are expected to show associations between an achieved level of lung function and both the cumulated long-term and recent short-term history of exposure. Conditional on the availability of both long-term and more recent exposure data, cross-sectional studies can be used to assess simultaneously the associations between both long- and short-term exposures and lung function (Ackermann-Liebrich et al. 1997; Schindler et al. 2001).

In contrast to cross-sectional studies, cohort studies are better suited to investigating changes in lung function over time that result from all endogenous and exogenous factors

experienced during a defined past time period. Longitudinal cohort studies can also assess how changes in exposure affect changes in functional lung development or decline. However, follow-up times need to be long, particularly among middle-aged adults, because of the rather slow decline of lung function. Both in cross-sectional and longitudinal analyses, healthy-survivor effects (the tendency for healthy people to remain in a workforce or other population, while unhealthy people are removed) and the fact that the ability to perform high-quality lung-function tests might depend on health status tend to result in underestimated associations with exposures.

All these approaches have been used in air-pollution epidemiology. A recent review concluded that there is strong evidentiary support for an adverse effect of air pollution on lung function in children and adolescents (Götschi et al. 2008). The effect on the decline of lung-function growth in adults are less conclusive; only one follow-up study in adults has been published (Downs et al. 2007). Only a fraction of these studies qualified for this review, because many of them were based on general assessments of exposure to urban air pollution rather than on more specific assessments of exposure to traffic-related pollution, as defined for this review.

Similar to what is observed for other health outcomes, a history of smoking (apart from age) is a very strong (if not the strongest) predictor of lung-function development, level, and decline. To the extent that smoking might be correlated with exposure to traffic-related air pollution because of the correlation between SES, smoking, and the environmental quality of neighborhoods, smoking and — particularly among children — exposure to secondhand smoke are of concern as potential confounders or modifiers of the effects of exposure to traffic-related pollution (Marshall 2008). Studies with appropriate adjustment for smoking and, in particular, studies that report associations among never-smokers are thus more valid sources of inference.

4.V.2 LUNG FUNCTION

The studies discussed in the following subsections include studies conducted in children and adults. Selected results are included in Figures 4.11a and 4.11b and Table 4.14 (at the end of the chapter). The studies in the figures are grouped according to the reported measure of lung function (e.g., odds of low FEV_1 and percent decline in FEV_1). Studies that reported FEV_1 declines expressed in mL (instead of percentages) and that did not provide the FEV_1 predicted or any confidence intervals are not shown in the figures.

4.V.2.A Cross-Sectional Studies of Long-Term Exposure

Studies Conducted in Children and Adolescents Several studies have compared the relation between traffic-related exposures within communities with lung-function measures in children. All but one (Fritz and Herbarth 2001) controlled for secondhand-smoke exposure.

Wjst and colleagues (1993) reported significant associations between traffic density in Munich school districts and measures of expiratory flow (PEF and MEF_{25}) in 4320 children, ages 9 to 11 years (see Figure 4.11b). For each increase of 25,000 cars per day that passed the district, MEF_{25} was estimated to decrease by 0.68% (95% CI, −1.11 to −0.25). Traffic-density contrasts ranged from 7000 to 125,000 cars/day. Models were adjusted for the daily number of cigarettes smoked at home, use of gas or coal, test compliance, month of examination, sex, height, weight, and parental history of asthma. Children who lived in the same residence for less than five years and those who reported respiratory infections at examination were excluded.

Hirsch and colleagues (1999) used data from an extensive measurement campaign (SO_2, NO_2, CO, benzene, and ozone) conducted on a 1-km^2 grid in Dresden (see Figure 4.11a). Estimated annual mean concentrations of these outdoor pollutants were assigned individually to the home locations of approximately 1130 children, ages 9 to 11 years. The authors found a significant association between home outdoor benzene (as a marker of traffic-generated pollution) and having $FEF_{25-75} < 70\%$ predicted. Results for FEV_1 were not significant nor was any result for any other marker of pollution, including NO_2. The contrasts in the assigned exposures were rather limited, such as an NO_2 IQR of 10 μg/m^3, for example. We also note that the 1-km^2 grid might have been too large to provide a reasonable assessment of local traffic-related exposure. Models were adjusted for maternal smoking and several covariates that included proxy measures of SES. Some might have led to overadjustment of the associations if SES was highly correlated with proximity to traffic and was not evaluated as an effect modifier.

Fritz and Herbarth (2001) conducted a descriptive study of lung function in relation to traffic pollution in 235 5-year-old preschoolers in Leipzig (see Figure 4.11b). Various pollutants were measured at and near the daycare centers ($N = 16$) of these children, and benzene ("low" versus "high") was used as a surrogate for local traffic-related pollution while SO_2 was used as a surrogate for coal heating based on an earlier source-apportionment analysis (Rehwagen et al. 1999). FEV_1 and FVC were both lower in the areas with heavy traffic (that had either high or low coal heating) than in areas with low traffic. The FEV_1/FVC ratio

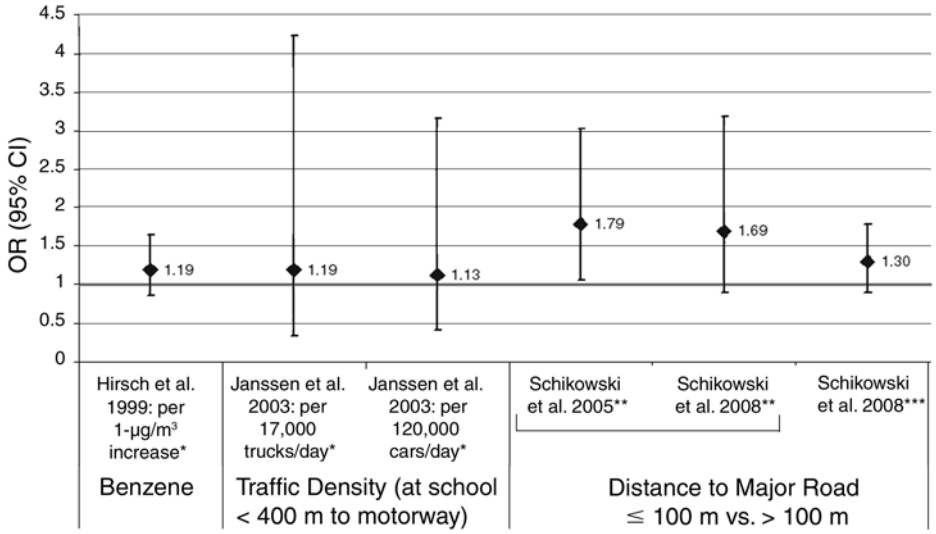

Figure 4.11a. Studies of exposure to traffic pollution and lung function (odds ratios for FEV_1 or FEV_1/FVC) in children and adults (by exposure metric). See Table 4.14 for data. Vertical lines indicate 95% confidence intervals. *In children; FEV_1 < 85% predicted. **In adults; FEV_1/FVC < 0.7. ***In adults; FEV_1 < 80% predicted.

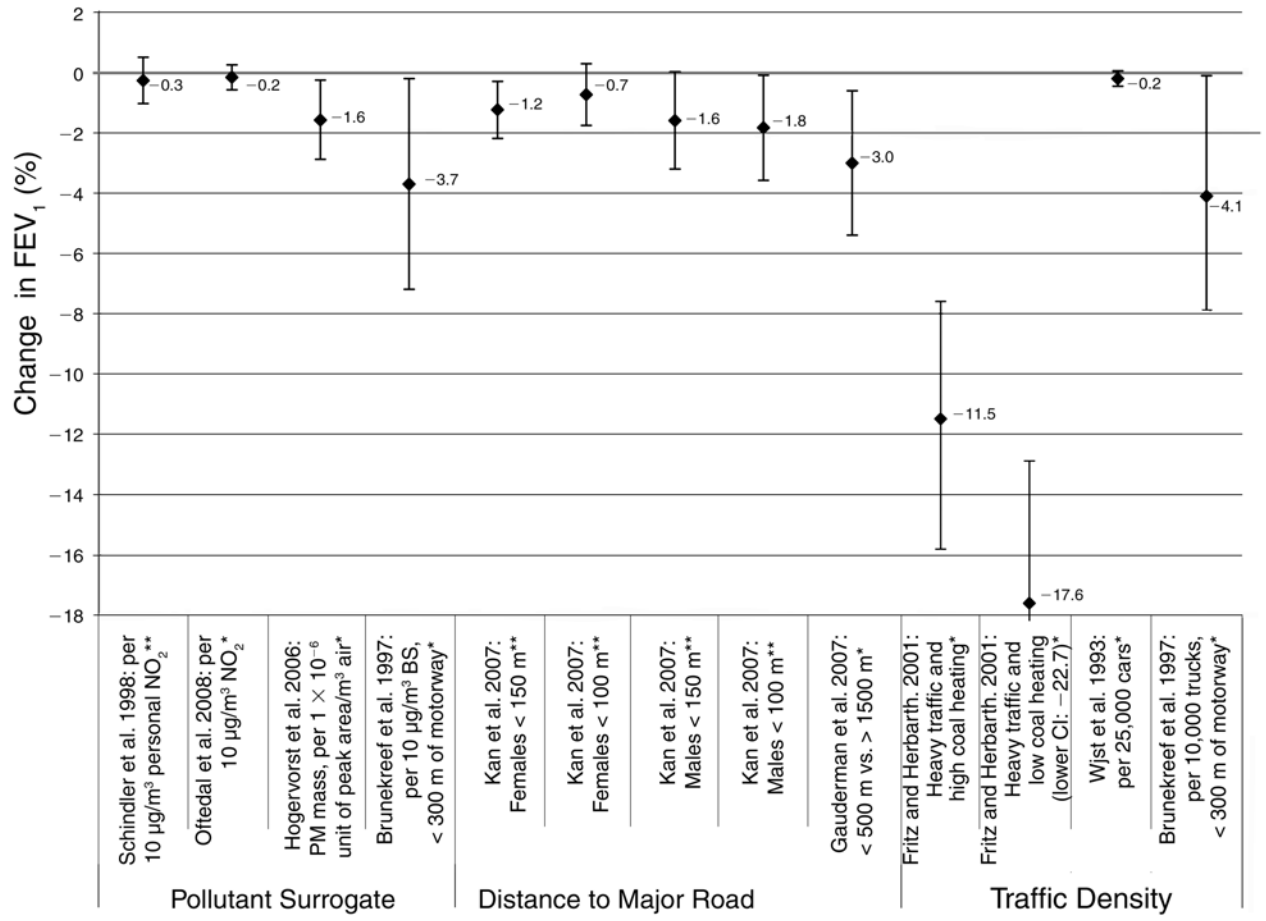

Figure 4.11b. Studies of exposure to traffic pollution and lung function in children and adults (percentage decline in FEV_1) (by exposure metric). See Table 4.14 for original data (data in figure have been rounded). Vertical lines indicate 95% confidence intervals. *In children. **In adults.

was similar across the categories of exposure, indicating similar proportional decreases in FEV_1 and FVC. Exposure to secondhand smoke was common but not directly controlled, which hampers the interpretation of results. Assignments of the authors' findings to traffic-related pollution is questionable given the method used to define exposure.

Brunekreef and colleagues (1997) studied 877 Dutch schoolchildren who lived within 1000 m of motorways in six areas of the Netherlands (Figure 4.11b). The authors found negative associations between weekday counts of truck- (but not car-) traffic density and decreases in various lung-function indicators (FEV_1, PEF, and FEF_{25-75}) that ranged between −2.5% and −8% (per 10,000 trucks). Changes in BS and NO_2 (measured inside the schools) were also correlated negatively with lung function, but most estimates did not reach statistical significance (not in Table 4.14). After restricting the analysis to children living within 300 m of a motorway (N = 308) the estimated effects of truck-traffic density were similar and that of BS increased. In a second study of the same design that included 24 schools, the same Dutch research group could not reproduce fully its earlier findings on lung function, although the associations between traffic indicators and symptoms remained (Janssen et al. 2003). In this study, higher truck- and car-traffic densities as well as BS and NO_2 concentrations for children in schools within 400 m of a motorway were associated with increased odds of low FEV_1, but the estimates did not reach statistical significance (Figure 4.11a). The reason for the discrepancy between the two similar studies is not clear. Although the level and range of traffic densities tended to be higher in the second study, the contrasts for BS and NO_2 concentrations were larger in the first study, which was based on only a short measurement campaign, compared with the second study and its more comprehensive exposure model. The differences in the exposure assessments preclude a clear explanation for the discrepant findings. Both studies adjusted for smoking.

Gauvin and colleagues (2001) analyzed the association between spirometry (FEV_1 and PEF) and NO_2 exposure (measured with personal and fixed monitors) and a "traffic index" based on traffic density and distance to roads (within 300 m buffer) from homes and schools, weighted by the time each child reportedly spent at these locations (results not shown in Figures 4.11a or 4.11b). The study was conducted in four French cities. The traffic index was correlated negatively with FEV_1 among the subjects in two of the cities and was statistically significant in one city. The association with PEF was inconsistent across cities. Personal NO_2 concentrations, monitored with passive samplers carried for only 48 hours, were not associated with lung function. The strongest predictors of personal NO_2 concentrations were the traffic index, cooking with gas, and outdoor pollution (measured at the closest fixed-site monitor). The study thus confirms that personal measurements of NO_2 do not necessarily represent a gold standard for assessing exposure to traffic-related pollution, because personal monitors are also affected by indoor sources of NO_2. The simpler traffic index was not affected by this inherent limitation of personal NO_2 monitoring. The city means of the index ranged from 1.7 to 6.5 units, but the quantitative meaning of this with respect to a specific exposure cannot be determined. Fifty percent of the children had asthma. The model did not adjust for the use of asthma medication but did adjust for second-hand smoke.

Nicolai and colleagues (2003) used traffic counts within 50 m of residences and an emission-based NO_2 model that considered stop-and-go traffic characteristics to assign exposure to 2019 children, ages 9 to 11 years, in Munich. Traffic counts were not associated with lung function despite significant adverse effects on respiratory symptoms (see section 4.IV.2.D). Because spirometric measures and spirometric changes were not specified, this study is not included in Table 4.14. No details (e.g., adjustment) were provided for these negative results, but secondhand smoke and a range of covariates were available and used in the symptom analyses (see section 4.IV.2.D on symptoms and section 4.VI on allergy). Contrasts in the assigned NO_2 concentrations were rather limited, at 43 to 47 $\mu g/m^3$ in the lowest tertile and > 57 $\mu g/m^3$ in the highest.

Hogervorst and colleagues (2006) used oxygen-radical (OH·) formation by particles in vitro as a novel marker of exposure. OH· radicals more directly reflect the oxidative properties of particles than the usual mass concentration does. OH· might thus provide a surrogate of exposure relevant to oxidative stress and inflammation. In 342 Dutch children, ages 8 to 13 years, from six schools varying in distance to and density of traffic, lung function (FEV_1, FVC, and FEF_{50}) was not associated with traffic density around the school; the analyses focused more on models with PM (mass and radical-generating capacity), which were collected at the playground of each school. However, for this review, these markers are not necessarily considered specific for traffic exposure. The investigators found negative associations for the $PM_{2.5}$ radical-formation capacity and FEV_1, FVC, and FEF_{50}; only the association with FEV_1 was statistically significant (Figure 4.11b). PM mass concentrations were not associated with lung function except in a few models, indicating even better function at higher PM concentrations. Models were adjusted for age, height, sex, and smokers at home. Exposures were assigned by school. Traffic densities ranged from 3400 to 9500 vehicles/day (250-m buffer) across five of the

schools; the sixth school had 45,000 vehicles/day. $PM_{2.5}$ mass concentrations varied very little. OH· formation appeared to be more strongly affected by traffic and had approximately a sixfold range across the schools.

Holguin and colleagues (2007) conducted a four-month panel study with 200 Mexican children with and without asthma, ages 6 to 12 years (not shown in Figures 4.11a or 4.11b). The authors reported adverse cross-sectional associations and trends between traffic metrics (school-based NO_2, road density around schools, and road density around homes) and FEV_1, FVC, and exhaled NO in the children with asthma. Although the results were mostly non-significant, they were larger among the children with asthma. Road density in the 200-m buffer was associated significantly with FEV_1 among the children with asthma, and trends across five distance-based buffers were significant as well. Associations between exhaled NO and lung function were not discussed.

Oftedal and colleagues (2008) used the cross-sectional lung-function data of all children who were lifetime Oslo residents in the Oslo 1992 Birth Cohort (see Figure 4.11b) . A total of 2170 children provided lung-function data at ages 9 to 10 years. Spatially resolved dispersion models for NO_2 and PM_{10} were used to obtain hourly exposure concentrations and derive exposure estimates for the first year of life and for the lifetime of each child. Models were adjusted for a range of covariates, including education and tobacco-smoke exposure. PEF, FEF_{25}, and FEF_{50} were all associated negatively with both early-life and lifetime exposure. Point estimates were in general two to three times larger in girls than in boys; the latter were not significant. For the same contrast in NO_2 concentration, the lifetime-exposure measure showed larger effects than the first-year-of-life exposure perhaps due, in part, to greater variability in the lifetime measure.

Studies Conducted in Adults As mentioned above, selected results of the studies on the association between exposure to traffic-related air pollution and changes in lung function in adults are shown in Figures 4.11a and 4.11b and Table 4.14. Only results for FEV_1 decline expressed as percentages or OR are shown in the Figures.

Nakai and colleagues (1999) selected women from three zones in Tokyo with the aim of capturing three levels of local exposure to traffic, defined by distances to busy roads. The first group lived within 20 m of such a road (> 30,000 cars during the day-time 12 hours), the second lived within 20 to 150 m of the same road, and the third lived in a residential district outside the city. Lung-function analysis among the 444 women who had never smoked, based on at least one spirometry session, did not show significant patterns of association but were not quantifiable. Because of this the results are not shown in Figures 4.11a or 4.11b. The analysis controlled only for age and height, which raises the real possibility of unmeasured confounding. Moreover, NO_2 concentrations were low in all three zones.

Schindler and colleagues (1998) reported an association between neighborhood-level NO_2 concentrations and lung function (FVC and FEV_1) in eight Swiss communities among adult participants in the SAPALDIA study. Because the neighborhoods were rather small, outdoor NO_2 measurements (using Palmes tubes) were considered markers of traffic as defined in this review. Basel, for example, one of the largest areas, in which all subjects were living within a maximum distance of 5 km from each other, was subdivided into 13 "NO_2 neighborhoods." Moreover, 560 subjects participated in personal NO_2 measurements performed with passive samplers. Negative associations with lung function were observed in all eight of the communities, but the precision of the overall estimates was modest. Models were adjusted for smoking and other covariates as well as community-level background pollution, which has been associated independently with lung function (Ackermann-Liebrich et al. 1997). Associations of lung-function decrements with increases in "neighborhood" or personal NO_2 within a community were smaller than associations with increases in NO_2 across communities. A 10-$\mu g/m^3$ increase in personal NO_2 within a community, for example, was associated with a 0.74% deficit in FVC (95% CI, −1.41 to −0.07); and a 0.26% deficit in FEV_1 (95% CI, −1.03 to −0.52) (Figure 4.11b). An increase of 10 $\mu g/m^3$ NO_2 between study communities was associated with a decrement in FVC of 1.67% (95% CI, −2.33 to −1.01) and in FEV_1 of 0.94 (−1.69 to −0.18). The latter does not qualify as "traffic-related" pollution in the sense defined for this review. The community-mean NO_2 was a marker of "urban background" pollution and did not capture local contrasts in traffic-related pollution.

Kan and colleagues (2007) characterized exposure to traffic among participants in the Atherosclerosis Risk in Communities (ARIC) study, who were sampled from four communities in Maryland, Minnesota, Mississippi, and North Carolina. Both traffic density and distance to major roads were assigned to each subject. Distance was partitioned for 150 m and 100 m. FEV_1 and FVC, but not FEV_1/FVC, were associated significantly with traffic surrogates in the women but not in the men (see Figure 4.11b). The associations (among women) were larger and statistically significant for the 150-m cutoff compared with the 100-m cut-off. The follow-up was only three years, and

lung-function change was not associated with pollution over this time period.

In the German cross-sectional SALIA study (Study on the influence of Air pollution on Lung function, Inflammation, and Aging), Schikowski and colleagues (2005) included proximity to the nearest busy road (> 10,000 vehicles/day). The authors found a significantly increased risk for COPD measured as $FEV_1/FVC < 0.7$ in women, ages 54 to 55 years, who were living closer than 100 m to such a road (OR = 1.79; 95% CI, 1.06–3.02) (Figure 4.11a). FEV_1 and FVC were significantly lower as well (−1.3% and −1.8%, respectively). All models were adjusted for age, smoking, occupational exposure, type of heating, body-mass index, and height. The estimates were very similar among a subset of 1200 women included in an analysis that focused on the contribution of SES to respiratory health in Germany (Schikowski et al. 2008) (see Figure 4.11a).

Collectively, these five studies preclude conclusive statements about causality because of inconsistent and possibly subgroup-specific results or because of exposure assignments that were not clearly specific to traffic. The most convincing study (Schikowski et al. 2005) related to women only.

4.V.2.B Longitudinal Studies in Children and Adults

Based on a review by Götschi and colleagues (2008) and our updated searches for this review, 18 longitudinal studies on air pollution and lung function were identified; however, only seven met the criteria for this review. Two of these studies included children, four reported data from adults, and one reported data from both children and adults. Three studies had a short follow-up of cohorts with repeated measurements (i.e., panel studies); four had a longer follow-up. Selected data from these studies are included in Figure 4.11b and Table 4.14.

Panel Studies of Short-Term Effects of Traffic Pollution on Pulmonary Function Chauhan and colleagues (2003) enrolled 114 children with asthma, ages 8 to 11 years, and a history of wheezing or cough who lived in nonsmoking households in Southampton, U.K. The children were selected from the asthma registers of general practitioners in the area and had a mean follow-up time of 37 weeks. PEF was measured twice daily. The weekly means of personal exposure were established by personal NO_2 passive sampling. During periods preceding viral infections, personal NO_2 was associated significantly with reduced PEF. There was a significant PEF decline (12 L/min) for picornavirus when personal NO_2 was > 14 $\mu g/m^3$ compared with < 7.5 g/m^3 (in tertiles). During post-infection periods, this association was absent. With personal monitoring of NO_2, clear assignment of associations to traffic is not possible, as both indoor and outdoor concentrations of NO_2 are included in the measurements. The authors mentioned outdoor concentrations, commuting by car, and gas cooking as major determinants of the personal concentrations. Because the authors did not partition the exposures, however, interpretation of the results is limited.

Hong and colleagues (2005) asked university students ages 20 to 30 years ($N = 293$) to carry personal 24-hour-average NO_2 samplers for one week, fill out time–activity questionnaires, and measure lung function once a day. Personal 24-hour concentrations of NO_2 correlated significantly with residential proximity to streets and the time spent in cars. In a multivariate model, FVC, FEV_1, FEV_1/FVC, and $FEF_{25–75}$ were associated negatively with personal concentrations of NO_2, but only $FEF_{25–75}$ was statistically significant in all models. The age-, sex-, height-, weight-, and smoking-adjusted model indicated a 0.14 L/sec deficit (standard error [SE]: 0.07; P value = 0.05) in $FEF_{25–75}$ per 10 ppb (18.9 $\mu g/m^3$) NO_2 (range of concentrations: 10–70 ppb). For FEV_1/FVC, the slope was −0.0772 (SE: 0.037; $P = 0.038$) in the univariate model but only −0.0427 (SE: 0.0356; $P = 0.232$) for the same 10-ppb NO_2 contrast in multivariate models. The analytic approach taken with the repeated measurements was not described. Active smoking and exposure to secondhand smoke were not associated with lung function in these data.

The investigations of Burr and colleagues fall into the category of accountability studies as defined by HEI (Burr et al. 2004; van Erp et al. 2008). Respiratory health in children and adults was investigated twice, once before and once after the opening of a street bypass that reduced congestion and related air pollution in the neighborhood. However, only PEF data were used to address day-to-day variations (reported as the coefficient of variation). There was a large loss to follow-up caused by moving and a small sample size (81 and 99 subjects in the congested and uncongested streets, respectively), both of which limited the authors' results.

Cohort Studies of Long-Term Effects of Traffic Pollution on Pulmonary Function The Southern California Children's Health Study is the largest and longest investigation of air-pollution-related health effects in children (initially reported by Peters et al. 1999). To date, five cohorts have been recruited; annual lung-function measurements, however, are available only for four (Gauderman et al. 2004, 2007). These studies have presented evidence of an adverse effect of ambient air pollution on lung development in children and adolescents that appears to be modifiable by a

change in exposure caused by moving to a residence location with a different concentration of air pollution (Avol et al. 2001). Traffic was a dominant source of pollution in these California study areas; all of the observed associations could thus have been caused by traffic-related pollution, at least to some extent. However, only one lung-function analysis qualified for this review, i.e., one in which markers of local traffic-related exposures were used (Gauderman et al. 2007) (Figure 4.11b). This study used three categories of distance to a freeway as marker of within-community contrasts of exposure, with adjustments for measured community-level background ambient pollution. The choice of pollutants (NO_2, $PM_{2.5}$, PM_{10}, or EC) to adjust for community-level air quality had no impact on the main effects of the association between distance to a freeway and lung-function measures. FVC, FEV_1, and $FEF_{25–75}$ were all associated with the traffic exposure; FEV_1 and $FEF_{25–75}$ were associated significantly with living within 500 m of a freeway. Subjects living within 500 m of a freeway, for example, had 81-mL (95% CI, −18 to −143) deficits in 8-year growth of FEV_1 and 127 mL/sec (95% CI, −11 to −243) deficits in $FEF_{25–75}$ (also referred to as maximum midexpiratory flow [MMEF]) compared with those living more than 1500 m from a freeway (see Table 1 in the original paper and also Figure 4.11b). Results were similar in subjects with and without asthma, stronger in boys, and not sensitive to model specifications. Findings for modeled concentrations of freeway-related pollution were similar. Results for distance to non-freeway roads (e.g., within 75 m) were less consistent and not statistically significant, but these models were not adjusted for distance to a freeway. Many of the Southern California Children's Health Study communities are in areas with a high density of freeways. The observed statistical independence between background (community-level) pollution and local (within-community) contrasts might be seen as the strongest evidence for an effect of pollutants found in high concentrations in proximity to heavy traffic. On the other hand, the distance buffers chosen were rather wide and were not consistent with roadside measurement studies carried out around freeways in the same region (Zhu et al. 2002). The studies observed pollutant concentrations up to 10-fold higher than background in zones adjacent to highways than farther from the highway that reached background levels within the first 50 to 100 m. Although it is appropriate to interpret the distance-based findings as associated with traffic-related pollution, the Southern California Children's Health Study analyses also underscore the difficulties related to the quantitative translation of results based on proximity measures instead of on measured pollutants or constituents.

Sekine and colleagues (2004) selected women from three zones defined by proximity to busy roads (up to 20 m, > 20–150 m, and within the same buffer but in a district with less traffic). The authors confirmed exposure contrasts across the zones using NO_2 measurements, with approximately 11-ppb (21 μg/m^3) differences between adjacent zones. An eight-year decline in FEV_1 followed a statistically significant trend across the levels of exposure in the three zones. The annual declines were 20 mL, 15 mL, and 9 mL, respectively (reported to be statistically significant). The cross-sectional lung-function data presented for each assessment across the eight study years suggested some influence of loss to follow-up, with higher loss among those who participated until the end of the study. This "censoring" was strongest in the group with medium exposure and seems unlikely to have led to spurious positive overall results. The analysis also adjusted for years of residence in the area, age, job status, smoking, type of heating, and housing structure. Moreover, the models included baseline lung function, which might be a source of bias. The selection of the population was not based on communities but on residential proximity to main roads; all subjects lived within 150 m of such a road.

Nakai and colleagues (1999) presented a longitudinal component among the adult subjects, with up to 10 measurements conducted over a three-year period in Tokyo (not in Table 4.14). A formal assessment of the results is not possible, however, given the limited information provided in the paper. Similarly, Kan and colleagues (2007) referred to a three-year follow-up of the ARIC study in adults in the United States but found associations with traffic only in the cross-sectional analyses (see section 4.V.2.A).

4.V.3 SUMMARY OF TRAFFIC EXPOSURE AND LUNG FUNCTION

In a recent review of the associations between spirometric measures and air pollution, Götschi and colleagues (2008) concluded that the diversity in study designs, measures of air pollution, approaches to assigning exposure, and choices of lung-function measures limited the comparability of studies and precluded unified quantitative summaries. Only a subset of the studies reviewed by Götschi and colleagues, complemented with a few more-recent publications, qualified for inclusion in the traffic-specific review presented here. For the same reasons noted by Götschi and colleagues, a quantitative assessment of the evidence discussed in this review is not possible. In fact, even a qualitative assessment is more difficult than that for air pollution in general. When taken in conjunction with the heterogeneity of the definitions of outcomes for respiratory

disease and the differences in measures of lung function used across the studies, we conclude that the evidence is "suggestive but not sufficient" to infer a causal role for exposure to traffic-related air pollution in the various respiratory measures that have been evaluated.

Although the studies related to lung function are suggestive of an adverse association with ambient air pollution in general both in the short and long term, an assessment of the public-health relevance of the small, short-term deficits observed cannot be made. Short-term changes in lung function are a marker of altered physiology, but the correlations between acute symptoms and acute changes in lung function are weak. In terms of long-term exposures to traffic-related pollution, there is some coherence in the data: (1) the data suggest that long-term exposure is associated with changes in lung function in adolescents and young adults, (2) there is suggestive evidence that lung-function measures are lower in people who live in more polluted areas, and (3) one study suggests that changing residence to areas with less pollution is associated with improvements in lung function. Points 1 and 2 are consistent with longer-lasting effects on lung structure and function. Moreover, decrements in lung function (in particular FEV_1) has been shown repeatedly to be a strong determinant of life expectancy (Higgins and Keller 1970; Ashley et al. 1975; Hole et al. 1996). The lung-function findings are thus in agreement with what one would expect if both lung-function development and life expectancy were associated with cumulative exposure to air pollutants. Point 3 can be interpreted to indicate that some component of the apparent effects on lung-function development is reversible or are more the result of short-term exposure.

A major problem with the data presented in this section is that it is difficult to disentangle the effects of urban air pollution in general from those of the traffic-related pollution of interest in this review. In fact, the surrogates of exposure used in the studies with the strongest design and evidence of a causal role for pollution in the growth and aging of lung function — namely the Southern California Children's Health Study and SAPALDIA (Downs et al. 2007) — are not easily characterized as pertaining specifically to traffic pollution rather than to general urban air pollution. The studies based on proximity or traffic density are mostly cross-sectional in nature and, despite presenting evidence suggestive of adverse effects on lung function, their results are not entirely consistent. The negative or unclear studies in children appeared to suffer from limited contrasts in exposure, but a formal assessment of this is not possible because of the use of heterogeneous exposure measures and terminology. The results of the adult ARIC study (Kan et al. 2007) were positive only among women, an observation for which there was no good explanation.

In summary, our statement about causal inference in the associations between traffic-related pollution and lung function is based on a limited and methodologically heterogeneous literature. Although several studies support the hypothesis that living close to high concentrations of traffic-related pollution is associated with reduced lung function, the evidence to date is "suggestive but not sufficient" to infer causality, and further data are needed to put the findings into a qualitative (e.g., types of traffic-related pollutants and composition of automobile fleets) and quantitative context for traffic-related pollution.

4.V.4 TRAFFIC EXPOSURE AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

COPD is a common disease that affects 5% to 10% of the U.S. population (Mannino et al. 2002; Halbert et al. 2003). During the past two decades, death and morbidity from COPD have continued to increase, especially among women (Murray and Lopez 1997; Mannino et al. 2002; Halbert et al. 2003). Although cigarette smoking is the most important single causal factor in the development of COPD, other factors are operative as well, because COPD is observed in people who have never smoked. Given the substantial overlap in chemical constituents found in cigarette smoke and ambient air pollution, the latter might be a relevant candidate for causing the disease; traffic-related pollutants as defined in this review are of particular interest in this regard. However, an assessment of the role of air pollution in general, and traffic-related pollution in particular, in the development of COPD is very difficult for a number of reasons.

First, the disease is poorly defined. Definitions used in various studies are rather heterogeneous and range from questionnaire-based information about doctors' diagnoses (such chronic bronchitis, emphysema, or COPD) and the occurrence of chronic symptoms (such as cough or phlegm) to objective measures of lung function (FEV_1 and preferably FEV_1/FVC). Post-bronchodilator lung-function measurements are considered the gold standard for defining COPD, but these are frequently not available — a situation that can lead to a failure to distinguish between COPD and asthma.

Second, the objective definition of COPD often dichotomizes the lung-function measure (FEV_1/FVC), defining the "diseased" as having a ratio of < 0.7. As a result, the continuous spectrum of the disease might not be captured, and it is not clear how to interpret associations between FEV_1/FVC taken as continuous measures and some exposure with respect to COPD. Moreover, the fixed ratio is

confounded by age (which raises concerns about the use of percentiles to define the disease).

Third, the link between lung development in early life and future COPD is poorly understood and not well defined. Childhood studies on air pollution and lung development cannot be used in the evidentiary assessment for COPD in adults, despite strong evidence of an association between FEV_1 growth and ambient air pollution (Gauderman et al. 2007; Rojas-Martinez et al. 2007).

Fourth, it is not clear whether obstructive airways disease among adult never-smokers can result in the same clinical phenotype as COPD among smokers.

Given these issues, this review of the evidence sought to rely on studies conducted among adult never-smokers that defined COPD objectively by providing data on lung function.

There are only two studies that fulfill these criteria, namely the cross-sectional SALIA (Schikowski et al. 2005) and ARIC studies (Kan et al. 2007) discussed above. Schikowski and colleagues, in a study of women in Germany living within 100 m of a busy road compared with those living farther away, reported an OR of 1.79 (95% CI, 1.06–3.02) for COPD (defined as $FEV_1/FVC < 70\%$). Associations were adjusted for smoking and reported to be similar for never-smokers and ever-smokers. Estimates for the same traffic marker were very similar, although not statistically significant, in a further analysis of a subset ($N = 1200$) of the same women focusing on their SES and respiratory health (Schikowski et al. 2008). These results contrast with those reported by Kan and colleagues (2007), who observed associations of a magnitude similar to those in SALIA between FEV_1 and FVC and traffic markers in both men and women in the United States. However, FEV_1/FVC was not associated with traffic density in either sex. Living within 100 m of roads was associated with non-significantly lower FEV_1/FVC (men: −0.3% [95% CI, −0.7 to 0.2]; women: −0.2% [95% CI, −0.5 to 0.2]).

In conclusion, the paucity of studies precludes a meaningful assessment of the evidence for the role of traffic-related air pollution in the occurrence of COPD. The available data are not consistent, and the evidence is "insufficient" to infer a causal association.

4.VI. TRAFFIC EXPOSURE AND ALLERGY

There is a substantial literature based on human and animal exposure, and in vitro studies that provides strong mechanistic support for a role for traffic-derived pollutants along pathways that lead to the enhancement of IgE-mediated responses to aeroallergens (see Chapter 5 for details).

In addition to the quality of the exposure data, studies included in this section had to report at least one of the following: (1) skin-prick testing for reactivity to common aeroallergens, (2) serum-specific IgE to common aeroallergens, (3) a doctor's diagnosis of eczema or allergic rhinitis, or (4) questionnaires that used the terms hay fever, seasonal runny nose or rhinitis, or conjunctivitis or itchy eyes.

Sixteen studies are reviewed here (see Table 4.15, at the end of the chapter). Selected results are shown in Figure 4.12a and Figure 4.12b. All but one (Cesaroni et al. 2008) of the studies involved children, and three (Brauer et al. 2002, 2006, 2007) involved the same study population (PIAMA cohort). One of these focused on otitis media (Brauer et al. 2006), which, although most frequently the result of an infection, can be an adverse consequence of persistent nasal congestion (serous otitis media) caused by allergic rhinitis (Bernstein 1996); the study is therefore included in this section.

Overall, the evidence for an association with non-asthma allergy is inconsistent both across and within the studies. Of these only two showed some consistent positive association (Krämer et al. 2000, Morgenstern et al. 2008). The study by Krämer and colleagues (2000), cited previously (see section 4.IV.2.D), that involved children from three areas of Düsseldorf showed reasonably consistent results for an association between allergy history and skin-prick-test reactivity in relation to NO_2 at children's residences as a marker of traffic (Figure 4.12b). The children were born in 1986 or 1987, and 317 of 844 eligible children participated. NO_2 concentrations at each child's residence were derived from interpolation of outdoor measurement at multiple sampling points and were highly correlated with a traffic index based on vehicle density (0.70).* A large number of confounders were considered (including exposure to secondhand smoke).

The study by Morgenstern and colleagues (2008), also cited previously, based on the LISA and GINI studies in Munich, presented increased ORs for hay fever and specific IgE (to outdoor but not indoor allergens) and modeled traffic-related $PM_{2.5}$ (Figure 4.12b) measured as absorbance of $PM_{2.5}$ filters or residential distances of < 50 m from a major roadway (Figure 4.12a). No associations were seen with traffic-related NO_2.

Hirsch and colleagues (1999), cited previously, studied children ages 5 to 7 years and 9 to 11 years in Dresden. Allergy was assessed based on results from skin-prick tests ($N = 3188$) and measurements of specific IgE to common aeroallergens ($N = 2757$). For each residence and school, exposure to traffic surrogates CO, NO_2, and benzene was

* The authors used a Pearson correlation despite the fact that the index was a three-level variable. It is therefore difficult to interpret this result.

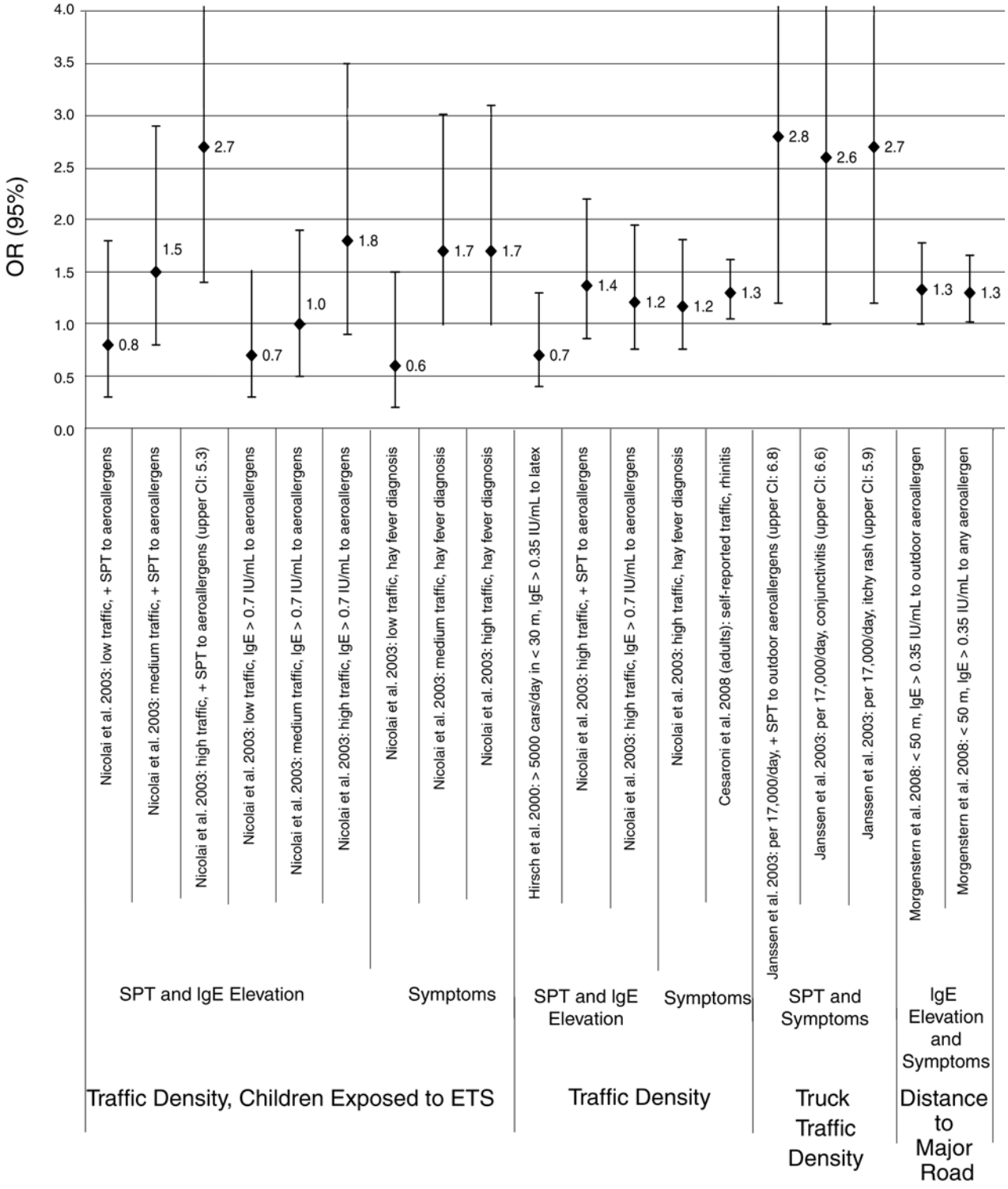

Figure 4.12a. Studies of exposure to traffic pollutants (traffic distance and density) and nonasthmatic respiratory allergy. See Table 4.15 for original data (some data in figure have been rounded The exposures are estimates at the residential address with the exception of the study by Janssen et al. (2003) in which they are estimated at the school. All studies are in children with the exception of Cesaroni et al. (2008). Vertical lines indicate 95% confidence intervals. Abbreviations: SPT = skin-prick test and SHS = second-hand smoke.

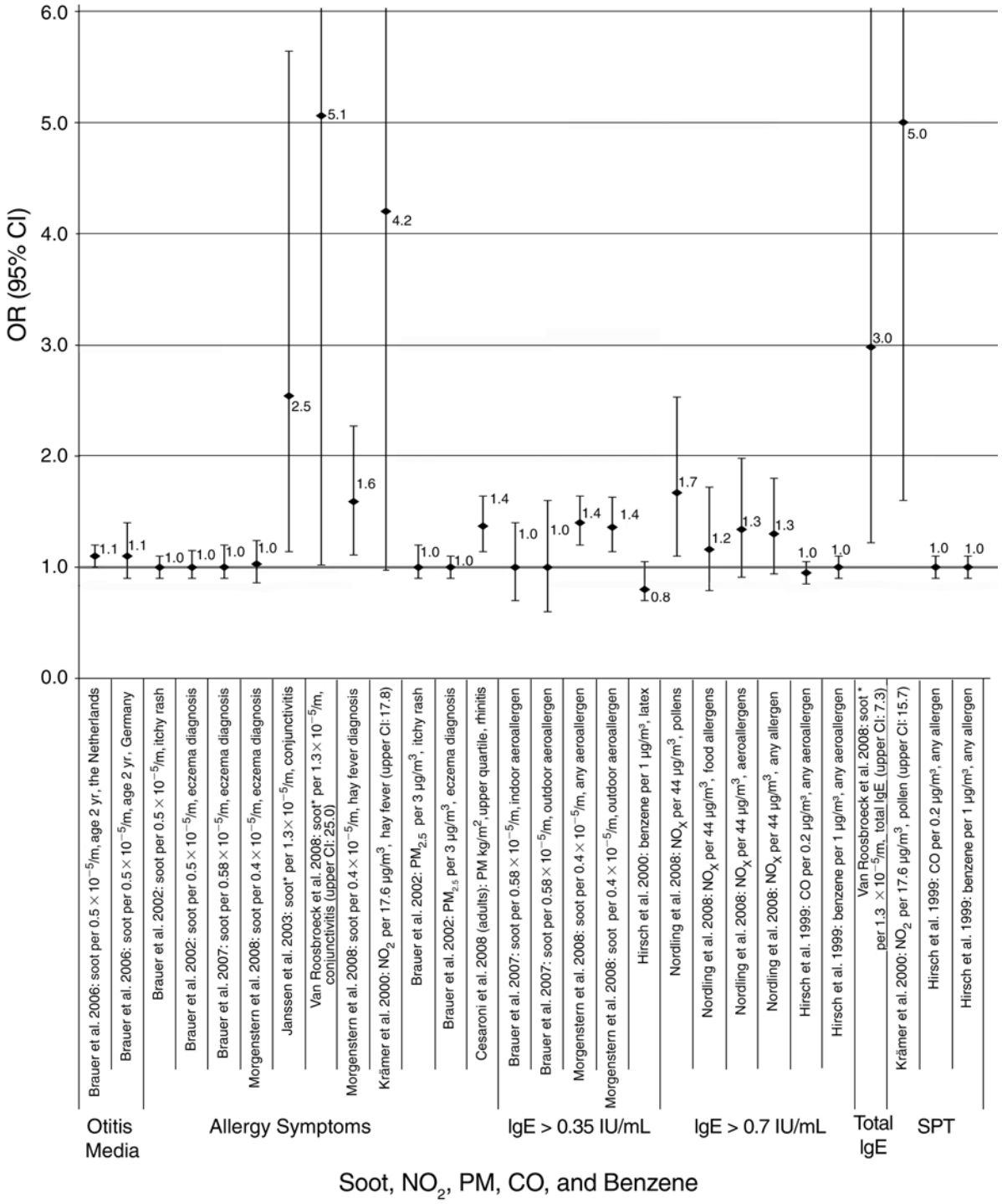

Figure 4.12b. Studies of exposure to traffic pollutants and nonasthmatic respiratory allergy (by outcome). See Table 4.15 for original data (some data in figure have been rounded). The exposures are estimates at the residential address with the exception of the study by Janssen et al. (2003) in which they are estimated at the school. All studies are in children with the exception of Cesaroni et al. (2008). Vertical lines indicate 95% confidence intervals. *Converted to measured absorbance from reported concentrations as described in footnote in Table 4.15. Abbreviations: LBW = low birth weight and SES = socioeconomic status.

estimated based on inverse-distance-weighted interpolation of measurements from the four nearest monitors in the four corners of a 1-km^2 grid. Health data and some validation data were reported for NO_2; measurements, but no validation data, were reported for CO and benzene. Inspection of the authors' Table 3 does not show any consistent pattern between benzene concentrations and the prevalence of positive skin-prick tests or specific IgE or between CO and NO_2 and the allergy markers (see Figure 4.12b). A second study by Hirsch and colleagues (2000) involved the same children as in the Hirsch et al. 1999 (ages 5 to 7 and 9 to 11 years) and used the same exposure estimates plus a direct measure of exposure — traffic counts on the street within 30 m of the residence. The study examined the prevalence of sensitization to latex (based on measurements of latex-specific IgE in serum). It showed no association between estimated traffic counts on the subjects' streets of residence or residence-based estimated exposure to benzene as a marker of traffic exposure and specific IgE to common aeroallergens in latex-sensitized children compared with non-latex-sensitized children. Unlike the 1999 study, the 2000 study provided some validation data for benzene as a suitable marker for traffic exposure. Both studies included multiple confounders, although not the same ones in both studies.

In another study of German children, Nicolai and colleagues (2003), cited earlier, studied ISAAC Phase Two participants (ages 5 to 7 and 9 to 11 years) in Munich. A validated traffic-exposure model (developed by Carr et al. 2002) produced R^2 values of 0.80 for benzene and soot and 0.77 for NO_2 relative to the measured concentrations. Exposure was also estimated based on traffic counts (vehicle/day divided into tertiles) and distance to roadway. Positive skin-prick test and specific IgE were associated significantly with high traffic (> 30,000 vehicles/day), with effect modification by exposure to secondhand smoke (see Figure 4.12a). Neither soot, benzene, nor NO_2 were associated with these markers of allergy in analyses with or without interaction terms for exposure to secondhand smoke. While SES was associated with traffic counts, there was no evidence of effect modification.

A recent study by Nordling and colleagues (2008) in a birth cohort from municipalities in Stockholm, cited earlier, reported associations for exposure during the first year of life for traffic-related modeled NO_x and PM_{10} and specific IgE to selected pollens (evaluated at age 4), but not for IgE to food allergens or all aeroallergens combined. No associations were reported for symptoms associated with hay fever.

The remaining studies — Oosterlee et al. 1996; Brauer et al. 2002, 2006, 2007; Janssen et al. 2003; Shima et al. 2003; Fritz and Herbarth 2004; and Van Roosbroeck et al. 2008 — reported inconsistent or null results. Oosterlee and colleagues (1996), cited earlier, developed a validated exposure model for traffic and used NO_2 concentrations on selected streets with an estimated 10,000 to 30,000 vehicles per day and control streets with less traffic in Haarlem, the Netherlands. Of 291 children (ages 0 to 15 years), 245 had data on exposure and all confounders. The adjusted OR for any doctor-diagnosed allergy was 1.4 (95% CI, 0.6–3.4).

Using data from the PIAMA birth-cohort in the Netherlands at age 4 years, Brauer and colleagues (2007), cited earlier, showed no association between lifetime exposure to soot or NO_2 and a history of eczema or specific IgE to indoor or outdoor aeroallergens (see Figure 4.12b). Unexpectedly, however, significant adjusted associations were found with specific IgE to food allergens. Soot and NO_2 were used as surrogates based on exposure models that combined measured concentrations at numerous monitoring points with GIS data or traffic data and the distance to road. The models explained 81% and 85% of the variance of soot and NO_2, respectively. In an earlier analysis of the children in the PIAMA cohort data at age 2 years, Brauer and colleagues (2002), reported no associations (adjusted for multiple confounders) between soot and NO_2 (derived from the same model noted above) and self-reported itchy rash or a doctor's diagnosis of eczema. As in the 2007 PIAMA study, a large number of confounders and modifiers were considered, including maternal smoking in pregnancy, breast feeding, gas stoves in homes, and use of mattress covers.

Janssen and colleagues used traffic counts (trucks and cars) and measured NO_2, $PM_{2.5}$, and soot concentrations at schools (all within 400 m of a roadway) (Janssen et al. 2001, 2003) to assess exposure of children ages 7 to 12 years who participated in ISAAC Phase Two in the Netherlands. Distance of homes and schools to motorways was also assessed (using GIS). Multiple confounders were considered for the children for whom specific IgE (N = 881) and skin-prick-test (N = 1141) data were available. Truck-traffic density, $PM_{2.5}$, and NO_2, but not soot, were associated with skin-prick-test reactivity). Self-reported history of hay fever was associated with $PM_{2.5}$ and NO_2 but not soot or truck traffic. Eczema was not associated with any traffic.

The study by Shima and colleagues (2003), cited earlier, of 3234 Japanese children ages 6 to 9 years at recruitment in schools in eight communities in Chiba Prefecture used only distance from a roadway (< 50 m or > 50 m) as the traffic metric. Six of the schools were near major roads with heavy traffic (37,000–83,000 vehicles/day; 18%–44% heavy vehicles); four schools were located in rural communities without "major roads" (no traffic data provided).

Allergy was defined as reporting by parents of a doctor's diagnosis of eczema, atopy, allergic rhinitis, pollinosis, or a history of hyposensitization therapy. Although data on multiple confounders were available, only crude point estimates (no variance estimates) of associations between traffic and allergy were presented; these estimates are therefore not provided in this review.

Fritz and Herbarth (2004) utilized source-apportionment analysis to attribute exposure to traffic-related and coal-fire–related pollution in children living in Leipzig, Germany. The exposure-measurement methods were described by Rehwagen and colleagues (1999). The children were classified into two main groups based on whether the kindergarten they attended (of 13 kindergartens total) was located in an area where coal heating was the predominant pollution source (using SO_2 as the indicator) or where traffic was the predominant pollution source (using benzene as the indicator). Fritz and Herbarth found only a marginal increment in the prevalence of allergy (using self-reports of specific allergies and allergy-related symptoms) in children living in the areas dominated by traffic (and low coal heating) over that of children in areas with both high coal heating and high traffic. The two types of areas did have higher reported prevalences compared with the areas where coal heating was the predominant pollutant source. The study considered only age, sex, and parental history of allergy or asthma as covariates. Assignment of the authors' findings to traffic-related pollution is not possible, given the methods used to define exposure (not shown in Figure 4.15).

Brauer and colleagues (2006) studied otitis media as the outcome at ages 1 and 2 years in the PIAMA cohort in the Netherlands and a cohort of children of similar ages in Munich. The authors reported marginal associations between NO_2 and otitis in the Netherlands cohort (N = 2970 at age 2 in the adjusted model) and the Munich cohort (N = 605 at age 2 in the adjusted model) (see Figure 4.12b). The latter was estimated less precisely, undoubtedly because of the smaller sample size.

Finally, one study evaluated the relation between exposure to traffic air pollution and allergy in adults. Cesaroni and colleagues (2008) reported consistent associations between self-reported rhinitis in adults and several measures of traffic exposure. Self-reported traffic density, distance to high-traffic roads, meters of high-traffic road within various buffers, traffic-generated PM emissions (from emission model), traffic-related NO_2 concentrations (estimated from land-use regression), and a summary score of all exposure metrics (Figure 4.12ab). The exposure metrics in the study were particularly strong, as was the control for confounding. However, the definition of rhinitis was vague in that it was not referenced to season, to specific allergen exposure, or to allergy in general. Of note, the associations appeared to be confined exclusively to non-smokers (see Table 5 of Cesaroni et al. 2008).

4.VI.1 METHODS OF EXPOSURE ASSESSMENT

The methods used to assign traffic exposure varied across the studies. The Brauer studies (2002, 2006, 2007) all used the same population and the same model, which was based on the factors noted above and described in detail in Brauer et al. 2003. With the exception of Shima and colleagues (2003), all the studies used at least some measure of traffic counting; many supplemented this with additional models.

Oosterlee and colleagues (1996) used information on types of vehicles and engines, traffic density, local topography (such as types of buildings and street canyons), urban background pollution, and regional meteorology to create a street dispersion model that was validated, in part, by measurement and wind-tunnel data. Based on data from 10 street segments, traffic-related NO_2 was predicted with a 9% error. Krämer and colleagues (2000) deployed 158 Palmes tubes for one week in three areas of Düsseldorf. NO_2 was correlated with a three-level traffic index (for a rural area and for areas with 2,000–25,000 and > 25,000 cars per day on a main road near children's homes). The correlation between the interpolated and measured NO_2 at the residences was 0.71.

In addition to a benzene marker, Hirsch and colleagues (1999) also considered self-reported characteristics of traffic on residential streets (i.e., frequency of congestion, frequency of trucks, maximum speed, and main or side roads) as well as traffic counts. Only subjects who lived on roads with > 5000 cars per day were included. None of the indices of traffic exposure were associated significantly with allergy.

Nicolai and colleagues (2003) used traffic counts, data on the percentage of time with traffic jams (not defined further), and other street characteristics for all road segments that were within buffers and had traffic counts of > 4000 vehicles per day. Traffic counts were weighted to account for the distances of the road segments from the residences. As noted previously, this model resulted in reasonable correlations with measured data.

Janssen and colleagues (2003) used a model reported earlier by the same group (Janssen et al. 2001), with outdoor sampling for $PM_{2.5}$, $PM_{2.5}$ reflectance (for soot), and NO_2 on roofs or patios of the schools. The authors' model also included weekday traffic counts, roadway distances, and the percentage of time the residences were downwind

of major roadways. Unfortunately, no information on the fit of these models to the data was provided (Janssen et al. 2001), and therefore the validity of the exposure model cannot be judged.

The model used by Fritz and Herbarth (2004) (described in Rehwagen et al. 1999) started with a principal-components analysis that identified three factors: one with SO_2 and NO_2 ("coal heating"); one with benzene, toluene, dust, and CO ("traffic"); and one with ozone alone. The coal-heating and traffic factors accounted for 55% and 17% of the variances, respectively. From this, the authors created a pollution quotient (Rehwagen et al. 1999; Fritz and Herbarth 2004) whose numerator was the ratio of the mean concentrations of the traffic marker SO_2 in areas of high and low coal-heating use and whose denominator was the same ratio, using benzene as the traffic marker. It was not clear on what basis "high" and "low" were determined; by implication it was on the basis of scores from the principal-components analysis, but this was not stated specifically. Moreover, CO, which was included in the traffic factor, had a quotient that seemed to be more consistent with coal heating predominance. No variance estimates for the quotients were provided. The validity and reliability of the traffic-exposure estimates are thus open to serious question.

Nordling and colleagues (2008) presented very specific traffic-exposure data based on emission inventories for NO_x and PM_{10}, by type of vehicle (nine categories of vehicles and emissions controls) combined with data on road type and traffic flow. Although the study provided some of the most detailed and specific exposure metrics, very few associations with respiratory allergy were reported, as noted previously. In an analysis designed to address measurement errors in the assignment of exposures to traffic-related pollution, Van Roosbroeck and colleagues (2008) used data from 24 schools in the Netherlands that participated in ISAAC Phase Two (Janssen et al. 2003) (see Table 4.15). Measurement-error–adjusted prevalence ratios for recent conjunctivitis and elevated total IgE were associated significantly with exposure to traffic-related soot and NO_2. However, the estimates were very imprecise because of the small number of subjects in the validation study (45 for soot, 67 for NO_2). The measurement-error models for soot and NO_2 had R^2 values of 0.71 and 0.77, respectively. The most complete exploration of the possible effects of choice of metrics was provided by Cesaroni and colleagues (2007), who evaluated self-reporting of traffic and four more-specific metrics. There was general agreement among the OR across all metrics used, an observation that makes it unlikely that the associations in the study were caused solely by mismeasurements of exposure to traffic-related pollution.

Finally, it should be noted that none of these studies considered the allergen content of road dust from nearby roads measured as settled dust or airborne components. A detailed study by Miguel and colleagues (1999) in the Los Angeles basin of Southern California from October 1995 through May 1996 demonstrated that dust from roads contained antigenic material (based on specific IgE binding) from fungi and pollens. In the study, dust was vacuumed from roadways immediately adjacent to monitors maintained by the South Coast Air Quality Management District. The authors estimated that between 3.5% and 9% of the total-suspended-particulate fraction of the dust was in the fine-particle fraction (below 2 µm in diameter) and between 45% and 75% was in the PM_{10} fraction (see Supporting Information, Figure S1, in Miguel et al. 1999). Between October 1995 and January 1996, the estimated paved-road dust contribution to airborne-particle antigenicity ranged from 0.6% to 12% (see Table 3 in Miguel et al. 1999). A potentially important component related to the association between traffic exposure and allergy could thus account for some of the disparate results discussed here, depending on the road-related antigen concentrations in the various studies.

The inconsistency across the studies reviewed might also reflect a failure to identify susceptible subgroups. A study by Melen and colleagues (2008) seemed to point in this direction. In the study's birth cohort, traffic-related pollution derived from local-NO_2 models was correlated with sensitization at age 4 only among a genetically defined subset of the population (see Table 4 in Melen et al. 2008 and Table 4.15 in this report).

4.VI.2 SUMMARY

Based on these data, there is "inadequate and insufficient evidence" to infer a causal association, or even a non-causal association, between exposure to traffic-related pollutants and allergy. This conclusion is not due to lack of control for confounding, because all of the studies, except that of Shima and colleagues (2003), addressed the most important confounders with statistical approaches that were reasonable. With a few, inconsistent, exceptions, results based on skin-prick-test reactivity or allergen-specific IgE failed to show any associations with a number of different traffic-exposure surrogates. Because of findings from human-exposure studies using diesel-exhaust particles (Bastain et al. 2003; Gilliland et al. 2004), one would have expected more consistent positive associations. Perhaps the use of nasal instillation in the diesel studies is not an appropriate model for what happens when exposure consists of inhalation through the nose and mouth, as occurs under normal circumstances. This would not be an

adequate explanation for enhanced responses to aeroallergens in controlled inhalation studies with NO_2 (Tunnicliffe et al. 1994). These studies also used concentrations far above those that would have been encountered in ambient conditions. The inconsistent results for self-reported histories in the epidemiologic studies are not entirely surprising, especially given the occasional use of categories such as "itchy rash," which, if not qualified in some detail, might not be sufficiently specific. Although exposure assessments can always be called into question, several of the studies (Hirsch et al. 1999; Brauer et al. 2002, 2006, 2007; Janssen et al. 2003; Nordling et al. 2008) used exposure models that went beyond simple distance measures. Hirsch and colleagues (1999) even accounted for the amount of time schools and residences were downwind of the traffic sources, a variable not usually considered in most of the epidemiologic studies reviewed in this chapter. The issue of these associations thus remains unsettled at this time.

4.VII. TRAFFIC EXPOSURE AND BIRTH OUTCOMES

A considerable body of data from around the world has identified consistent associations between exposure to air pollutants and various birth-outcome measures, including low birth weight, small for gestational age, and perinatal or postnatal mortality (see, for example, Ritz and Yu 1999; Bobak 2000; Dolk et al. 2000; Ritz et al. 2000). However, this consistency did not extend to the specific critical periods during pregnancy or specific pollutants or sources. Although the directness, intensity, and temporal profiles of exposures differ, ambient pollution contains many of the same chemical species that are found in tobacco smoke, the latter being a well-known causal factor for adverse birth outcomes (Bernstein et al. 2005). Recently, several studies have been conducted that specifically addressed associations between exposure to traffic-related pollutants and birth outcomes. The results are shown in Figure 4.13 and Table 4.16 (at the end of the chapter).

Two studies (Wilhelm and Ritz 2003; Ponce et al. 2005) based on the same data from Los Angeles County birth certificates and population spatial distribution, have addressed this question. Both used the same annual average distance-weighted traffic density for all roads within a 750-foot (230-m) buffer around each birth residence; the weights were derived from a simple Gaussian dispersion that assumed 96% dispersion at 500 feet (150 m) without considering meteorologic data, roadway geometry, or vehicle-emission rates. Although these studies controlled for a wide variety of relevant individual- and group-level potential confounders, none had data on maternal smoking during pregnancy. In the first study Wilhelm and Ritz (2003) evaluated the association of traffic density with low birth weight and preterm births. They found significant association between the highest traffic density (> 80th percentile of density) and both outcomes only for births whose third trimester of gestation fell in the fall or winter. Because subsequent analyses of their data suggested confounding by SES (based on unemployment, public assistance, and income below poverty line) (Ponce et al. 2005), smoking was likely to have been an empirical confounder, because of its association with low SES (Centers for Disease Control and Prevention 2007) and birth outcomes, as well as a potential effect modifier. The latter possibilities are suggested by the finding that the effects observed for distance-weighted traffic density were stronger for women who resided in lower-SES areas; the greatest differences in effect estimates were observed when the authors stratified on the median proportion of children in poverty. Moreover, the data indicated that, in general, mothers of lower SES lived in more polluted areas than those of higher SES (Ponce et al. 2005). These issues of potential bias or modification cloud the interpretation of the data shown in Table 4.16 for these studies, which is of some importance, because the effect sizes were small and were estimated imprecisely. The most consistent effects were observed for pregnancies whose third trimester was in the November-to-April period, which includes the times of year with the highest $PM_{2.5}$ concentrations and the lowest ozone concentrations. A subtle but important point with regard to the use of these data at the population level is the evidence for effect modification by a variety of social factors (Ponce et al. 2005). Consequently, the OR estimates for exposure in Table 4.16 must be interpreted as conditional (i.e., stratum-specific) and cannot be assumed to apply across the board to the population of women studied, meaning they cannot be marginal population estimates even if the models were properly specified (the latter being, in addition, difficult if not impossible to determine).

Slama and colleagues (2007) use land-use regression to estimate annual traffic-related pollutants ($PM_{2.5}$ mass, $PM_{2.5}$ absorbance, and NO_2) around birth residences for births in the LISA cohort in the Munich metropolitan area (from January 1998 to January 1999), whose fetal development took place at the same residence. The land-use model (developed as part of the TRAPCA study) included road distances and length in a buffer around the residence, population density, and land coverage around the home address (not defined) and was based on a 40-site measurement campaign conducted over two weeks (during March 1999 and July 2000). In an attempt to attribute exposures to specific seasons and thus to trimesters, the investigators averaged

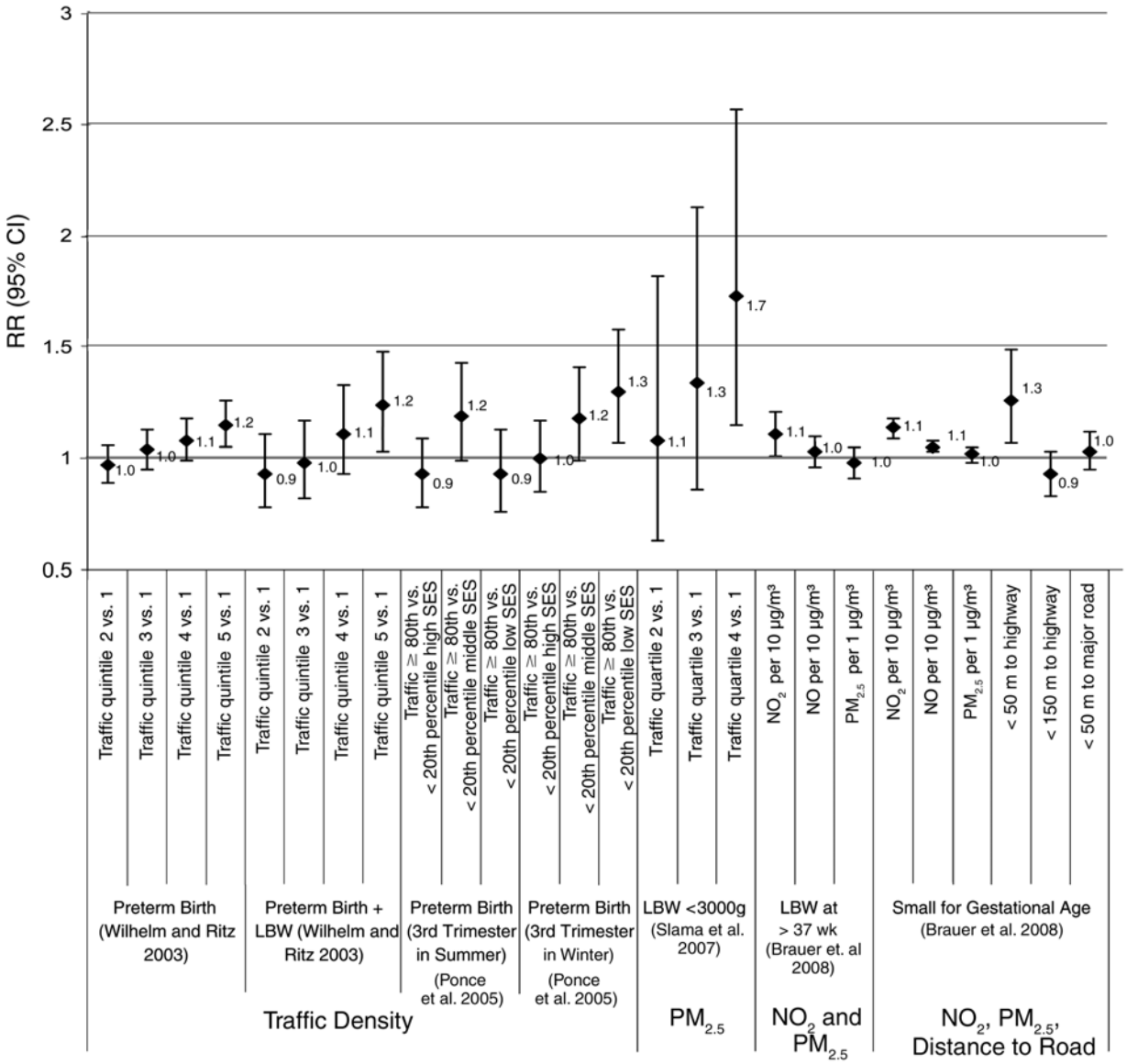

Figure 4.13. Studies of exposure to traffic pollution and birth outcomes. See Table 4.16 for original data (data in figure have been rounded). Vertical lines indicate 95% confidence intervals. Abbreviation: LBW = low birth weight and SES = socioeconomic status.

NO_2 daily mean concentrations (from a background regulatory monitor away from roadways) over the pregnancy of each woman and divided them by average NO_2 concentrations from the TRAPCA measurement campaign and multiplied the resulting coefficient by the NO_2 estimate for each woman from the TRAPCA II spatial land-use model. A similar procedure was carried out for $PM_{2.5}$ absorbance; temporal variability was assumed to be the same as that for PM_{10}, which itself was estimated, in part, from total-suspended-particulate measurements. The authors did not provide clear definitions of land cover and the model provided only 47% and 51% of the variance for soot and NO_2, respectively (Morgenstern et al. 2007) and the specific coefficient for traffic and their partial R^2 were not reported, as noted in section 4.IV.2.A. The estimates in Table 4.16 for this study are therefore difficult to interpret with respect to traffic-related associations. A strength of this study was that it did adjust for maternal smoking throughout pregnancy and during specific trimesters as well as for many other important potential confounders.

Recently, Brauer and colleagues (2008) reported an ecologic analysis of 70,249 births from 1999 to 2002 in Vancouver. Three types of exposure to traffic were considered: (1) inverse-distance weighted CO, NO, NO_2, ozone, SO_2,

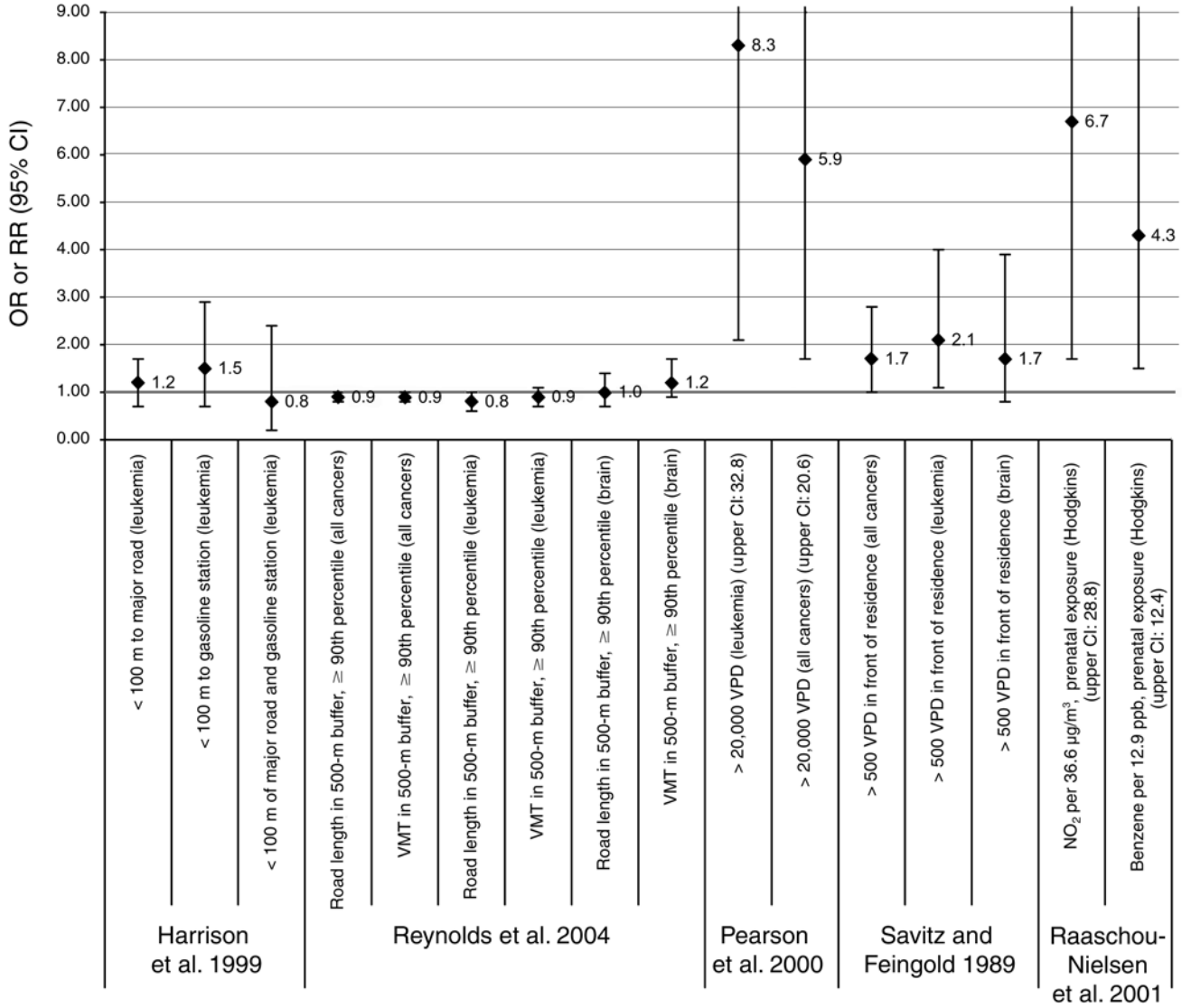

Figure 4.14a. Studies of exposure to traffic pollution and cancer in children. See Table 4.17 for original data (some data in figure have been rounded). Vertical lines indicate 95% confidence intervals. Abbreviation: VMT = vehicle miles traveled and VPD = vehicles per day.

$PM_{2.5}$, and PM_{10} measured at regulatory monitoring sites; (2) modeled NO, NO_2, $PM_{2.5}$, and BC from measurement at multiple monitoring points and land-use regression based on roads within residential buffers; and (3) measures of distance from roadways. There were generally small but consistent higher ORs for associations between exposure to NO, NO_2, and $PM_{2.5}$ during the entire period of gestation and residence within 50 m of a highway and small-for-gestation-age birth weight (defined as births below the tenth percentile weight of the cohort for each week of gestation. The results are less consistent for low birth weight for infants born ≥ 37 weeks of gestation.

Data on congenital anomalies associated with exposure to traffic and related pollutants has not been studied to any great extent (see review article by Srám et al. 2005). The one report that has investigated this found associations between certain cardiovascular congenital defects and CO in the Los Angeles basin, but there were no exposure metrics related directly to traffic exposures (Ritz et al. 2002). There are, in addition, virtually no useful data on associations between exposure to traffic-related pollutants and fertility.

Taken together, the small number of studies with limited geographic coverage and the uncertainty of the traffic metric in one study (Slama et al. 2007) lead to a classification

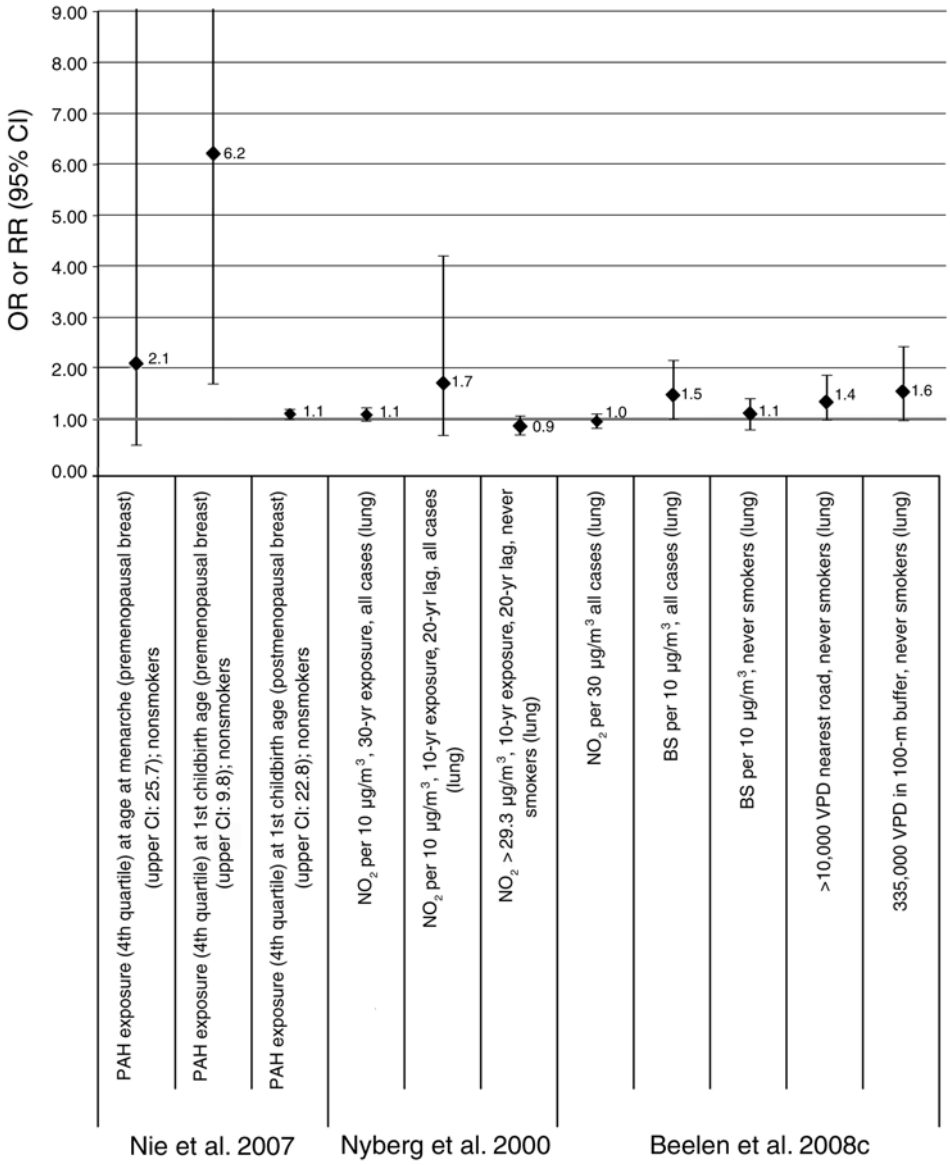

Figure 4.14b. Studies of exposure to traffic pollution and cancer in adults. See Table 4.17 for data. Vertical lines indicate 95% confidence intervals. Abbreviations: BS = black smoke, PAH = polycyclic aromatic hydrocarbons, and VPD = vehicles per day.

of the evidence as "inadequate and insufficient" to infer a causal relation, despite the very consistent findings in a study by Brauer and colleagues (2008).

4.VIII. TRAFFIC EXPOSURE AND CANCER

This section reviews the epidemiologic data on the associations between exposure to traffic-related air pollution and cancer. Among children, the most studied cancers are leukemias, lymphomas, and cancers of the central nervous system (also referred to as brain cancer). The studies in adults are restricted to individuals not exposed in occupational settings (e.g., studies in occupations with exposure to components of traffic pollution such as diesel exhaust and benzene). The studies reviewed here are shown in Figure 4.14a (children) and Figure 4.14b (adults) and summarized in Table 4.17 (at the end of the chapter).

4.VIII.1 CHILDHOOD CANCERS

One of the earliest studies, by Savitz and Feingold (1989), compared the occurrence of leukemias and brain and other types of cancers in children ages 0 to 14 years in Denver who

lived near roads with > 500 vehicles/day and < 500 vehicles/day. An extensive set of potential confounders was evaluated; relatively imprecise estimates of positive associations were observed for leukemias and brain cancer (see Figure 4.14a). The same population was studied by Pearson and colleagues (2000) with a more detailed traffic-exposure assessment that used more updated traffic data (for the year 1990), identified the street with the highest traffic within 1500 ft of the residence (by GIS), and computed traffic volume (for the year 1990) by distance weight for different width (250, 500, and 750 ft) of Gaussian distribution curves at the street-to-home distance (but ignored winds and topography). The same set of confounders in Savitz and Feingold (1989) were included in the analysis. Significant associations with 750-ft distance weighted traffic density were observed for cases of leukemias and all tumors combined in the highest category of traffic density (> 20,000 vehicles per day), but there was no consistent pattern for lower traffic densities. Because of the small numbers (8 leukemia cases, 18 total cancer cases, and 3 controls), the estimates were highly imprecise (see Table 2 in Pearson 2000 and Figure 4.14a in this chapter).

Based on ecologic data, Harrison and colleagues (1999) computed age-standardized incidence-rate ratios for presence of high traffic roads (with mean 23,400 vehicles per day) or presence of a gasoline station within 100 m of residences and cancer in children 0 to 15 years of age in West Midlands, U.K. Although the authors had very large numbers of children in their population base, there were only 24 leukemia cases and 31 solid tumors. All but one community had ≤ 4 observed cases. The only group-level confounder considered was a deprivation index that had a very low association with tumor incidence. The results are reported as OR for leukemias versus solid tumors (not show in Table 4.17) and as IR (calculated from the number of leukemia cases relative to the expected number of cases in the population) (see Figure 4.14a). In neither analysis were the associations statistically significant.

A study by Raaschou-Nielsen and colleagues (2001) based on data from the Danish cancer registry reported significant associations between prenatal benzene and NO_2 exposures (99th percentile versus 50th percentile) and Hodgkin's disease in children less than 15 years old who were diagnosed before 11.2 years of age, based on modeled estimates of front-door concentrations. There were no significant associations between prenatal exposures and leukemias, brain tumors, or all selected cancers combined. Exposures during childhood were not associated significantly with any major cancer type. A large number of confounders were considered; however, data on maternal smoking during pregnancy and parental occupations were not available. The exposure model incorporated street width, building height, distance of residence from street, average traffic speed, percentage of vehicles > 3500 kg, presence of other streets within 50 m with traffic density higher than the street of residence, emissions factors, meteorologic data, and background pollution. A validation study in 204 children, with six-month measurements at the front door and one week of personal exposure, showed that misclassification was only between adjacent exposure categories based on front-door measurements and that the errors were independent of calculated values with constant variance. On this basis, the authors concluded that the errors were consistent with Berkson-type error and therefore that their estimates were not likely to be biased by measurement error. It is not clear that this is the case, because the classical error model would also be consistent with the misclassification data reported. Moreover, the approximate fivefold range of the distribution of NO_2 at the front door (see Figure 1 in Raaschou-Nielsen et al. 2001) was, again, equally consistent with classical error and does not provide strong support for a Berkson-type error; thus bias toward the null might have been present.

A large case–control study by Reynolds and colleagues (2004) based on data from the California statewide population-based cancer registry (1728 leukemias, 746 brain tumors) failed to find evidence of any associations between road density within a 500-foot radius around the residence (miles/mile^2) or traffic density within that radius ([{vehicles/day}/segment length, VMT] per square mile) and any cancer in children diagnosed at less than 5 years of age between 1988 and 1997. Age- and sex-matched controls were derived from state birth-certificate data. Race or ethnicity and U.S. Census Block Group median family income were the only other confounders that were considered.

4.VIII.2 ADULT CANCERS

Four studies evaluated cancers in adults. Nyberg and colleagues (2000) studied lung-cancer cases in men ages 40 to 75 years living in Stockholm between 1985 and 1990. Lifetime exposure to traffic-related NO_2 at each residence before diagnosis was derived from a detailed regional emissions database for 1993, with NO_x/NO_2 as the traffic marker. A Gaussian dispersion model was used at a resolution of 100 × 100 m. Estimated exposures were derived from these data for the 1960s, 1970s, and 1980s, based on assumptions about traffic growth and historical traffic counts, adjusted for street-canyon effects, over these years. An extensive set of confounders was considered, including adjustment for smoking habits, diesel-exhaust exposure, radon exposure, and occupational exposure to carcinogens. Weak associations were found with exposure over the 20 and 30 years before diagnosis; these were confined largely to nonsmokers living at the residence for more than 20 years and

whose estimated NO_2 exposure was (above 90th percentile, i.e., 29.3 μg/m^3) relative to those whose exposures were below the 90th percentile (OR 1.68; 95% CI, 0.67–4.19). A case–control study by Nie and colleagues (2007) in Niagara and Erie counties in western New York evaluated exposure to traffic emissions of benzo[*a*]pyrene (as a surrogate for PAHs) and breast cancer. Emissions were derived from a detailed exposure model developed for Long Island, N.Y. (Beyea et al. 2006). This model used tailpipe emissions of aromatic hydrocarbons (PAHs), vehicle counts, and included a factor to account for higher emissions at intersections (with accelerations and decelerations) and for emissions for cold and hot engines. Vehicle and meteorologic data for the model were obtained from the two counties. A large number of relevant covariates were considered in the model. PAH adducts in soil and carpet dust at residences were used to evaluate the model; blood PAH–DNA adducts were also measured. Benzo[*a*]pyrene was used as the principal traffic marker. Plots of predicted traffic emissions and cold-start emissions showed considerable variability (see Figures S-2 and S-3 in Beyea et al. 2006). All significant associations were found only in nonsmokers and only for selected life-course times (see Figure 4.14b).

Beelen and colleagues (2008c) published a separate case–cohort study of incident lung cancer (between 1986 and 1997) from the NLCS cohort discussed previously in relation to mortality (Beelen et al. 2008b; see also Brunekreef et al. 2009.)* Analyses were carried out separately for the full cohort (approximately 120,000 subjects and for a case–cohort in a randomly selected subset of the full cohort (approximately 22,000 subjects). Important associations with exposure were confined exclusively to nonsmokers, who accounted for 252 cases in the full cohort analysis (person–years not provided). Because the full cohort analysis did not have the same extensive covariate data as the case–cohort subset did, there remains some concern about residual confounding caused by the lack of data on occupation for the full cohort analysis.

A nested case–control study by Vineis and colleagues (2006) in a subset of the European Prospective Investigation into Cancer and Nutrition cohort (GenAir study cohort) assigned exposure to traffic based on distance of residences from a "major" street (based on traffic count) but the distribution of distances represented by being "located in a major street" was not presented. Only never-smokers or those who had smoked less than 10 years were included. Bladder, lung, oral, pharyngeal, and laryngeal cancer and leukemia were considered as a group. Lung cancer was also analyzed separately. Numerous confounders were controlled by matching or inclusion on appropriate regressions. The results showed nonsignificant associations between lung cancer and living near roads with heavy traffic; only one of the four models evaluated showed a lower confidence interval greater than 1. This study is not presented in Figure 4.14b.

* See section 4.II.2.A on cardiopulmonary mortality for description of exposure methods and metrics.

4.VIII.3 SUMMARY

Overall, the database from which to draw inferences related to cancers other than lung cancer is rather limited, and our comments are confined to this database. Data on childhood cancers is inconclusive in terms of overall consistency and in terms of specific childhood cancers. Too few data were available for adult exposure to traffic-related pollution to draw any meaningful inference related to cancers other than lung cancer. We therefore rate the evidence as "inadequate and insufficient" to infer a causal relation for cancers not related to lung cancer. The same rating could be applied to the studies of lung cancer in nonoccupational settings.

4.IX. HEALTH EFFECTS ASSOCIATED WITH TRAFFIC EXPOSURE IN OCCUPATIONAL SETTINGS

Occupational settings potentially offer a very useful environment in which to study health effects related to exposure to traffic-related pollutants. At least in theory, the exposure settings are more clearly defined, both in terms of place and the burden of exposure to traffic exhaust and specificity of type of exposure. In this section, studies of health-effects–associated exposure to traffic-related pollutants are evaluated.

Despite the apparent benefits of studies of occupational exposure to traffic-related pollutants, in practice there are three major problems with such studies (see Table 4.18, at the end of the chapter):

1. Exposure to traffic is almost always based on job status without specific estimates of traffic density or volume, specific pollutant surrogates at the sites, or specific measures of personal exposure (e.g., BC and NO_x).
2. Most of the studies were carried out in relatively small samples of exposed individuals who were then compared with similar workers in indoor environments. However, the proximity of these indoor environments to sources of traffic was usually not specified. In several cases, the control groups were not optimal with regard to their equivalence.

3. The range of potential confounders was frequently limited or the extent to which confounding was evaluated was not adequate. At least one study (Ingle et al. 2005) was excluded from the table because only crude estimates of association were provided.

Specific examples are provided in Table 4.18. What is not immediately evident from the table is that most of the studies either recruited only a small to moderate fraction of their target work populations or failed to specify what fraction their samples represented. Most of these studies also failed to account adequately for confounding in their analyses, despite the availability in many cases of a large amount of data on potential confounders and effect modifiers. We therefore conclude that it is not possible to present any association or effect estimates that have validity from any of these studies. On the whole, then, this group of studies has contributed no useful information about possible health effects related to exposure to traffic-related pollutants in work situations.

4.X. OVERALL SUMMARY AND DISCUSSION

In trying to provide a summary statement of the topics reviewed in this chapter, it is important to reiterate the limitations placed on any quantitative summary because of the variety of differences across studies: (1) the differences in emission patterns caused by qualitative and quantitative differences and by changes in vehicle fleets and fuel formulas, (2) population differences, (3) survivor-cohort effects, (4) differences in urban structure, and (5) differences in methods of exposure assessment between, and sometimes within, studies that do not translate easily from one to the other. Although these factors make quantitative summaries difficult, they do not preclude qualitative summaries of the overall evidence as it pertains to causal associations between the exposures and reported health outcomes.

The aggregate evidence with respect to mortality, especially cardiovascular mortality, is suggestive of a causative role for traffic-related pollutants. Although limitations were noted for given studies and groups of studies, the overall evidence pointed consistently to the existence of such associations. The studies related to the types of dysregulation of autonomic control and electrophysiology that have been associated with an increased risk of mortality added weight to the causal role of traffic pollution, as did the studies reviewed in the section in Chapter 5 on toxicology related to inflammatory mechanisms.

There was sufficient evidence to support the hypothesis that asthma is more common among children living in the street buffers with the highest concentrations of traffic-related pollution. The evidence for a causal relation was considered to be a grey zone between "sufficient" and "suggestive but not sufficient." There was "sufficient evidence" that children with asthma living in hot spots of traffic-related pollution experience more symptoms and exacerbations. The evidence for allergic sensitization, which is often associated with asthma, was insufficient; it remains unsettled at this time whether traffic-related air pollution causes allergic sensitization.

With only one relevant study, the evidence was not sufficient to decide whether adult onset of asthma is caused by exposure to traffic-related pollution. Studies on symptom exacerbations in adults were less abundant than studies of asthma onset in children, and the evidence was considered as only "suggestive but not sufficient" to infer a causal relation.

Although plausibly related to higher hospitalization rates for asthma, the evidence for inferring causal associations between traffic-related pollution and health-care use was insufficient, both in children and adults. Methodologic limits of both the positive and negative studies precluded conclusive statements.

Conclusions about associations between traffic-related air pollution and lung function are based on a limited and methodologically hetero-geneous literature. Although several studies supported the hypothesis that living close to a high concentration of traffic-related pollution is associated with reduced lung function, the evidence is suggestive but not sufficient to infer causality. Despite the sufficient evidence for a causal association between ambient air pollution in general and lung growth (i.e., the amount of growth achieved by age 18 years), and possibly lung-function decline in adults, it is not yet clear whether these health effects also result specifically from traffic-related exposure. To the extent that traffic-related pollution is the dominant contributor to certain ambient environments, extrapolation from studies on background pollution could provide supporting evidence for a causal association, conditional on control of appropriate confounders and modifiers and appropriately fitted statistical models.

With only two studies on COPD, the evidence was insufficient about a potential role for traffic-related air pollution in the development of COPD.

A number of studies have tried to address the effects of exposure to traffic-related pollution on a variety of birth outcomes. However, the current data, even though they do show some apparently consistent associations, were considered to be insufficient at this time to infer a causality.

The data reviewed here were also insufficient to infer that traffic-related pollutants contribute to childhood cancers (principally leukemia, lymphoma, and cancers of the central

nervous system). The data on cancers, including lung cancer, from general population studies in adults is too sparse to make any statement at all.

Common to all of the health outcomes discussed here is the insufficiency of our knowledge about the underlying susceptibility factors that might ultimately determine whether, or to what degree, some people might be affected by traffic-related pollution. As is the case for smoking, it is very unlikely that traffic-related pollution affects all people equally. Heterogeneity in susceptibilities can explain inconsistencies found across studies. To strengthen the evidence, future studies ought to be designed specifically to identify susceptible subpopulations.

4.XI. CHAPTER 4 TABLES 4.3–4.18

Table 4.3. Studies of Long-Term Exposure to Traffic Pollution and All-Cause Mortality[a]

Study / Location	Years of Study (N = deaths)	Effect Estimate RR (95% CI)	Effect Scale and Exposure Metric[b]
Beelen et al. 2008b the Netherlands	1987–1996 (15,287)		Full cohort
		1.05 (0.97 to 1.12)	Distance from major road per 2.3 m natural log of distance
		1.05 (1.00 to 1.11)	Per 10 μg/m^3 BS, background and local
Finkelstein et al. 2004 Ontario, Canada	1992–2001 (923)		≤ 50 m from major road or ≤ 100 m from highway
		1.18 (1.02 to 1.38)	All subjects
		1.27 (0.92 to 1.75)	Subjects not diagnosed with chronic pulmonary disease
Gehring et al. 2006 North Rhine-Westphalia, Germany	2001–2003 (399)[c]	**1.29 (0.93 to 1.78)**	Distance from major road ≤ 50 m vs. > 50 m
Hoek et al. 2002 the Netherlands	1986–1994 (489)	1.04 (0.65 to 1.64)	Per 10 μg/m^3 in modeled BS, background
		1.31 (0.95 to 1.80)	Per 10 μg/m^3 in modeled BS, background and local (95th−5th percentile)
		1.53 (1.01 to 2.33)	Distance from major road ≤ 50 m vs. > 50 m
Jerrett et al. 2005 Los Angeles, Calif.	1982–2000 (5856)	1.17 (1.05 to 1.30)	Per 10 μg/m^3 $PM_{2.5}$ (controlling for 44 individual covariates)
		1.11 (0.99 to 1.25)	Per 10 μg/m^3 $PM_{2.5}$ (controlling for 44 individual covariates and parsimonious contextual covariates)
Lipfert et al. 2006a United States	1999–2001 (5638)[d]	Exponentialized coefficients	
		1.041 (1.001 to 1.084)	Ln (traffic density)[e] with vanadium and nickel
		1.051 (1.007 to 1.097)	Ln (traffic density)[e] with EC and NO_3^-
Lipfert et al. 2006b United States	1976–1981	1.024 (1.006 to 1.042)	Ln (traffic density)[e]
	1997–2001	**1.020 (0.996 to 1.040)**	Ln (traffic density)[e]
	1976–1981	1.021 (1.000 to 1.042)	Ln (traffic density),[e] with 1 log increment for the log of population density
	1997–2001	1.019 (0.991 to 1.048)	
	1976–1981	1.024 (1.003 to 1.044)	Ln (traffic density),[e] with 1 log increment for the log of housing density
	1997–2001 (11,785 and 5638)	1.019 (0.991 to 1.048)	

[a] Models adjusted for covariates unless noted. **Bold** indicates RRs are plotted in Figure 4.1. Abbreviations: RR = relative risk.

[b] Estimates at residential address unless otherwise indicated.

[c] Females only.

[d] Males only.

[e] Traffic density = (road km per km^2) × (vehicles traveled/day on selected county roads).

Table 4.4. Relative Risk (RR) of 100-μg/m^3 Increases in BS on Mortality in Total Population and in Population Exposed to Traffic (Adapted from Roemer and van Wijnen 2001)

Lag	Total Population Using Background Sites RR (95% CI)	Population Exposed to Traffic Using Background Sites RR (95% CI)	Total Population Using Traffic Sites RR (95% CI)
Lag 1 Day	1.383 (1.153 to 1.659)	1.887 (1.207 to 2.949)	1.122 (1.023 to 1.231)
Lag 2 Days	1.217 (1.011 to 1.466)	1.730 (1.096 to 2.732)	1.124 (1.024 to 1.234)
Mean of lag 0–lag 6	1.254 (1.100 to 1.431)	1.294 (0.929 to 1.801)	1.132 (1.050 to 1.220)

Table 4.5. Studies of Long-Term Exposure to Traffic Pollution and Cardiovascular and Cardiopulmonary Mortality[a]

Study / Location	Years (*N* = deaths)	Effect Estimate RR (95% CI)	Effect Scale and Exposure Metric[b]
Beelen et al. 2008b the Netherlands	1987–1996 (904)		Respiratory (full cohort)
		1.22 (0.99 to 1.50)	Per 10 µg/m^3 BS, background and local
		1.37 (1.00 to 1.87)	Per 30 µg/m^3 NO_2, background and local
		1.19 (0.91 to 1.56)	Distance from major road per 2.3 m natural log of distance
			Cardiovascular (full cohort)
		1.04 (0.95 to 1.13)	Per 10 µg/m^3 BS, background and local
		1.07 (0.94 to 1.21)	Per 30 µg/m^3 NO_2 , background and local
		1.05 (0.93 to 1.18)	Distance from major road per 2.3 m natural log of distance
Finkelstein et al. 2005 Ontario, Canada	1992–2001 (310)		Cardiovascular (*N* = 58)
		1.38 (1.07 to 1.78)	Distance ≤ 50 m of major road or ≤ 100 m of highway
			Cerebrovascular (*N* = 252)
		1.84 (1.09 to 3.10)	Distance ≤ 50 m of major road or ≤ 100 m of highway
			Both without the deprivation index
Gehring et al. 2006 North Rhine-Westphalia, Germany	2001–2003 (139)[c]		Cardiopulmonary
		1.70 (1.02 to 2.61)	Distance ≤ 50 m vs > 50 m
Hoek et al. 2002 the Netherlands	1986–1994 (185)		Cardiopulmonary
		1.34 (0.68 to 2.64)	Per 10 µg/m^3 in modeled BS, background only
		1.71 (1.10 to 2.67)	Per 10 µg/m^3 in modeled BS, background and local
		1.95 (1.09 to 3.51)	Distance ≤ 50 m of major road or ≤ 100 m of highway
Jerrett et al. 2005 Los Angeles, Calif.	1982–2000 (3136)		Cardiopulmonary
		1.12 (0.97 to 1.30)	Per 10 µg/m^3 modeled $PM_{2.5}$ (44 individual covariates)
		1.07 (0.91 to 1.26)	Per 10 µg/m^3 modeled $PM_{2.5}$ (44 individual covariates and parsimonious contextual model [based on 11 covariates])
Jerrett et al. 2009 Toronto	2002–2004 (80)		Circulatory[d]
		1.45 (1.10 to 1.92)	Per IQR NO_2 (4 ppb = 7.65 µg/m^3)
		1.22 (0.74 to 2.02)	Distance ≤ 50 m of major road or ≤ 100 m of highway
		1.39 (1.05 to 1.85)	Distance from major road and IQR increase in NO_2
Maheswaran and Elliott 2003 England and Wales	1991–1992 (189,966)		Stroke
			Distance to major road, reference ≥ 1000 m[e]
		1.05 (1.04 to 1.07)	< 200 m
		1.03 (1.01 to 1.05)	200 to < 500 m
		1.02 (1.00 to 1.03)	500 to < 1000 m

[a] Models adjusted for covariates unless noted. **Bolded** RRs are plotted in Figure 4.3.

[b] Estimates at residential address unless otherwise indicated.

[c] Females only.

[d] No associations for noncirculatory, respiratory, or lung cancer deaths; overall *N* = 2360.

[e] Calculated from the centroid of each 1991 census enumeration district in England and Wales.

Table 4.6. Studies of Exposure to Traffic Pollution and Cardiac Electrophysiologic Response[a]

Study / Location	Protocol (*N* and Age)	Selected Traffic Surrogate	Selected Outcomes	Estimated Effect Change (95% CI or ± SE)
Adar et al. 2007 St. Louis, Mo.	1-hr bus trip, several off-bus activities, 1-hr bus trip (*N* = 44, age ≥ 60 yr)	5-, 30-, 60-min and 4- and 24-hr BC and $PM_{2.5}$ expsoures (moving averages) BC IQR magnitude: On bus: 2.6 μg/m^3 Off bus: 0.27 μg/m^3	HRV SDNN (msec) 5-min mean overall 24-hr mean overall 5-min on bus 5-min off bus LF/HF 5-min mean overall 24-hr mean overall 5-min on bus 5-min off bus	% change per IQR BC −0.3 (−0.1 to −0.5) −4.7 (−3.5 to −5.9) −4.6 (−3.0 to −6.1) −0.1 (0.1 to −0.3) 0.3 (0.1 to 0.6) 6.5 (4.5 to 8.6) −0.8 (−3.1 to 1.7) 0.8 (0.5 to 1.1)
Gold et al. 2005 Boston, Mass.	12 weekly tests; rest, stand walk, rest, paced breathing (*N* = 28, age 61–89 yr)	5-hr BC (measured ≤ 500 m of residence) 90th−10th percentile = 1.60 μg/m^3	ST segment ↓ (mm) Rest Exercise Post exercise and rest	mm change per 90th−10th percentile of BC −0.11 (−0.02 to −0.20) −0.08 (0.00 to −0.17) −0.11 (−0.05 to −0.18)
Lanki et al. 2006 Helsinki	Biweekly tests for 6 mo, 6-min submax bicycle ergometry (*N* = 47, age ≥ 50 yr)	"Local traffic" $PM_{2.5}$ from source apportionment (measured at fixed site)	Any ST segment ↓ (mV) Lag 1 day Lag 2 days	OR for > 0.1 mV per 1-μg $PM_{2.5}$ 1.22 (0.88 to 1.69) 1.53 (1.19 to 1.97)
Riediker et al. 2004a North Carolina	4 consecutive days of testing and monitoring (*N* = 9, age 23–29 yr)	In-vehicle (police patrol car) $PM_{2.5}$ during 9-hr shift by gravimetric and light scattering	Morning after exposure HRV SDNN (msec) Light scatter Gravimetric Total Power (msec) Light scatter Gravimetric VPBs per hr Light scatter Gravimetric	Slope per 10-μg/m^3 $PM_{2.5}$ 15.2 (± 5.02) 10.3 (± 9.45) 13.4 (± 8.20) 20.7 (± 13.7) 2.76 (± 1.31) 3.00 (± 13.7)
Riediker et al. 2004b North Carolina	4 consecutive days of monitoring (*N* = 9, age 23–29 yr)	Source apportionment of in-vehicle $PM_{2.5}$ 1. crustal material 2. automotive steel wear 3. gasoline combustion 4. speed-changing traffic (emissions/brake wear)	Morning after exposure HRV MCL	% change[b] per 1 SD of speed-change factor + 16% (HRV) + 7% (MCL) Only graphic data available for other factors.
Schwartz et al. 2005 Boston, Mass.	12 weekly tests; rest, stand walk, rest, paced breathing (*N* = 28, age 61–89 yr)	24-hr BC	HRV SDNN (msec) LF/HF	% change per IQR increase in BC −5.1 (−1.5 to −8.6) 7.2 (0.7 to 14.1)

[a] Abbreviations: BC = black carbon; HF = high frequency; HRV = heart-rate variability; IQR = interquartile range; LF = low frequency; MCL = mean cycle length of the normal-to-normal intervals; SDNN = standard deviation of the normal-to-normal intervals; and VPB = ventricular premature beats.

[b] Percent change was estimated from a graph.

Table 4.7. Studies of Exposure to Traffic Pollution and Cardiovascular Morbidity[a,b]

Study / Location	Years of Study (*N* and Age)	Outcome	Selected Effect Estimate OR or % Change (95% CI)	Effect Scale and Exposure Metric[c]
Hoffmann et al. 2006 Rhine-Ruhr region in Germany	2000–2003 (3399, age 45–75 yr)	Prevalence of clinical CHD	**1.85 (1.21 to 2.84)**	≤ 150 m vs. > 150 m from a major road (30–110 × 10^3 vehicles/day)
Hoffmann et al. 2007 Rhine-Ruhr region in Germany	2000–2003 (4494, age 45–75 yr)	High CAC (CAC above age- and gender-specific 75th percentile)	**1.45 (1.15 to 1.82)** 7.0% (0.1 to 14.4) higher CAC	≤ 100 m vs > 100 m from a major road 50% reduction in distance of residence to roadway
Rosenlund et al. 2006 Stockholm	1992–1994 (1397 cases, 1870 controls, age 45–70 yr)	First MI	Non-fatal **0.89 (0.67 to 1.19)** (*n* =1085) In-hospital death **1.28 (0.75 to 2.17)** (*n* = 188) Out-hospital death **2.17 (1.05 to 4.51)** (*n* = 84)	NO_2 from dispersion-modeled traffic-generated pollution per 30 μg/m^3 (95th − 5th percentile)
Tonne et al. 2007 Worcester, Mass.	1995–2003, odd years (5049 cases, 10,277 controls, age ≥ 25 yr)	AMI	**1.06 (1.03 to 1.09)** **1.06 (1.02 to 1.10)**	Natural log of daily traffic ≤ 100 m buffer (cumulative traffic) Distance from major roadway (per km) Adjusted for spatial autocorrelation

[a] See Figure 4.4. Models adjusted for covariates unless noted. **Bold** indicates odds ratios plotted in Figure 4.4.

[b] Abbreviations: AMI = acute myocardial infarction; CAC = coronary artery calcification; CHD = coronary heart disease; MI = myocardial infarction; OR = odds ratio.

[c] Estimates at residential address unless otherwise indicated.

Table 4.8. Studies of Exposure to Traffic Pollution and Incidence of Doctor-Diagnosed Asthma in Children[a,b]

Study / Location	Birth Year (*N*) Age at Observation	Effect Estimate OR or HR (95% CI)	Effect Scale and Exposure Metric[c]
Brauer et al. 2002	1996–1997 (2989)		OR per IQR:
the Netherlands	0–12 mo	1.27 (1.01 to 1.59)	Per 0.54 × 10^{-5}/m local "soot"
(PIAMA cohort)	12–24 mo	1.12 (0.88 to 1.43)	(= 0.8 μg/m^3 EC)
	0–24 mo	1.14 (0.94 to 1.38)	
	2 yr	1.12 (0.88 to 1.43)	
	0–12 mo	**1.25 (1.00 to 1.57)**	Per 10.3 μg/m^3 local NO_2
	12–24 mo	**1.18 (0.88 to 1.43)**	
	0–24 mo	1.16 (0.96 to 1.40)	
	2 yr	1.18 (0.93 to 1.51)	
Brauer et al. 2007	1996–1997 (2826)		OR per IQR:
the Netherlands	All subjects at age 4 yr	1.30 (0.98 to 1.71)	Per 0.58 × 10^{-5}/m local "soot"
(PIAMA cohort)	Children with full follow-up	1.26 (1.02 to 1.56)	(= 0.84 μg/m^3 EC)
	All subjects at age 4 yr	**1.29 (0.99 to 1.69)**	Per 10.6 μg/m^3 local NO_2
	Children with full follow-up	**1.19 (1.04 to 1.56)**	
Gehring et al. 2002	1995–1999		
Munich	Diagnosis of obstructive/		
(GINI and LISA cohorts)	asthmoid bronchitis		OR per IQR:
	Age 1 yr (1597)	0.99 (0.81 to 1.22)	Per 0.4 × 10^{-5}/m local "soot"
	Age 2 yr (1517)	0.94 (0.79 to 1.12)	Per 0.4 × 10^{-5}/m local "soot"
	Age 1 yr (1597)	**0.97 (0.77 to 1.23)**	Per 8.5 μg/m^3 local NO_2
	Age 2 yr (1517)	**0.90 (0.74 to 1.10)**	Per 8.5 μg/m^3 local NO_2
Jerrett et al. 2008	1983 or 1986 (217)		HR per IQR:
Southern California	Age 10 yr	**1.29 (1.07 to 1.56)**	Per 6.2 ppb measured (or 11.7 μg/m^3)
(Children's Health Study cohort)	Incident cases (23) during 8 yr of follow-up, 11 communities		annual local NO_2
Morgenstern et al. 2007	1995–1999 (3059 age 1 yr;		OR per IQR:
Munich	2861 age 2 yr)		
(GINI and LISA cohorts)	Age 1 yr	1.14 (0.88 to 1.48)	Per 0.22 × 10^{-5}/m local "soot"
	Age 2 yr	0.85 (0.31 to 2.34)	
	Age 1 yr	**1.30 (1.03 to 1.66)**	Per 5.7 μg/m^3 local NO_2
	Age 2 yr	**0.82 (0.33 to 2.03)**	
	Age 1 yr	**1.12 (0.88 to 1.44)**	≤ 50 m to major road vs. > 50 m
	Age 2 yr	**1.23 (1.00 to 1.51)**	
Morgenstern et al. 2008	1995–1999, (2436)		
Munich	Diagnosis of obstructive	1.56 (1.03 to 2.37)	Per IQR 0.2 × 10^{-5}/m local "soot"
(GINI and LISA cohorts)	/asthmoid bronchitis	**1.04 (0.67 to 1.39)**	Per IQR 6.4 μg/m^3 local NO_2
		1.66 (1.01 to 2.59)	≤ 50 m from main road
Shima et al. 2003	1983–1986 (2506) (4-yr study)	Male: **1.99 (0.79 to 4.99)**	≥ 50 m from trunk road
Chiba Prefecture, Japan	Age 6–9 yr	Female: **1.74 (0.63 to 4.81)**	(~ 70,000 vehicles/12 hr) (rural = reference)
		Male: **3.77 (1.00 to 14.16)**	0–49 m from trunk road
		Female: **4.03 (0.9 to 17.69)**	(rural = reference)
Zmirou et al. 2004	1984–1996	Exposure before age 3 yr:	Traffic density, < 11.2 vehicles/day/
France	(217 pairs of cases and	**1.48 (0.74 to 3.02)**	m (distance)
(VESTA studies)	controls)	**2.28 (1.14 to 4.56)**	2nd tertile 11.2–28.8 vehicles/day/m
	Age 4–14 yr	1.30 (1.04 to 1.62)	3rd tertile ≥ 30 vehicles/day/m
			Per unit increase in log-transformed traffic density
		In atopics:	
		11.03 (1.3 to 100.9)	3rd tertile

[a] Models adjusted for covariates unless noted. **Bold** indicates an OR plotted in Figure 4.5.

[b] Abbreviations: GINI = German Infant Nutrition Intervention Programme; HR = hazard ratio; IQR = interquartile range; LISA = Influences of Lifestyle Related Factors on the Human Immune System and Development of Allergies in Children; OR = odds ratio; PIAMA = Prevention and Incidence of Asthma and Mite Allergy; and VESTA = Five (V) Epidemiological Studies of Transport and Asthma.

[c] Estimates at residential address unless otherwise indicated.

Table 4.9. Studies of Exposure to Traffic Pollution and Prevalence of Doctor-Diagnosed Asthma in Children[a,b]

Study / Location	Years of Study (*N*) Age at Observation	Effect Estimate OR (95% CI)	Effect Scale and Exposure Metric[c]
Gauderman et al. 2005 Southern California	1993 and 1996 (208) Age 10 yr	**1.83 (1.04 to 3.21)** **1.89 (1.19 to 3.02)** 1.45 (0.73 to 2.91)	NO_2 (per IQR 5.7 ppb [= 10.8 µg/m^3] Distance to freeway (per IQR 1.2 km) Traffic volume within 150 m
Gordian et al. 2006 Anchorage, Alaska	2003 (671 in adjusted model) Age 5–7 yr	Traffic density within 100 m of residence All children: **1.40 (0.77 to 2.55)** **2.83 (1.23 to 6.51)** Children without parental asthma: 2.43 (1.12 to 5.28) 5.34 (2.08 to 13.74)	Reference, < 4 × 10^6 (vm) Medium traffic (4 × 10^6 to 8 × 10^6 vm) High traffic (> 8 × 10^6 vm) Medium traffic High traffic
Hirsch et al. 1999 Dresden, Germany	1995–1996 (4477 and 4350) Age 5–7 yr and 9–11 yr	All children: 1.11 (0.97 to 1.25) Non-atopic children: 1.32 (1.07 to 1.62) All children: **1.16 (0.94 to 1.42)** Non-atopic children: **1.49 (1.04 to 2.16)** All children: 1.07 (0.94 to 1.21) Non-atopic children: 1.29 (1.05 to 1.59)	Benzene (per 1 µg/m^3) NO_2 (per IQR 10 µg/m^3) CO (per 0.2 µg/m^3)
Janssen et al. 2003 the Netherlands	1997–1999 (2053) Age 7–12 yr	**1.02 (0.43 to 2.44)** **1.04 (0.74 to 1.45)** 1.36 (0.62 to 2.98) **1.39 (0.75 to 2.56)**	Truck traffic density within 400 m of school per 17,000/weekday Distance to motorway (< 100 m vs. 100–400 m) Soot (per 10 µg/m^3) at school NO_2 (per 18 µg/m^3) at school
Kim et al. 2004 San Francisco Bay area	1991–1993 (1109) Age 8–10 yr	All: 1.05 (0.98 to 1.12) LTR: **1.08 (1.0 to 1.15)** LTR girls: 1.19 (1.03 to 1.36) LTR boys: 1.02 (0.94 to 1.12)	NO (per IQR 11.6 ppb [= 21.9 µg/m^3]) at school
Kim et al. 2008 San Francisco Bay area	2001 (1080) Age 8–10 yr (3rd–5th graders from 10 schools)	**1.43 (1.04 to 1.54)** **3.80 (1.20 to 11.71)** **1.87 (0.71 to 4.90)** **1.25 (0.5 to 3.11)** 1.41 (0.81 to 2.46) 1.05 (0.58 to 1.91)	Log-distance to freeway, continuous, per 939 m Distance to freeway with reference > 300 m ≤ 75 m > 75–150 m > 150–300 m Distance to freeway by wind direction ≤ 300 m downwind vs. > 300 m ≤ 300 m upwind vs. > 300 m

Table continues next page

[a] Models adjusted for covariates unless noted. **Bold** indicates ORs plotted in Figure 4.6.

[b] Abbreviations: IQR = interquartile range; LTR = long-term resident; OR = odds ratio; and vm = vehicle meter.

[c] Estimates at residential address unless otherwise indicated.

Table 4.9 (*Continued*). Studies of Exposure to Traffic Pollution and Prevalence of Doctor-Diagnosed Asthma in Children[a,b]

Study / Location	Years of Study (*N*) Age at Observation	Effect Estimate OR (95% CI)	Effect Scale and Exposure Metric[c]
Lewis et al. 2005 United Kingdom	2003 (11,562) Age 4–6 yr	**1.14 (0.96 to 1.36)**	Distance from main road vs. >150 m
		1.02 (0.87 to 1.21)	90–149 m
		0.90 (0.69 to 1.18)	30–89 m
			< 30 m
McConnell et al. 2006 Southern California	2003 (4742, LTR: 1856) Age 5–7 yr	All children: **1.29 (1.01 to 1.66)**	< 75 m from a major road vs. > 300 m
		No parental asthma: 1.85 (1.11 to 3.09)	
		No allergic symptoms: 2.27 (1.04 to 4.94)	
		Female LTR: 2.51 (1.39 to 4.54)	
		Male LTR: 0.94 (0.54 to 1.64)	
Nicolai et al. 2003 Munich	1995–1996 (3946) Age 5–7 yr and 9–11 yr	All children: **1.19 (0.76 to 1.87)**	Traffic density < 50 m, vehicles/day (> 30,000) vs. rest of population
		1.42 (0.92 to 2.2)	Soot (> 10.7 µg/m^3): highest tertile vs. rest of population
		1.28 (0.81 to 2.01)	NO_2 (> 57.4 µg/m^3): highest tertile vs. rest of population
		Children exposed to environmental tobacco smoke: 1.75 (0.98 to 3.12)	Soot (> 10.7 µg/m^3) highest tertile
van Vliet et al. 1997 South Holland	1993 (878 living < 1000 m from freeway) Age 7–12 yr	1.68 (0.68 to 4.14)	≤ 100 m of freeway vs. > 100 m
		0.54 (0.18 to 1.60)	Truck density on freeway
		0.22 (0.04 to 1.13)	BS concentration in school
		0.37 (0.11 to 1.24)	NO_2 concentration in school
Wjst et al. 1993 Munich	1989–1990 (6537) Age 9–11 yr	Lifetime: **1.06 (0.97 to 1.16)** Present past year: 1.04 (0.89 to 1.21)	Traffic density in school district per 25,000 vehicles/day

[a] Models adjusted for covariates unless noted. **Bold** indicates ORs plotted in Figure 4.6.

[b] Abbreviations: IQR = interquartile range; LTR = long-term resident; OR = odds ratio; and vm = vehicle meter.

[c] Estimates at residential address unless otherwise indicated.

Table 4.10. Studies of Exposure to Traffic Pollution and Wheeze in Children[a,b]

Study / Location	Birth Year (*N*) Age at Observation	Effect Estimate OR (95% CI)	Effect Scale and Exposure Metric[c]
Cohort			
Brauer et al. 2002 the Netherlands	1996–1997 (2991) Age 2 yr	**1.11 (0.97 to 1.26)**	Per IQR 0.54×10^{-5}/m (= 0.8 µg/m^3 EC) local "soot"
		1.13 (0.99 to 1.29)	Per IQR 10.3 µg/m^3 local NO_2
Brauer et al. 2007 the Netherlands	1996–1997 (2825) Age 3 mo–4 yr	Full cohort at 4 yr of age	
		1.18 (1.00 to 1.40)	Per IQR 0.58×10^{-5}/m (= 0.8 µg/m^3 EC) local "soot"
		1.16 (0.98 to 1.36)	Per IQR 10.6 µg/m^3 local NO_2
		Children with full follow-up at 4 yr (*N* = 2575)	
		1.18 (1.04 to 1.34)	Per IQR 0.58×10^{-5}/m local "soot"
		1.19 (1.05 to 1.34)	Per IQR 10.6 µg/m^3 local NO_2
		Children with food allergies at 4 yr (*N* = 708)	
		1.64 (1.21 to 2.23)	Per IQR 0.58×10^{-5}/m local "soot"
		1.49 (1.13 to 1.97)	Per IQR 10.6 µg/m^3 local NO_2
Gehring et al. 2002 Munich	1995–1999 (1722) Age 1 yr	0.93 (0.78 to 1.12)	Per IQR 0.4×10^{-5}/m local "soot"
		0.87 (0.70 to 1.08)	Per IQR 8.5 µg/m^3 local NO_2
	(1627) Age 2 yr	0.98 (0.84 to 1.14)	Per IQR 0.4×10^{-5}/m local "soot"
		0.94 (0.79 to 1.12)	Per IQR 8.5 µg/m^3 local NO_2
Morgenstern et al. 2007 Munich	1995–1999		
	Age 1 yr (*N* = 3037)	0.97 (0.77 to 1.23)	Per IQR 0.4×10^{-5}/m local "soot"
	Age 2 yr (*N* = 2882)	1.09 (0.9 to 1.33)	
	Age 1 yr	**1.09 (0.88 to 1.35)**	Per IQR 5.7 µg/m^3 local NO_2
	Age 2 yr	**1.09 (0.90 to 1.31)**	
	Age 1 yr	**1.14 (0.92 to 1.42)**	≤ 50 m of road vs. > 50 m
	Age 2 yr	**1.06 (0.88 to 1.27)**	
Shima et al. 2003 Chiba Prefecture, Japan	1983–1986 (1858)	Male: 1.02 (0.44 to 2.36)	≥ 50 m of trunk road (rural = reference)
		Female: 0.79 (0.26 to 2.39)	
		Male: 1.35 (0.34 to 5.32)	0–49 m of trunk road
		Female: 0.76 (0.08 to 7.00)	
Cross-Sectional			
Gauderman et al. 2005 Southern California	1983 and 1986 (208) Age 10 yr	**1.72 (1.07 to 2.77)**	Per IQR 5.7 ppb (= 10.8 µg/m^3) measured NO_2
		1.59 (1.06 to 2.36)	Distance to freeway (per IQR 1.2 km)
		1.70 (1.12 to 2.58)	Per IQR 1.27 ppb NO_2 (= 2.4 µg/m^3) from freeway traffic; estimated from dispersion model
		Wheeze with exercise:	
		2.01 (1.08 to 3.72)	Per IQR 5.7 ppb (= 10.8 µg/m^3) measured NO_2
		2.57 (1.50 to 4.38)	Distance to freeway (per IQR 1.2 km)
		2.56 (1.50 to 4.38)	Per IQR 1.27 ppb NO_2 (= 2.4 µg/m^3) from freeway traffic; estimated from dispersion model

Table continues next page

[a] Estimates from cohort and cross-sectional studies adjusted for covariates unless noted. **Bold** indicates ORs plotted in Figures 4.7a and 4.7b.

[b] Abbreviations: IQR = interquartile range; OR = odds ratio; SES = socioeconomic status; and LTR = long-time resident.

[c] Estimates at residential address unless otherwise indicated.

Table 4.10 (*Continued*). Studies of Exposure to Traffic Pollution and Wheeze in Children[a,b]

Study / Location	Birth Year (*N*) Age at Observation	Effect Estimate OR (95% CI)	Effect Scale and Exposure Metric[c]
Cross-Sectional (*Continued*)			
Hirsch et al. 1999 Dresden	1984–1991 (4518 and 4379) Age 5–7 and 9–11 yr	**1.13 (0.93 to 1.37)** Non-atopic: 1.16 (0.79 to 1.70)	Per IQR 10 μg/m^3 NO_2
Janssen et al. 2003 the Netherlands	1985–1991 (2071) Age 7–12 yr	1.20 (0.89 to 1.62) 1.43 (0.66 to 3.07) **1.74 (0.99 to 3.05)** **1.96 (0.88 to 4.38)** Sensitized to outdoor allergens: 5.31 (CI not available), $P = 0.04$	Distance to motorway (100 m vs. 400 m) Soot per 9.3 μg/m^3 at school NO_2 per 18 μg/m^3 at school Both, maximum − minimum Truck traffic per 17,000/day within 400 m of school (maximum − minimum) NO_2 per 18 μg/m^3
Krämer et al. 2000 Dusseldorf	1986–1987 (317) Age 9 yr	Female: 20.41 (1.81 to 230.62) Male: 17.38 (0.91 to 330.72)	Per 10 μg/m^3 NO_2
McConnell et al. 2006 Southern California	1996–1998 (4742; LTR: 1856) Age 5–7 yr	**1.40 (1.09 to 1.78)** No parental asthma: 2.74 (1.71 to 4.39) No allergic symptoms: 2.58 (1.14 to 5.86) Long-term residents Female: 1.95 (1.11 to 3.41) Male: 1.41 (0.84 to 2.37)	Living < 75 m of major road (reference > 300 m of major road)
Nicolai et al. 2003 Munich	1995–1996 (3889) Age 5–7 and 9–11 yr	Current asthma: 1.79 (1.05 to 3.05) Current wheeze: **1.66 (1.07 to 2.58)** Current asthma: 1.66 (0.94 to 2.90) Current wheeze: **1.58 (1.01 to 2.48)**	Traffic density < 50 m, vehicles/day (> 30,000) vs. rest of population NO_2 (> 57.4 μg/m^3), highest tertile vs. rest of population (reference)
Nordling et al. 2008 Four municipalities in Sweden	1990–1992 (3515) Age 4 yr	Persistent wheezing up to 4 yr 1.64 (0.90 to 3.00) **1.60 (1.09 to 2.36)**	From source-specific dispersion models Per 6 μg/m^3 PM_{10} (95th−5th percentile) Per 44 μg/m^3 NO_x (95th−5th percentile) and 10,000–30,000 vehicles/day
Oosterlee et al. 1996 Haarlem, the Netherlands	1976–1991 (291) Age 0–15 yr	Wheeze in past year Girls: **5.3 (1.1 to 25.0)** Boys: **0.7 (0.2 to 2.5)**	Living on busy streets (high NO_2) vs. living on quiet streets

Table continues next page

[a] Estimates from cohort and cross-sectional studies adjusted for covariates unless noted. **Bold** indicates ORs plotted in Figures 4.7a and 4.7b.

[b] Abbreviations: IQR = interquartile range; OR = odds ratio; SES = socioeconomic status; and LTR = long-time resident.

[c] Estimates at residential address unless otherwise indicated.

Table 4.10 (*Continued*). Studies of Exposure to Traffic Pollution and Wheeze in Children[a,b]

Study / Location	Birth Year (*N*) Age at Observation	Effect Estimate OR (95% CI)	Effect Scale and Exposure Metric[c]
Cross-Sectional (*Continued*)			
Pierse et al. 2006 Leicestershire, U.K.	1993–1997 (2584) Follow-up in 2001 (2331) Age 1–5 yr	Prevalence in 1998: 0.99 (0.88 to 1.12) Prevalence in 2001: 1.28 (1.04 to 1.58) Incidence in 2001: 1.42 (1.02 to 1.97)	Per 1 μg/m^3 primary PM_{10} (estimated from dispersion model)
Pikhart et al. 1997 Prague	(3340) Age 7–10 yr	Crude association 1.06 (0.90 to 1.24) 1.36 (1.15 to 1.61) Adjusted associations 0.81 (0.65 to 1.01) 1.47 (1.20 to 1.79)	NO_2 per 10 μg/m^3 NO_2 home NO_2 school Adjusted for SES, traffic noise, and other covariates with both home and school NO_2 in the model NO_2 home NO_2 school
Ryan et al. 2005 Cincinnati, Ohio	2002–2003 (622) Age < 1 yr	Wheeze without cold **2.50 (1.15 to 5.42)**	Living < 100 m from stop-and-go truck traffic (< 50 mi/hr) on a state route (reference: > 100 m to state route or > 400 m to highway)
Van Roosbroeck et al. 2008 the Netherlands	1985–1992 (1862) Age 7–12 yr	2.15 (0.59 to 7.74) **2.94 (0.85 to 10.18)**	Soot per 9.3 μg/m^3 at school NO_2 per 17.6 μg/m^3 at school (maximum−minimum) Adjusted for measurement error
van Vliet et al. 1997 South Holland	1983–1988 (878 living < 1000 m from freeway) Age 7–12 yr	Wheeze: **2.00 (0.99 to 4.03)** Asthma attacks: 0.87 (0.32 to 2.37) Wheeze in females only: 3.05 (1.11 to 8.41) Asthma attacks in females only: 1.00 (0.26 to 3.94)	≤ 100 m vs. > 100 m of freeway (80,000–150,000 vehicles/day)
Venn et al. 2000 Nottingham, U.K.	1979–1992 Age 4–11 yr (22,968) Age 11–16 yr (27,826)	Age 4–11 yr Medium: **1.11 (1.02 to 1.22)** High: **1.13 (1.03 to 1.24)** Age 11–16 yr Medium: **0.99 (0.92 to 1.06)** High: **0.94 (0.87 to 1.01)**	Per 10-unit increase in the traffic activity index (vm/day/km^2) at school within 1×1 km grid
Venn et al. 2001 Nottingham, U.K.	Same as above	Age 4–11 yr All: 1.08 (1.00 to 1.16) Girls: **1.14 (1.01 to 1.28)** Boys: **0.98 (0.87 to 1.09)** Age 11–16 yr All: 1.16 (1.02 to 1.32)	Per 30-m distance of school to main road (within 150 m)

Table continues next page

[a] Estimates from cohort and cross-sectional studies adjusted for covariates unless noted. **Bold** indicates ORs plotted in Figures 4.7a and 4.7b.

[b] Abbreviations: IQR = interquartile range; OR = odds ratio; SES = socioeconomic status; and LTR = long-time resident.

[c] Estimates at residential address unless otherwise indicated.

Table 4.10 (*Continued*). Studies of Exposure to Traffic Pollution and Wheeze in Children[a,b]

Study / Location	Birth Year (*N*) Age at Observation	Effect Estimate OR (95% CI)	Effect Scale and Exposure Metric[c]
Cross-Sectional (*Continued*)			
Venn et al. 2005 Jimma, Ethiopia	(1413) children Age < 16 yr (See Table 4.13 for adults)	All subjects ≤ 150 m of road **1.17 (1.01 to 1.36)** Children < 16 yr: **1.27 (0.93 to 1.73)**	Per 30-m distance to main road (within 150 m)
		1.26 (1.03 to 1.53)	Closest road > median flow (653 vehicles/12 hr)
		1.08 (0.86 to 1.35)	Closest road < median flow
Wjst et al. 1993 Munich	1978–1981 (6537) Age 9–11 yr	**1.08 (1.01 to 1.16)**	Traffic density on street with maximum traffic volume within school district (~2 km radius, 117 districts) per 25,000 cars/day.
Yang et al. 2002 Kaohsiung, Taiwan	1987–1992 (3221 high-traffic; 2969 low-traffic) Age 6–11	1.01 (0.84 to 1.21)	Two-school comparison (high-traffic = 36.3 ppb [68.6 μg/m^3] NO_2; low-traffic = 23.2 ppb [43.8 μg/m^3] NO_2)

[a] Estimates from cohort and cross-sectional studies adjusted for covariates unless noted. **Bold** indicates ORs plotted in Figures 4.7a and 4.7b.

[b] Abbreviations: IQR = interquartile range; OR = odds ratio; SES = socioeconomic status; and LTR = long-time resident.

[c] Estimates at residential address unless otherwise indicated.

Table 4.11. Studies of Exposure to Traffic Pollution and Other Respiratory Symptoms in Children[a,b]

Study / Location	Birth Year (*N*) Age at Observation	Effect Estimate OR (95% CI)[c]	Effect Scale and Exposure Metric[d]
Dry Cough at Night			
Brauer et al. 2002 the Netherlands	1996–1997 (2969) Age 2 yr	1.02 (0.88 to 1.17)	Per IQR 0.54 × 10^{-5}/m local "soot"
		1.02 (0.89 to 1.18)	Per IQR 10.3 μg/m^3 local NO_2
Brauer et al. 2007 the Netherlands	1996–1997 (2830) Age 4 yr	1.14 (1.00 to 1.31)	Per IQR 0.58 × 10^{-5}/m local "soot"
		1.11 (0.97 to 1.26)	Per IQR 10.6 μg/m^3 local NO_2
Gehring et al. 2002 Munich	1995–1999 (1607) Age 1 yr	All: 1.27 (1.04 to 1.55) Males: 1.31 (1.04 to 1.67) Females: 1.26 (0.79 to 1.71)	Per IQR 0.4 × 10^{-5}/m local "soot"
		All: **1.36 (1.07 to 1.74)** Males: 1.45 (1.07 to 1.98) Females: 1.20 (0.78 to 1.84)	Per IQR 8.5 μg/m^3 local NO_2
	(1507) Age 2 yr	All: 1.16 (0.98 to 1.37) Males: 1.17 (0.95 to 1.44) Females: 1.12 (0.84 to 1.48)	Per IQR 0.4 × 10^{-5}/m local "soot"
		All: **1.24 (1.02 to 1.51)** Males: 1.28 (0.99 to 1.66) Females: 1.17 (0.86 to 1.60)	Per IQR 8.5 μg/m^3 local NO_2
Morgenstern et al. 2007 Munich	1993–1997 (3056) Age 1 yr	1.09 (0.78 to 1.51)	Per IQR 0.4 × 10^{-5}/m local "soot"
		1.34 (1.00 to 1.81)	Per IQR 8.5 μg/m^3 local NO_2
		0.84 (0.61 to 1.16)	≤ 50 m to road
	(2866) Age 2 yr	1.18 (0.93 to 1.50)	Per IQR 0.4 × 10^{-5}/m local "soot"
		1.16 (0.92 to 1.47)	Per IQR 8.5 μg/m^3 local NO_2
		0.93 (0.73 to 1.18)	≤ 50 m to road
Pierse et al. 2006 Leicestershire, U.K.	1998 (~ 2570) Follow-up 2001 (~ 2310 prevalence; ~ 1430 incidence) Age 1–5 yr	Nighttime cough Prevalence in 1998: 1.06 (0.94 to 1.19) Prevalence in 2001: 1.25 (1.06 to 1.47) Incidence in 2001: **1.19 (0.96 to 1.47)**	Per 1 μg/m^3 primary PM_{10} (estimated from dispersion model)
		Cough without cold Prevalence in 1998: 1.21 (0.107 to 1.38) Prevalence in 2001: 1.56 (1.32 to 1.84) Incidence in 2001: **1.62 (1.31 to 2.00)**	

Table continues next page

[a] Models adjusted for covariates unless noted. **Bold** indicates OR plotted in Figures 4.8a and 4.8b.

[b] Abbreviations: IQR = interquartile range; LTR = long-term resident; OR = odds ratio; SES = socioeconomic status; and VMT = vehicle miles traveled.

[c] # $P < 0.10$, * $P < 0.05$, ** $P < 0.01$.

[d] Estimates at residential address unless otherwise indicated.

Table 4.11 (*Continued*). Studies of Exposure to Traffic Pollution and Other Respiratory Symptoms in Children[a,b]

Study / Location	Birth Year (*N*) Age at Observation	Effect Estimate OR (95% CI)[c]	Effect Scale and Exposure Metric[d]
Other Symptoms			
Braun-Fahrländer et al. 1992 Zurich and Basel	1980–1986 (625) Age 0–5 yr	Upper respiratory symptoms: **1.19 (0.99 to 1.42)** Duration of symptoms: **1.13 (1.01 to 1.27)** Duration of episodes of breathing difficulty: **1.50 (1.04 to 2.16)**	NO_2 per 20 μg/m^3
Gauderman et al. 2005 Southern California	1983 and 1986 (208) Age 10 yr	Current asthma medication use **2.19 (1.20 to 4.01)**	NO_2 per IQR 5.7 ppb (= 10.8 μg/m^3), measured
		2.04 (1.25 to 3.31)	Distance to freeway, per IQR 1.2 km (75th−25th percentile)
		1.92 (1.18 to 3.12)	NO_2 from freeway traffic per IQR 1.27 ppb (= 2.4 μg/m^3) estimated from dispersion model
Hirsch et al. 1999 Dresden	1984–1991 (3585–4515) Age 5–7 and 9–11 yr	Morning cough All children: **1.22 (1.04 to 1.44)** Non-atopic children: **1.42 (1.10 to 1.84)** Bronchitis All children: **1.23 (1.11 to 1.38)** Non-atopic children: **1.37 (1.17 to 1.62)**	NO_2 per IQR 10 μg/m^3
Janssen et al. 2003 the Netherlands	1985–1992 (~ 2040) Age 7–12 yr	Current phlegm:	Traffic density within 400 m of school:
		2.14 (0.73 to 6.30)	Trucks per 17,000/weekday
		0.48 (0.19 to 1.22)	Cars per 120,000/weekday
		1.52 (0.80 to 2.91)	School motorway distance per 300 m
		2.41 (0.96 to 6.04)#	Soot per 10 μg/m^3 at school
		1.72 (0.82 to 3.62)	NO_2 per 18 μg/m^3 at school
		Current bronchitis:	
		2.41 (0.82 to 7.13)	Trucks per 17,000/weekday
		1.21 (0.87 to 1.68)	Home–highway distance per 300 m
		1.32 (0.44 to 3.94)	Soot per 9.3 μg/m^3 at school
		1.37 (0.60 to 3.12)	NO_2 per 18 μg/m^3 at school

Table continues next page

[a] Models adjusted for covariates unless noted. **Bold** indicates OR plotted in Figures 4.8a and 4.8b.

[b] Abbreviations: IQR = interquartile range; LTR = long-term resident; OR = odds ratio; SES = socioeconomic status; and VMT = vehicle miles traveled.

[c] # $P < 0.10$, * $P < 0.05$, ** $P < 0.01$.

[d] Estimates at residential address unless otherwise indicated.

Table 4.11 (*Continued*). Studies of Exposure to Traffic Pollution and Other Respiratory Symptoms in Children[a,b]

Study / Location	Birth Year (*N*) Age at Observation	Effect Estimate OR (95% CI)[c]	Effect Scale and Exposure Metric[d]
Other Symptoms (*Continued*)			
Kim et al. 2004 San Francisco Bay area	1991–1993 (1109) Age 8–10 yr	Bronchitis symptoms **1.05 (1.02 to 1.09)** 1.04 (1.00 to 1.08)	 NO per IQR 11.6 ppb (= 22 μg/m^3) at school BC per IQR 0.15 μg/m^3 at school
Kim et al. 2008 San Francisco Bay area	1991–1993 (1080) Age 8–10 yr	Bronchitis symptoms 1.47 (1.11 to 1.96) 2.81 (0.94 to 8.39) 1.82 (0.75 to 4.40) 2.00 (0.93 to 4.29) 1.42 (0.87 to 2.33) 1.13 (0.66 to 1.95)	 Log-distance to freeway, continuous, per 939 m Distance to freeway, reference > 300 m ≤ 75 m > 75–150 m > 150–300 m Distance to freeway by wind direction ≤ 300 m vs. > 300 m downwind ≤ 300 m vs. > 300 m upwind
Meng et al. 2008 Los Angeles and San Diego county	1984–2001 (1792) Age 0–17 yr	Asthma symptoms **1.40 (1.04 to 1.86)** **1.72 (1.23 to 2.32)** 2.80 (1.04 to 4.91)	Traffic density (daily VMT/ mi^2) in 500-ft buffer (reference ≤ 20,000) 20,001–200,000 (total population) > 200,000 (total population) > 200,000 (population below federal poverty level)

Table continues next page

[a] Models adjusted for covariates unless noted. **Bold** indicates OR plotted in Figures 4.8a and 4.8b.

[b] Abbreviations: IQR = interquartile range; LTR = long-term resident; OR = odds ratio; SES = socioeconomic status; and VMT = vehicle miles traveled.

[c] # $P < 0.10$, * $P < 0.05$, ** $P < 0.01$.

[d] Estimates at residential address unless otherwise indicated.

Table 4.11 (*Continued*). Studies of Exposure to Traffic Pollution and Other Respiratory Symptoms in Children[a,b]

Study / Location	Birth Year (*N*) Age at Observation	Effect Estimate OR (95% CI)[c]	Effect Scale and Exposure Metric[d]
Other Symptoms (*Continued*)			
Mukala et al. 1996 Helsinki	1985-1988 (172) Age 3–6 yr	Winter and Spring	Living in central urban area (27.4 µg/m^3 median personal NO_2) vs. living in suburban area (18.2 µg/m^3 median personal NO_2)
		Prevalence Cough: **1.66 (1.03 to 2.68)** Nasal symptoms: 1.97 (1.10 to 3.52) Incidence Cough: **1.15 (0.83 to 1.59)** Nasal symptoms: 1.23 (0.91 to 1.67)	
		Spring	Personal NO_2 by tertile (vs. lower tertile)
		Prevalence of cough: 1.17 (0.58 to 2.40)	Medium tertile (17.9 to 26.5 µg/m^3)
		2.18 (0.9 to 5.33)	Upper tertile (26.6 to 45.8)
		Incidence of cough: 1.24 (0.75 to 2.07)	Medium tertile (17.9 to 26.5 µg/m^3)
		1.75 (0.85 to 3.49)	Upper tertile (26.6 to 45.8)
Nicolai et al. 2003 Munich	1984–1991 (7509) Age 5–7 and 9–11 yr	Morning cough: **1.62 (1.16 to 2.27)****	Traffic density < 50 m, > 30,000 vehicles/day, vs. rest of population
		1.60 (1.14 to 2.23)**	NO_2: highest tertile (> 57.4 µg/m^3) vs. rest
Oosterlee et al. 1996 Haarlem, the Netherlands	1976–1991 (291) Age 0–15 yr	Asthma medication — current: 4.8 (0.9 to 27.5) Respiratory medication — ever : 2.2 (1.1 to 4.6)	Living on busy streets (with high NO_2 and 10,000–30,000 vehicles/day) vs. living on quiet streets
Van Roosbroeck et al. 2008 the Netherlands	1987–1992 (~ 1850) Age 7–12 yr	Phlegm: 5.29 (1.24 to 22.62)	Soot (BC) per 9.3 µg/m^3 at school
		3.82 (1.03 to 14.21)	NO_2 per 17.6 µg/m^3 at school (both highest − lowest)
		Conjunctivitis: 5.06 (1.02 to 24.96)	Soot per 9.3 µg/m^3 at school
		6.60 (1.33 to 32.77)	NO_2 per 17.6 µg/m^3 at school Adjusted for measurement error

Table continues next page

[a] Models adjusted for covariates unless noted. **Bold** indicates OR plotted in Figures 4.8a and 4.8b.

[b] Abbreviations: IQR = interquartile range; LTR = long-term resident; OR = odds ratio; SES = socioeconomic status; and VMT = vehicle miles traveled.

[c] # $P < 0.10$, * $P < 0.05$, ** $P < 0.01$.

[d] Estimates at residential address unless otherwise indicated.

Table 4.11 (*Continued*). Studies of Exposure to Traffic Pollution and Other Respiratory Symptoms in Children[a,b]

Study / Location	Birth Year (*N*) Age at Observation	Effect Estimate OR (95% CI)[c]	Effect Scale and Exposure Metric[d]
Other Symptoms (*Continued*)			
van Vliet et al. 1997 South Holland	1983–1988 (1068) Age 7–12 yr	Chronic cough All: **1.64 (0.98 to 2.74)#** Females: **2.45 (1.16 to 5.16)*** Bronchitis past year All: **0.99 (0.39 to 2.52)** Females: **0.99 (0.27 to 3.68)**	≤ 100 m vs. 100 m to freeway
Wilhelm et al. 2008 Los Angeles and San Diego county	1983–2001 (612) Age 0–17 yr	Asthma symptoms **0.95 (0.44 to 2.06)** **0.61 (0.22 to 1.69)**	Traffic density (daily VMT/mi^2) in 500-ft buffer (reference = 20,000) 20,001–200,000 > 200,000
Wjst et al. 1993 Munich	1978–1981 (6537) Age 9–11 yr	Recurrent bronchitis: **1.05 (0.98 to 1.12)** Common cold at exam: 1.20 (1.08 to 1.34) Recurrent dyspnea: 1.10 (1.00 to 1.20) Lifetime cough: **1.06 (0.99 to 1.13)** Lifetime croup: 1.09 (1.00 to 1.18) > 10 upper respiratory infections: 0.95 (0.76 to 1.19)	Traffic density on street with maximum traffic volume within school district (~2 km radius, 117 districts) per 25,000 cars/day
Yang et al. 2002 Kaohsiung, Taiwan	1988–1994 Primary school children (grades 1–6)	Cough: **1.12 (0.92 to 1.35)** Dyspnea: 0.99 (0.83 to 1.17) Bronchitis: **0.99 (0.88 to 1.12)** Upper respiratory symptoms: 1.03 (0.91 to 1.15)	Two-school comparison: high traffic (36.34 ppb NO_2 [= 68.3 μg/m^3]) vs. low traffic (23.22 ppb NO_2 [= 43.8 μg/m^3])

[a] Models adjusted for covariates unless noted. **Bold** indicates OR plotted in Figures 4.8a and 4.8b.

[b] Abbreviations: IQR = interquartile range; LTR = long-term resident; OR = odds ratio; SES = socioeconomic status; and VMT = vehicle miles traveled.

[c] # $P < 0.10$, * $P < 0.05$, ** $P < 0.01$.

[d] Estimates at residential address unless otherwise indicated.

Table 4.12. Studies of Exposure to Traffic Pollution and Health-Care Utilization for Respiratory Problems in Children[a,b]

Study / Location	Years of Study (*N*) Age at Observation	Effect Estimate OR or RR (95% CI)	Effect Scale and Exposure Metric[c]
Buckeridge et al. 2002 Southeast Toronto	1990–1992 (1779)	Hospital admissions for respiratory problems (RR)	Traffic-related $PM_{2.5}$ from dispersion model (per a $\log_{10}$ increase; adjusted for SES)
		1.24 (1.05 to 1.45)	
Edwards et al. 1994 Birmingham, U.K.	1988–1989 (715 cases; 736 hospital controls; 736 community controls) Age 0–4 yr	Hospital admission for asthma (OR) (CIs not available)	Traffic density < 500 m to main road (vehicles/24 hr), reference < 14,000
		1.02	14,000–19,000
		1.35	20,000–23,000
		1.84	24,000–27,000
		1.90	28,000–35,000
		1.52	> 35,000
		P for trend < 0.006	Unadjusted
		1.52 (1.22 to 1.90)	< 200 m vs. > 200 m to a major road
English et al. 1999 San Diego county, Calif.	1993 (5996 cases; 2284 controls) Age 0–14 yr	Paid claim for asthma (medication) (OR)	Traffic density (vehicles/day) on nearest street by percentile (reference ≤ 5500)
		0.80 (0.64 to 1.00)	90th (> 27,500)
		0.92 (0.69 to 1.22)	95th (> 41,000)
		0.90 (0.47 to 1.74)	99th (> 161,000)
		Two or more medical visits (in- or outpatient) vs. one visit for cases only	
		1.86 (0.82 to 4.18)	90th (> 27,500)
		2.91 (1.23 to 6.91)	95th (> 41,000)
		3.58 (0.78 to 16.44)	99th (> 161,000)
Ising et al. 2004 Osterode, Germany	2001 (371) Age 5–12 yr	Number of pediatrician contacts/yr (OR): Asthma	Measured NO_2 and sedimented dust; reference = NO_2 (10.7 µg/m^3), dust (0.06 mg/m^2, day)
		4.22 (2.79 to 8.16)	
			High exposure: NO_2 (26 µg/m^3) and dust (0.36 mg/m^2, day)
		1.41. (0.83 to 2.37)	Medium exposure: NO_2 (11.8 µg/m^3) and dust (0.1 mg/m^2, day)
		Bronchitis	High exposure
		13.8 (7.19 to 26.4)	Medium exposure
		1.95 (1.11 to 3.42)	Models included exposure to pollutants and noise

Table continues next page

[a] Models adjusted for covariates unless noted. **Bold** indicates OR or RR plotted in Figure 4.9.

[b] Abbreviations: OR = odds ratio; RR = relative risks; SES = socioeconomic status; and VMT = vehicle miles traveled.

[c] Estimates at residential address unless otherwise indicated.

Table 4.12. (*Continued*) Studies of Exposure to Traffic Pollution and Health-Care Utilization for Respiratory Problems in Children[a,b]

Study / Location	Years of Study (*N*) Age at Observation	Effect Estimate OR or RR (95% CI)	Effect Scale and Exposure Metric[c]
Lin et al. 2002 Erie county, N.Y. (excluding city of Buffalo)	1990–1993 (417 cases; 461 controls) Age 0–14 yr	Hospital admissions for asthma (OR)	Traffic density (VMT = daily traffic × length of route) on state routes within 200-m buffer by tertile vs. no state route
		1.31 (0.79 to 2.16)	≤ 2366
		1.06 (0.64 to 1.76)	2367–4042
		1.93 (1.13 to 3.29)	≥ 4043
		1.43 (1.03 to 1.99)	Heavy-truck density (% of trucks) at < 200 m
		0.99 (0.72 to 1.35)	Heavy-truck density (% of trucks) at < 500 m
Livingstone et al. 1996 London	1994 (436 cases; 1138 controls) Age 2–15 yr	Asthma treatment (OR)	
		0.96 (0.78 to 1.22)	≤ 150 m to a main road
Pershagen et al. 1995 Stockholm	1986–1988 (197 cases; 350 controls) Age 4 mo–4 yr	Hospital admission for breathing difficulty with wheezing (RR):	Time-weighted NO_2 (Reference = < 35 µg/m^3 NO_2)
		Boys: **1.7 (0.9 to 3.3)** Girls: **1.7 (0.6 to 4.4)**	35–45 µg/m^3 NO_2
		Boys: **1.0 (0.5 to 1.8)** Girls: **1.5 (0.6 to 3.6)**	46–70 µg/m^3 NO_2
		Boys: **0.7 (0.4 to 1.3)** Girls: **2.7 (1.1 to 6.8)** *P*-trend boys: 0.1; girls: 0.02	> 70 µg/m^3 NO_2
Wilhelm et al. 2008 Los Angeles and San Diego county, Calif.	2001 (612) Age 0–17 yr	Emergency visit or hospitalization for asthma symptoms (OR):	Traffic density (daily VMT/mi^2 in 500-ft buffer), reference: < 20,000 (lower tertile)
		2.45 (0.87 to 6.88)	20,001 to ≤ 200,000
		3.27 (1.08 to 9.89)	> 200,000
		2.48 (1.14 to 5.38)	O_3 and $PM_{2.5}$ from stationary monitoring sites within 5 mi in two-pollutant model
Wilkinson et al. 1999 Northwest London	1992–1994 (1380 cases / 5703 controls) Age 5–14 yr	Emergency visit for asthma (OR):	
		0.93 (0.82 to 1.06)	≤ 150 m of main road vs. 150 m Traffic density (VMT/hr in 150-m buffer), reference < 1500
		1.03 (0.87 to 1.22)	1500–14,999
		0.80 (0.68 to 0.95)	15,000–49,999
		0.88 (0.74 to 1.06)	> 49,999

[a] Models adjusted for covariates unless noted. **Bold** indicates OR or RR plotted in Figure 4.9.

[b] Abbreviations: OR = odds ratio; RR = relative risks; SES = socioeconomic status; and VMT = vehicle miles traveled.

[c] Estimates at residential address unless otherwise indicated.

Table 4.13. Studies of Exposure to Traffic Pollution and Asthma or Respiratory Symptoms and Health-Care Utilization in Adults[a,b]

Study / Location	Years of Study (*N*) Age at Observation	Effect Estimate OR (95% CI)	Effect Scale and Exposure Metric[c]
Bayer-Oglesby et al. 2006 Switzerland	1991; 2002 follow-up (8555 reenrolled; 5922 never smokers) Age 18–60 yr	Results for never smokers Wheezing and breathing problems in "last 12 months":	
		0.91 (0.79 to 1.05)	Distance to closest main road (per 100 m)
		1.15 (0.97 to 1.35)	Length of main road segments ≤ 200 m (per 500 m)
		1.34 (1.00 to 1.79)	≤ 20 m to main road
		Wheezing without cold:	
		0.91 (0.78 to 1.06)	Distance to closest main road (per 100 m)
		1.18 (1.01 to 1.39)	Length of main road segments ≤ 200 m (per 500 m)
		1.05 (0.76 to 1.45)	≤ 20 m to main road
		Attack of breathlessness	
		0.88 (0.78 to 1.00)	Distance to closest main road (per 100 m)
		1.20 (1.05 to 1.38)	Length of main road segments ≤ 200 m (per 500 m)
		1.06 (0.82 to 1.37)	≤ 20 m to main road
		Cough:	
		1.00 (0.91 to 1.10)	Distance to closest main road (per 100 m)
		1.08 (0.96 to 1.21)	Length of main road segments ≤ 200 m (per 500 m)
		0.93 (0.75 to 1.17)	≤ 20 m to main road
		Phlegm:	
		1.01 (0.91 to 1.12)	Distance to closest main road (per 100 m)
		1.06 (0.94 to 1.20)	Length of main road segments ≤ 200 m (per 500 m)
		1.06 (0.84 to 1.34)	≤ 20 m to main road
Burr et al. 2004 North Wales, U.K.	1993 and 1996 (448 adults with repeats; 811 at baseline)	Net improvement (%) in respiratory symptom prevalence, including wheeze, cough, and doctor's consultations (no detailed quantification given)	After opening of a bypass road, relative to before
		up to 5.7%	Congested streets
		up to 8.5%	Uncongested streets (within same geographic area)
Garshick et al. 2003 Southeastern Massachu-setts	1988–1992 (2985) U.S. male veterans Mean age 60.6 yr	Persistent wheeze: **1.31 (1.00 to 1.71)** Chronic cough: **1.24 (0.92 to 1.68)** Chronic phlegm: **1.18 (0.88 to 1.56)**	≤ 50 m vs. > 400 m from main road
		Persistent wheeze: **1.71 (1.22 to 2.40)** Chronic cough: **1.29 (0.87 to 1.91)** Chronic phlegm: **1.40 (0.97 to 2.02)**	Traffic density (within 50 m): < 10,000 vs. ≥ 10,000 per day (reference > 50 m)

Table continues next page

[a] Models adjusted for covariates unless noted. **Bold** indicates OR plotted in Figure 4.10.

[b] Abbreviations: CVD = cardiovascular disease; OR = odds ratio; SES = socioeconomic status; and TB = tuberculosis.

[c] Estimates at residential address unless otherwise indicated.

Table 4.13 (*Continued*). Studies of Exposure to Traffic Pollution and Asthma or Respiratory Symptoms and Health-Care Utilization in Adults[a,b]

Study / Location	Years of Study (*N*) Age at Observation	Effect Estimate OR (95% CI)	Effect Scale and Exposure Metric[c]
Livingstone et al. 1996 London	1994 (630 cases; 5059 controls) Age 16–64 yr	Asthma prescriptions **1.00 (0.84 to 1.19)**	< 150 m from a main road
Modig et al. 2006 Luleå, Sweden	1995–1999 (203 cases; 203 controls) Age 20–60 yr	Asthma incidence: 2.4 (0.9 to 6.2) 1.1 (0.9 to 1.2) Positive skin test: 1.2 (1.0 to 1.3)	 High traffic flow per day (reference = low) Outdoor NO_2, measured 1 wk 0.5 m from home Outdoor NO_2, measured 1 wk 0.5 m from home
Morris et al. 2000 East London	1991–1992 (125 asthma and 124 chronic obstructive airways cases with matched controls) Age 15–90 yr	Asthma admissions: **0.78 (0.46 to 1.32)** COPD admissions: 0.94 (0.57 to 1.54)	≤ 150 m vs. > 150 m from main road
Nakai et al. 1999 Tokyo	1987–1990 (1986) Age 30–59 yr (females only)	 Persistent wheezing: **1.17 (0.59 to 2.34)** **1.00 (0.48 to 2.04)** Chronic cough: **1.87 (1.02 to 3.42)** **2.18 (1.08 to 4.42)** Chronic phlegm: **1.40 (0.88 to 2.21)** **1.79 (1.07 to 3.01)** Breathlessness: 0.83 (0.50 to 1.38) 1.16 (0.66 to 2.04)	Traffic density by zone: A, 0 to < 20 m from heavy traffic; B, 20–150 m from heavy traffic; C, suburban Zone A vs. Zone B Zone A vs. Zone C Zone A vs. Zone B Zone A vs. Zone C Zone A vs. Zone B Zone A vs. Zone C Zone A vs. Zone B Zone A vs. Zone C

Table continues next page

[a] Models adjusted for covariates unless noted. **Bold** indicates OR plotted in Figure 4.10.

[b] Abbreviations: CVD = cardiovascular disease; OR = odds ratio; SES = socioeconomic status; and TB = tuberculosis.

[c] Estimates at residential address unless otherwise indicated.

Table 4.13 (*Continued*). Studies of Exposure to Traffic Pollution and Asthma or Respiratory Symptoms and Health-Care Utilization in Adults[a,b]

Study / Location	Years of Study (*N*) Age at Observation	Effect Estimate OR (95% CI)	Effect Scale and Exposure Metric[c]
Nitta et al. 1993 Tokyo suburbs (3 cross-sectional studies)	1979 (1173)	Chronic wheezing: **2.75 (1.65 to 4.73)** Chronic cough: **1.62 (1.07 to 2.46)** Chronic phlegm: **1.47 (1.03 to 2.11)** Shortness of breath: 1.41 (0.89 to 2.24) Chest cold and phlegm: 1.35 (1.04 to 1.77)	Traffic density by zones < 20 m vs. 20–150 m from heavy traffic road
	1982 (2015)	Chronic wheezing: **1.52 (0.91 to 2.55)** Chronic cough: **1.35 (0.88 to 2.07)** Chronic phlegm: **1.87 (1.31 to 2.68)** Shortness of breath: 1.42 (0.94 to 2.15) Chest cold/phlegm: 1.21 (0.91 to 1.59)	< 20 m vs. 50–150 m from heavy traffic road
	1983 (2023)	Chronic wheezing: **0.94 (0.61 to 1.42)** Chronic cough: **1.45 (0.98 to 2.13)** Chronic phlegm: **1.26 (0.94 to 1.70)** Shortness of breath: 1.66 (1.12 to 2.48) Chest cold and phlegm: 0.94 (0.76 to 1.17)	< 20 m vs. 20–150 m from heavy traffic road
Oosterlee et al. 1996 Haarlem, the Netherlands	1991 (1117 adults) (see Tables 4.10 and 4.11 for children)	Doctor-diagnosed asthma: 1.2 (0.8 to 1.9) Current asthma medication: **1.2 (0.4 to 3.2)** Wheeze > 1 wk, past 2 yr: **1.1 (0.6 to 1.8)** COPD, medication, chronic cough, and chronic phlegm: All negative associations	Living on busy streets (high NO_2 and 10,000–30,000 vehicles/day) vs. living on quiet streets

Table continues next page

[a] Models adjusted for covariates unless noted. **Bold** indicates OR plotted in Figure 4.10.

[b] Abbreviations: CVD = cardiovascular disease; OR = odds ratio; SES = socioeconomic status; and TB = tuberculosis.

[c] Estimates at residential address unless otherwise indicated.

Table 4.13 (*Continued*). Studies of Exposure to Traffic Pollution and Asthma or Respiratory Symptoms and Health-Care Utilization in Adults[a,b]

Study / Location	Years of Study (*N*) Age at Observation	Effect Estimate OR (95% CI)	Effect Scale and Exposure Metric[c]
Schikowski et al. 2005 Rhine-Ruhr basin, Germany	1985–1994 (4205–4262) Age 54–55 yr (females)	Doctor-diagnosed chronic bronchitis: **1.15 (0.89 to 1.50)** Chronic cough with phlegm: **1.07 (0.83 to 1.37)** Frequent cough: **1.24 (1.03 to 1.49)**	< 100 m of main road vs. ≥ 100 m to major road (> 10,000 cars per day)
Schikowski et al. 2008 Rhine-Ruhr basin, Germany	1985–1994 (~1200) Age 54–55 yr (females)	Frequent cough with phlegm: 1.02 (0.68 to 1.53) Frequent cough: 1.13 (0.83 to 1.53)	< 100 m vs. ≥ 100 m to major road (> 10,000 cars/day) Reanalysis of same data as Schikowski et al. 2005 on small sample; focus was SES and respiratory health
Smargiassi et al. 2006 Montreal	2001–2002 (5805 cases; 39,260 controls) Age ≥ 60 yr	Hospitalization for respiratory vs. all diagnoses (except trauma /CVD/cancer/TB) 1.08 (1.00 to 1.15) 1.24 (1.12 to 1.38) Compared to genitourinary diagnoses 1.13 (1.02 to 1.26) 1.57 (1.32 to 1.87)	Traffic density during 3-hr-morning peak on nearest road segment; reference: off-traffic network. Adjusted for SES. 1–3160 vehicles > 3160 vehicles 1–3160 vehicles > 3160 vehicles
Sunyer et al. 2006 21 cities in European community	2000–2002 (1620) Age 43 yr (mean)	Prevalence of chronic phlegm All women (886): **1.38 (0.97 to 1.95)** 2.71 (1.03 to 7.16) Women > 16 yr of education: 1.90 (1.23 to 2.93) 5.81 (1.22 to 27.7) All men (734): **0.85 (0.56 to 1.31)** 0.99 (0.40 to 2.46)	Per 30 μg/m^3 NO_2 High vs. low NO_2 : < 20 μg/m^3 vs. > 50 μg/m^3 Per 30 μg/m^3 NO_2 High vs. low NO_2: < 20 μg/m^3 vs. > 50 μg/m^3 Per 30 μg/m^3 NO_2 High vs. low NO_2: < 20 μg/m^3 vs. > 50 μg/m^3
Venn et al. 2005 Jimma, Ethiopia	1996 (3592 children and adults; 2179 adults) Age ≥ 16 yr (see table 4.10 for children)	Wheeze All subjects: 1.17 (1.01 to 1.36) Adults only: **1.14 (0.97 to 1.33)** 1.26 (1.03 to 1.53)	< 150 m to nearest road (per 30 m) Nearest road with median flow (653 vehicles/12 hr daylight) within 150 m vs. nearest road with low flow

[a] Models adjusted for covariates unless noted. **Bold** indicates OR plotted in Figure 4.10.

[b] Abbreviations: CVD = cardiovascular disease; OR = odds ratio; SES = socioeconomic status; and TB = tuberculosis.

[c] Estimates at residential address unless otherwise indicated.

Table 4.14. Studies of Exposure to Traffic Pollution and Lung Function[a,b]

Study / Location	Year of Study (*N*) Age at Observation	Group Characteristics	Time Frame of Effect	Effect Estimate[c] (95% CI)	Effect Scale and Exposure Metric[d]
Brunekreef et al. 1997 6 cities in the Netherlands	1995 (308) Age 7–12 yr	Students from 13 schools	Long-term	% change: FEV_1 **−4.1 (−7.9 to −0.1)** **−3.7 (−7.2 to −0.2)**	Truck volume/weekday within 300 m of motorway (per 10,000) BS in school (per 10 μg/m^3)
Burr et al. 2004 North Wales, U.K.	1996–1997; 1999–2000 (after street bypass) (180) children and adults	Population-based	Long-term (or subacute / before–after street bypass)	PEF: No difference No significant difference in PEF variability	Congested–uncongested after bypass (cross-sectional) Before–after (longitudinal) traffic decreased ~ 50% PM_{10} decreased 8 and 3.4 μg/m^3 in congested and uncongested areas, respectively
Chauhan et al. 2003 Southampton, U.K.	1994; ~37 wk (114) Age 8–11 yr	Asthmatic children with respiratory infections	Acute	PEF change: −12 L/min (−0.8 to −23.6)* for picornavirus infection	Personal NO_2 exposure > 14 μg/m^3 vs. < 7.5μg/m^3
Fritz and Herbarth 2001 Leipzig	1994–1995 (235) Age 4–6 yr	Cross-section of pre-schoolers from 16 daycare centers	Long-term	% change: FVC: −14.5 (−19.2 to −10.2) FEV_1: **−11.5 (−15.8 to −7.6)** FVC: −21.1 (−26.5 to −16.1) FEV_1: **−17.6 (−22.7 to −12.9)** FVC −9.5 (−13.5 to −6.0) FEV_1 −8.2 (−11.9 to −4.9)	Exposure at daycare based on 2 main sources Heavy traffic and high coal-heating area Heavy traffic and low coal-heating area Low traffic and high coal-heating area
Gauderman et. al 2007 Southern California	2000 (3677) Age 18 yr (followed from age 10)	Asthma; no asthma	Long-term	FEV_1 % change: **−3.0 (−5.4 to −0.6)**** (calculated from volume)	< 500 m vs. > 1500 m to a freeway

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[a] **Bold** indicates effect estimates plotted in Figures 4.11a (for studies that report ORs for low FEV_1 or decline of FEV_1) and 4.11b (for studies that report percent change in FEV_1).

[b] Abbreviations: ARIC = Atherosclerosis Risk in Communities study ; BS = black smoke; COPD = chronic obstructive pulmonary disease; $FEF_{25–75\%}$ = forced expiratory flow between 25% and 75% of forced vital capacity; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; IQR = interquartile range; MEF = maximum expiratory flow; PEF = peak expiratory flow.

[c] Adjusted for covariates unless otherwise noted. # $P < 0.10$, * $P < 0.05$, ** $P < 0.01$.

[d] Estimates at residential address unless otherwise indicated.

Table 4.14 (*Continued*). Studies of Exposure to Traffic Pollution and Lung Function[a,b]

Study / Location	Year of Study (*N*) Age at Observation	Group Characteristics	Time Frame of Effect	Effect Estimate[c]	Effect Scale and Exposure Metric[d]
Gauvin et al. 2001 4 French metropolitan areas	1998 (~600) Age 4–14 yr	Volunteers; half had asthma	Long-term	FEV_1 regression slope (SE): Grenoble: −0.23* (± 0.04) Toulouse: −0.47# (± 0.15) Nice: 0.02 (± 0.04) Paris: −0.001 (± 0.01)	Traffic exposure index (time-weighted traffic density within 300-m buffer)
Hirsch et al.1999 Dresden	1995–1996 (~ 990) Age 9–11 yr	Random sample of 4th graders	Long-term	OR, for $FEF_{25–75\%}$ < 70% predicted: 1.27 (1.03 to 1.58) FEV_1 < 85% predicted: **1.19 (0.86 to 1.64)**	Per 1 µg/m³ benzene (home outdoor)
Hogervorst et al. 2006 Maastricht, the Netherlands	2002 (342) Age 8–13 yr	Students from 6 schools	Long-term	FEV_1: **−1.57% (−2.88 to −0.24)** (Only significant result)	$PM_{2.5}$ radical-generating capacity per 1×10^{-6} unit increase of peak area/m³ air from Electro Spin Resonance Spectrum
Holguin et al. 2007 Alerquim, Mexico	2003; 4 mo (196) Age 6–12 yr	Asthma; no Asthma	Acute; subacute	FEV_1 change (L) (children with asthma)	Road density mean ~ 18–24 km roads/km² area at different distances
				− 0.091 (− 0.174 to − 0.007)#	50 m buffer area
				− 0.072 (− 0.134 to − 0.009)*	100 m buffer area
				− 0.106 (− 0.171 to − 0.041)**	200 m buffer area
Hong et al. 2005 Incheon, Korea	2002 (293) Age ~23–27 yr	University student sample	Long-term	Regression coefficients (SE) multivariate model $FEF_{25–75}$: −0.0140* (0.007) FEV_1: − 0.0063# (0.0035) FEV_1/FVC: 0.0427 (0.0356)	Personal NO_2 (1-wk mean) per 10 ppb (18.9 µg/m³)
Ingle et al. 2005 Jalgaon, India	2003–2004 (120) Age 25–55 yr	60 policemen; 60 controls	Long-term	FVC % of predicted: 82% vs. 99%** FEV_1: 73% vs. 118%**	Working traffic policemen vs. control (office workers)
Janssen et al. 2003 the Netherlands	1997–1998 (1724) Age 7–12 yr	Students from 24 schools < 400 m of busy roads	Long-term	OR for FEV_1 < 85% predicted	Traffic density within 400 m of school
				1.19 (0.34 to 4.23)	Trucks/day per 17,000
				1.13 (0.40 to 3.16)	Cars/day per 120,000
				1.45 (0.43 to 4.85)	Soot outside school (per 10 µg/m³)

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[a] **Bold** indicates effect estimates plotted in Figures 4.11a (for studies that report ORs for low FEV_1 or decline of FEV_1) and 4.11b (for studies that report percent change in FEV_1).

[b] Abbreviations: ARIC = Atherosclerosis Risk in Communities study ; BS = black smoke; COPD = chronic obstructive pulmonary disease; $FEF_{25–75\%}$ = forced expiratory flow between 25% and 75% of forced vital capacity; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; IQR = interquartile range; MEF = maximum expiratory flow; PEF = peak expiratory flow.

[c] Adjusted for covariates unless otherwise noted. # $P < 0.10$, * $P < 0.05$, ** $P < 0.01$.

[d] Estimates at residential address unless otherwise indicated.

Table 4.14 (*Continued*). Studies of Exposure to Traffic Pollution and Lung Function[a,b]

Study / Location	Year of Study (*N*) Age at Observation	Group Characteristics	Time Frame of Effect	Effect Estimate[c]	Effect Scale and Exposure Metric[d]
Kan et al. 2007 4 U.S. communities	1987–1989; (13,972) mean age 54 yr	ARIC population sample	Long-term	FEV_1 change, mL and % (% is calculated) Females (7789) −17.4 mL (−41.9 to 7.1) **−0.73 % (−1.75 to 0.30)** Males (6183) −43.9 mL (−85.9 to −2.0)* **−1.83 % (−3.58 to −0.08)** Females −29.5 mL (−52.2 to −6.9)* **−1.23 % (−2.18 to −0.29)** Males −38.1 mL (−76.7 to 0.6)# **−1.59 % (−3.20 to 0.03)** FEV_1/FVC % change Females −0.3 % (−0.7 to 0.0) Males −0.5 % (−0.1 to 0.0)	Distance to major road; age-adjusted model < 100 m vs. ≥ 100 m < 150 m vs. ≥ 150 m < 100 m vs. ≥ 100 m
Nordling et al. 2008 4 municipalities in Swedish	1994–1996 (2565) Age 4 yr	Birth cohort with peak flow measured at age 4 yr	Cross-sectional	PEF (L/min) −5.36 (−10.67 to −0.053) −3.08 (−6.84 to 0.68)	From source-specific dispersion models Per 6 μg/m^3 PM_{10} (95th − 5th percentile) Per 44 μg/m^3 NO_x (95th − 5th percentile)

Table continues next page

[a] **Bold** indicates effect estimates plotted in Figures 4.11a (for studies that report ORs for low FEV_1 or decline of FEV_1) and 4.11b (for studies that report percent change in FEV_1).

[b] Abbreviations: ARIC = Atherosclerosis Risk in Communities study ; BS = black smoke; COPD = chronic obstructive pulmonary disease; $FEF_{25–75\%}$ = forced expiratory flow between 25% and 75% of forced vital capacity; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; IQR = interquartile range; MEF = maximum expiratory flow; PEF = peak expiratory flow.

[c] Adjusted for covariates unless otherwise noted. # $P < 0.10$, * $P < 0.05$, ** $P < 0.01$.

[d] Estimates at residential address unless otherwise indicated.

Table 4.14 (*Continued*). Studies of Exposure to Traffic Pollution and Lung Function[a,b]

Study / Location	Year of Study (*N*) Age at Observation	Group Characteristics	Time Frame of Effect	Effect Estimate[c]	Effect Scale and Exposure Metric[d]
Oftedal et al. 2008 Oslo	2001–2002 (2170) Age 9–10 yr	All children who were lifetime residents with valid lung function	Long-term (acute also estimated)	0–1 yr exposure: PEF mL/sec −60.7 (−97.0 to −24.4) $FEF_{25\%}$ mL/sec −61.5 (−102.2 to 20.7) $FEF_{50\%}$ mL/sec −39.1 (−74.6 to −3.7) FEV_1 mL −6.3 (−18.9 to 6.5) FVC mL −1.5 (−15.3 to 12.4) Lifetime exposure: PEF mL/sec −79.2 (−127.9 to −30.5) $FEF_{25\%}$ mL/sec −73.9 (−128.7 to −19.1) $FEF_{50\%}$ mL/sec −45.6 (−93.2 to 2.1) FVC mL −1.4 (−20.1 to 17.2) FEV_1 mL −6.3 (−23.3 to 10.7) Percent change in FEV_1 (calculated): **−0.15 (−0.57 to 0.26)**	NO_2 (and PM_{10}) from source-specific dispersion models Per IQR 19.7 µg/m³ (scaled down from 27.4 reported in paper) Per IQR 19.7 µg/m³ NO_2 Per IQR 10 µg/m³ NO_2 (scaled down from 19.7 µg/m³)
Schikowski et al. 2005 Rhine-Ruhr basin	1985–1994 (2581) Age 54–55 yr	German females	Long-term	OR for COPD (FEV_1/FVC < 0.7) **1.79 (1.06 to 3.02)**	≤ 100 m vs. > 100 m to a major road (> 10,000 cars/day)
Schikowski et al. 2008 Rhine-Ruhr basin	1985–1994 (1216) Age 54–55 yr	German females	Long-term	OR: COPD (FEV_1/FVC < 0.7) **1.69 (0.90 to 3.18)** For FEV_1 < 80%: **1.30 (0.94 to 1.79)** For FVC < 80%: 1.07 (0.79 to 1.45)	≤ 100 m vs. > 100 m to a major road (> 10,000 cars/day) Reanalysis of same data as Schikowski et al. 2005 on small sample; focus was SES and respiratory health
Schindler et al. 1998 Switzerland	1991 (7641) Age 18–60 yr	Random population sample	Long-term	FVC % change: −0.74% (−1.41 to −0.07) FEV_1 % change: **−0.26% (−1.03 to 0.52)**	Personal NO_2 per 10-µg/m³ difference between zones of residence within a community (with indoor exposure subtracted)

Table continues next page

[a] **Bold** indicates effect estimates plotted in Figures 4.11a (for studies that report ORs for low FEV_1 or decline of FEV_1) and 4.11b (for studies that report percent change in FEV_1).

[b] Abbreviations: ARIC = Atherosclerosis Risk in Communities study ; BS = black smoke; COPD = chronic obstructive pulmonary disease; $FEF_{25-75\%}$ = forced expiratory flow between 25% and 75% of forced vital capacity; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; IQR = interquartile range; MEF = maximum expiratory flow; PEF = peak expiratory flow.

[c] Adjusted for covariates unless otherwise noted. # $P < 0.10$, * $P < 0.05$, ** $P < 0.01$.

[d] Estimates at residential address unless otherwise indicated.

Table 4.14 (*Continued*). Studies of Exposure to Traffic Pollution and Lung Function[a,b]

Study / Location	Year of Study (*N*) Age at Observation	Group Characteristics	Time Frame of Effect	Effect Estimate[c]	Effect Scale and Exposure Metric[d]
Sekine et al. 2004 Tokyo	1987–1994; 8 yr (733) Age 30–59 yr	Population sample (females only)	Long-term	Change in FEV_1 per year: −20 mL −15 mL −9 mL *P* for trend < 0.001	Distance to major road ≤ 20 m (88.7 to 105.0 μg/m^3 NO_2) 20–150 m (71.7 to 86.8 μg/m^3 NO_2) 0–150 m in district with low NO_2 (45.3 to 67.9 μg/m^3)
Wjst et al. 1993 Munich	1989–1990 (4320) Age 9–11 yr	4th graders	Long-term	FEV_1: **−0.20 % (−0.45 to 0.06)** MEF_{25}: −0.68%(−1.11 to −0.25)** MEF_{50}: 20.72% (21.25 to 20.18)** MEF_{50}/FVC: −0.66% (−1.20 to −0.12)* PEF: − 0.71 (−1.08 to −0.33)***	Traffic density on street with maximum traffic volume within school district (~ 2 km radius, 117 districts), per 25,000 cars/day

[a] **Bold** indicates effect estimates plotted in Figures 4.11a (for studies that report ORs for low FEV_1 or decline of FEV_1) and 4.11b (for studies that report percent change in FEV_1).

[b] Abbreviations: ARIC = Atherosclerosis Risk in Communities study ; BS = black smoke; COPD = chronic obstructive pulmonary disease; $FEF_{25–75\%}$ = forced expiratory flow between 25% and 75% of forced vital capacity; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; IQR = interquartile range; MEF = maximum expiratory flow; PEF = peak expiratory flow.

[c] Adjusted for covariates unless otherwise noted. # $P < 0.10$, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

[d] Estimates at residential address unless otherwise indicated.

Table 4.15. Studies of Exposure to Traffic Pollution and Nonasthmatic Respiratory Allergy[a,b]

Study / Location	Years of Study / Age at Observation	Selected Effect Estimate: Effect (*N*)	Selected Effect Estimate: Adjusted OR (unless otherwise specified) (95% CI)	Effects Scale and Metric[c]
Brauer et al. 2002 the Netherlands (PIAMA cohort)	1999–2001 Age 2 yr			Pollutant modeled from spatial measurements and GIS traffic data[d] (exposure from 1 to 2 yr)
		Itchy rash (2995)	**1.01 (0.88 to 1.16)**	$PM_{2.5}$ per IQR 3 μg/m^3
			1.02 (0.91 to 1.15)	Soot[e] per IQR 0.5×10^{-5}/m
			1.02 (0.91 to 1.15)	NO_2 per IQR 10 μg/m^3
		Doctor-diagnosed eczema (2970)	**0.95 (0.83 to 1.10)**	$PM_{2.5}$ per IQR 3 μg/m^3
			0.96 (0.85 to 1.08)	Soot[e] per IQR 0.5 $\times 10^{-5}$/m
			0.96 (0.85 to 1.08)	NO_2 per IQR 10 μg/m^3
Brauer et al. 2006 the Netherlands (PIAMA cohort) and Munich (LISA cohort)	1998–2001 Age 1 and 2 yr	Otitis media	Netherlands cohort	Same as Brauer et al. 2002 (lifetime exposure)
		(2984)	Age 1 yr	
			1.11 (0.98 to 1.26)	Soot per IQR 0.5 $\times 10^{-5}$/m
			1.17 (1.03 to 1.34)	NO_2 per IQR 10 μg/m^3
		(2970)	Age 2 yr	
			1.10 (1.00 to 1.22)	Soot[e] per IQR 0.5 $\times 10^{-5}$/m
			1.14 (1.03 to 1.27)	NO_2 per IQR 10 μg/m^3
			Munich cohort	
		(620)	Age 1 yr	
			1.12 (0.83 to 1.51)	Soot per IQR 0.5 $\times 10^{-5}$/m
			1.09 (0.78 to 1.54)	NO_2 per IQR 10 μg/m^3
		(605)	Age 2 yr	
			1.10 (0.86 to 1.41)	Soot[e] per IQR 0.5 $\times 10^{-5}$/m
			1.14 (0.87 to 1.49)	NO_2 per IQR 10 μg/m^3

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[a] **Bold** indicates OR values plotted in Figure 4.12a and 412b.

[b] Abbreviations: EC = elemental carbon; ETS = environmental tobacco smoke; GINI = German Infant Nutrition Intervention; GIS = geographic information system; IgE = immunoglobulin E; IQR = interquartile range; ISAAC = International Study of Asthma and Allergies in Children; LISA = Influences of Lifestyle Related Factors on the Human Immune System and Development of Allergies in Children; LUR = land use regression; OR = odds ratio; PIAMA = Prevention and Incidence of Asthma and Mite Allergy study; SPT = skin prick test.

[c] Estimates at residential address unless otherwise indicated.

[d] The models explained 73%, 81%, and 85% of the variability of $PM_{2.5}$, soot, and NO_2, respectively.

[e] Measured as absorbance of $PM_{2.5}$ collected on filters; 1×10^{-5}/m absorbance = 1.45 μg/m^3 EC (Brauer et al. 2002 and Morgenstern et al. 2007).

[f] Pearson correlation between NO_2 concentrations and traffic volume in front of the residence of 0.70 (likely overestimated).

[g] The conversion from the measured absorbance to μg/m^3 was made using the following equation: BS = $-3.633 + 9.897 \times$ absorption (from Janssen et al. 2001) (Nicole Janssen, personal communication, October 2009).

Table 4.15 (*Continued*). Studies of Exposure to Traffic Pollution and Nonasthmatic Respiratory Allergy[a,b]

Study / Location	Years of Study / Age at Observation	Selected Effect Estimate: Effect (*N*)	Selected Effect Estimate: Adjusted OR (unless otherwise specified) (95% CI)	Effects Scale and Metric[c]
Brauer et al. 2007 the Netherlands (PIAMA cohort)	2001–2003 Age 4 yr	Doctor-diagnosed eczema (2819)	OR adjusted for early-life risk factors	Same as Brauer et al. 2002 (lifetime exposure)
			0.97 (0.83 to 1.14)	Soot[e] per IQR 0.58 $\times 10^{-5}$/m
			0.97 (0.83 to 1.14)	NO_2 per IQR 10 μg/m^3
		IgE to indoor aeroallergens ≥ 0.35 IU/mL (524)	**1.02 (0.71 to 1.46)**	Soot[e] per IQR 0.58 $\times 10^{-5}$/m
			0.97 (0.69 to 1.36)	NO_2 per IQR 10 μg/m^3
		IgE to outdoor aeroallergens ≥ 0.35 IU/mL (488)	**0.95 (0.59 to 1.52)**	Soot[e] per IQR 0.58 $\times 10^{-5}$/m
			0.92 (0.59 to 1.43)	NO_2 per IQR 10 μg/m^3
		IgE to food allergens ≥ 0.35 IU/mL (506)	1.64 (1.21 to 2.23)	Soot[e] per IQR 0.58 $\times 10^{-5}$/m
			1.49 (1.13 to 1.97)	NO_2 per IQR 10 μg/m^3
Cesaroni et al. 2008 Rome	2001 Adults with 3-year residence at current home Age 25–59 yr	Self-reported rhinitis (1227)	**1.30 (1.05 to 1.62)**	Self-reported traffic density (absent, low, moderate, high) high vs. absent
			1.18 (0.96 to 1.44)	Distance to high traffic road (traffic not defined) < 50 m vs. > 200 m
			1.37 (1.14 to 1.64)	PM emissions (kg/km^2) from road vehicles (calculated from emission factors for all diesel vehicles, number and types of vehicles, miles driven, etc.) upper vs. lower quartile
			1.30 (1.08 to 1.56)	NO_2 (modeled from spatial measurements and LUR) upper quartile (50–63 μg/m^3) versus lower quartile (21.0–37.3 μg/m^3)

Table continues on next page

[a] **Bold** indicates OR values plotted in Figure 4.12a and 412b.

[b] Abbreviations: EC = elemental carbon; ETS = environmental tobacco smoke; GINI = German Infant Nutrition Intervention; GIS = geographic information system; IgE = immunoglobulin E; IQR = interquartile range; ISAAC = International Study of Asthma and Allergies in Children; LISA = Influences of Lifestyle Related Factors on the Human Immune System and Development of Allergies in Children; LUR = land use regression; OR = odds ratio; PIAMA = Prevention and Incidence of Asthma and Mite Allergy study; SPT = skin prick test.

(*Footnotes continue on next page.*)

Table 4.15 (*Continued*). Studies of Exposure to Traffic Pollution and Nonasthmatic Respiratory Allergy[a,b]

Study / Location	Years of Study / Age at Observation	Selected Effect Estimate: Effect (*N*)	Selected Effect Estimate: Adjusted OR (unless otherwise specified) (95% CI)	Effects Scale and Metric[c]
Fritz and Herbarth 2004 Leipzig, Germany	1993-1995 Children from centrally located daycare centers Age 2 to 7 yr	Prevalence of allergic disorders (allergies, hay fever, rhinitis) (734)		Exposure at daycare center based on measurements of benzene (for traffic) and SO_2 (for coal heating)
			2.47 (1.02 to 6.00)	Heavy traffic and low coal-heating areas
			2.63 (1.03 to 6.72)	Heavy traffic and high coal-heating area
Hirsch et al. 1999 Dresden	1995–1996 Age 5–7 yr and 9–11 yr	SPT reaction > 3 mm to at least one allergen (2729)		Pollutant interpolated from 4 monitors at corners of 1 km^2 grid)
			1.01 (0.86 to 1.19)	NO_2, per 10 µg/m^3
			0.99 (0.89 to 1.10)	CO, per 0.2 µg/m^3
			1.02 (0.92 to 1.14)	Benzene, per 1 µg/m^3
		IgE against aeroallergens (> 0.7 IU/mL) (2361)		
			0.96 (0.82 to 1.12)	NO_2, per 10 µg/m^3
			0.95 (0.86 to 1.06)	CO, per 0.2 µg/m^3
			0.98 (0.88 to 1.09)	Benzene, per 1 µg/m^3
Hirsch et al. 2000 Dresden	1995–1996 Atopic children age 5–7 and 9–11 yr	IgE against latex (IgE > 0.35 IU/mL) (854; 151 were sensitized to latex)	**0.7 (0.4 to 1.3)**	Traffic density (> 5000 cars/day vs. ≤ 5000 cars/day) in residential street
				Pollutants interpolated from 4 monitors at corners of 1-km^2 grid
			0.8 (0.7 to 1.05)	Benzene, per 1 µg/m^3

Table continues on next page

[c] Estimates at residential address unless otherwise indicated.

[d] The models explained 73%, 81%, and 85% of the variability of $PM_{2.5}$, soot, and NO_2, respectively.

[e] Measured as absorbance of $PM_{2.5}$ collected on filters; 1×10^{-5}/m absorbance = 1.45 µg/m^3 EC (Brauer et al. 2002 and Morgenstern et al. 2007).

[f] Pearson correlation between NO_2 concentrations and traffic volume in front of the residence of 0.70 (likely overestimated).

[g] The conversion from the measured absorbance to µg/m^3 was made using the following equation: BS = $-3.633 + 9.897 \times$ absorption (from Janssen et al. 2001) (Nicole Janssen, personal communication, October 2009).

Table 4.15 (*Continued*). Studies of Exposure to Traffic Pollution and Nonasthmatic Respiratory Allergy[a,b]

Study / Location	Years of Study / Age at Observation	Selected Effect Estimate: Effect (*N*)	Selected Effect Estimate: Adjusted OR (unless otherwise specified) (95% CI)	Effects Scale and Metric[c]
Janssen et al. 2003 the Netherlands	1997–1998 Children from 24 schools within 400 m of motorway Age 7–12 yr	Conjunctivitis, current (2053)	**2.57 (1.00 to 6.58)**	Truck traffic density within 400 m of school, per 17,000/weekday (max–min)
			0.61 (0.41 to 0.91)	Distance of home to motorway, per 300 m
			2.54 (1.15 to 5.60)	Soot at school per 9.3 μg/m^3 (= 1.3 × 10^{-5}/m absorbance)[g]
			2.60 (1.38 to 4.90)	NO_2 at school per 17.6 μg/m^3
		Itchy rash, current (2060)	**2.65 (1.20 to 5.85)**	Truck traffic density within 400 m of school, per 17,000/weekday (max–min)
		SPT to outdoor aeroallergens ≥ 3 mm diameter (1141)	**2.83 (1.18 to 6.82)**	
		SPT to indoor aeroallergens ≥ 3 mm diameter (1141)	1.94 (1.13 to 3.33)	NO_2 at school per 17.6 μg/m^3
Krämer et al. 2000 Dusselfdorf	1996–1997 Children living in urban area near major roads Age 9 yr	Hay fever (306)	**4.24 (1.01 to 17.84)**	NO_2 (interpolated from spatial monitors)[f], per 10 μg/m^3
		Itchy skin (205)	1.97 (0.65 to 6.03)	
		SPT reaction ≥ 2 mm to pollen (232)	**4.96 (1.56 to 15.74)**	
		SPT reaction ≥ 2 mm to house dust mite or cat allergen (232)	3.51 (1.03 to 11.96)	

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[a] **Bold** indicates OR values plotted in Figure 4.12a and 412b.

[b] Abbreviations: EC = elemental carbon; ETS = environmental tobacco smoke; GINI = German Infant Nutrition Intervention; GIS = geographic information system; IgE = immunoglobulin E; IQR = interquartile range; ISAAC = International Study of Asthma and Allergies in Children; LISA = Influences of Lifestyle Related Factors on the Human Immune System and Development of Allergies in Children; LUR = land use regression; OR = odds ratio; PIAMA = Prevention and Incidence of Asthma and Mite Allergy study; SPT = skin prick test.

[c] Estimates at residential address unless otherwise indicated.

[d] The models explained 73%, 81%, and 85% of the variability of $PM_{2.5}$, soot, and NO_2, respectively.

[e] Measured as absorbance of $PM_{2.5}$ collected on filters; 1 × 10^{-5}/m absorbance = 1.45 μg/m^3 EC (Brauer et al. 2002 and Morgenstern et al. 2007)

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Table 4.15 (*Continued*). Studies of Exposure to Traffic Pollution and Nonasthmatic Respiratory Allergy[a,b]

Study / Location	Years of Study / Age at Observation	Selected Effect Estimate: Effect (*N*)	Selected Effect Estimate: Adjusted OR (unless otherwise specified) (95% CI)	Effects Scale and Metric[c]
Melen et al. 2008 Stockholm metropolitan area	1998–2002 Swedish birth cohort Age 4 yr	IgE to aeroallergens ≥ 0.35 IU/mL (266 cases, 362 controls) (by GSTP1 and TNF genotype)	STP1 Ile/Ile; TNF-308 GG (72 cases, 115 controls) 0.6 (0.2 to 2.0)	NO_x from traffic (dispersion model using source-specific emissions, traffic data, and road network) per 44 μg/m³ during first year of life
			STP1 Ile/Val, Val/Val; TNF-308 GG (87 cases,142 controls) 1.7 (0.7 to 4.1)	
			STP1 Ile/Ile; TNF-308 GA/AA (33 cases, 37 controls) 0.5 (0.1 to 4.0)	
			STP1 Ile/Val, Val/Val; TNF-308 GA/AA (52 cases, 42 controls) 22.0 (1.6 to 298)	
Morgenstern et al. 2008 Munich metropolitan area	1997–2002 GINI and LISA birth cohorts Age 4 yr and 6 yr			Pollutants (modeled from spatial measurements, distance to and type/density of roads, etc.) or distance to main road
		Doctor-diagnosed hay fever (2488)	**1.59 (1.11 to 2.27)** (age as continuous variable)	$PM_{2.5}$ absorbance[e] per IQR 0.4×10^{-5}/m
			1.05 (0.77 to 1.45) (age as continuous variable)	NO_2 per IQR 8.5 μg/m³
		Doctor-diagnosed eczema (2430)	**1.03 (0.86 to 1.24)** (age as continuous variable)	$PM_{2.5}$ absorbance[e] per IQR 0.4×10^{-5}/m
			1.18 (1.00 to 1.39) (age as continuous variable)	NO_2 per IQR 8.5 μg/m³
		IgE ≥ 0.35 IU/mL against any aeroallergen (at age 6 yr) (1353)	**1.40 (1.20 to 1.64)**	$PM_{2.5}$ absorbance[e] per IQR 0.4×10^{-5}/m
			1.03 (0.86 to 1.25)	NO_2 per IQR 8.5 μg/m³
			1.30 (1.02 to 1.66)	< 50 m to nearest road (yes/no)
		IgE ≥ 0.35 IU/mL against outdoors aeroallergens (at age 6 yr (1351)	**1.36 (1.14 to 1.63)**	$PM_{2.5}$ absorbance[e] per IQR 0.4×10^{-5}/m
			1.00 (0.81 to 1.23)	NO_2 per IQR 8.5 μg/m³
			1.33 (1.00 to 1.78)	< 50 m to nearest road (yes/no)

Table continues on next page

[f] Pearson correlation between NO_2 concentrations and traffic volume in front of the residence of 0.70 (likely overestimated).

[g] The conversion from the measured absorbance to μg/m³ was made using the following equation: BS = −3.633 + 9.897 × absorption (from Janssen et al. 2001) (Nicole Janssen, personal communication, October 2009).

Table 4.15 (*Continued*). Studies of Exposure to Traffic Pollution and Nonasthmatic Respiratory Allergy[a,b]

Study / Location	Years of Study / Age at Observation	Selected Effect Estimate: Effect (*N*)	Selected Effect Estimate: Adjusted OR (unless otherwise specified) (95% CI)	Effects Scale and Metric[c]
Nicolai et al. 2003 Munich	1995–1996 ISAAC survey Age 5–7 yr and 9– 11 yr		OR for children with ETS	Traffic density < 50 m (vehicles/day) by tertile, vs. rest of population
		Hay fever (1179)	**0.58 (0.23 to 1.47)**	Low: 2600 to 15,000 vehicles/day
			1.68 (0.94 to 2.98)	Medium: 15,0001 to 30,000 vehicles/day
			1.74 (0.97 to 3.13)	High: > 30,000 vehicles/day
		SPT reaction > 3 mm to at least one aeroallergen (695)	**0.79 (0.34 to 1.82)**	Low
			1.54 (0.81 to 2.92)	Medium
			2.67 (1.53 to 5.27)	High
		IgE ≥ 0.7 IU/mL (496)	**0.65 (0.30 to 1.45)**	Low
			1.00 (0.52 to 1.92)	Medium
			1.76 (0.90 to 3.46)	High
			OR for all children	
		Hay fever (3082)	**1.17 (0.76 to 1.81)**	High
		SPT reaction > 3 mm to at least one aeroallergen (1762)	**1.37 (0.86 to 2.20)**	High
		IgE ≥ 0.7 IU/mL (1311)	**1.21 (0.76 to 1.95)**	High
Nordling et al. 2008 Stockholm metropolitan area	1998–2002 Swedish birth cohort Age 4 yr			PM_{10} or NO_x from traffic (dispersion model using source-specific emissions, traffic data, and road network) per 44 μg/m^3 during first year of life
				Same as Melen et al. 2008
		IgE to pollens ≥ 0.35 IU/mL (281)	2.30 (1.23 to 4.29)	PM_{10} per 6 μg/m^3
			1.67 (1.10 to 2.53)	NO_x per 44 μg/m^3
		IgE to any aeroallergens ≥ 0.35 IU/mL (389)	1.73 (0.98 to 3.04)	PM_{10} per 6 μg/m^3
			1.34 (0.91 to 1.98)	NO_x per 44 μg/m^3
		IgE to food ≥ 0.35 IU/mL (406)	1.06 (0.60 to 1.88)	PM_{10} per 6 μg/m^3
			1.16 (0.79 to 1.72)	NO_x per 44 μg/m^3
		IgE to any aeroallergens or food ≥ 0.35 IU/mL (614)	1.42 (0.88 to 2.29)	PM_{10} per 6 μg/m^3
			1.30 (0.94 to 1.80)	NO_x per 44 μg/m^3

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Table 4.15 (*Continued*). Studies of Exposure to Traffic Pollution and Nonasthmatic Respiratory Allergy[a,b]

Study / Location	Years of Study / Age at Observation	Selected Effect Estimate: Effect (*N*)	Selected Effect Estimate: Adjusted OR (unless otherwise specified) (95% CI)	Effects Scale and Metric[c]
Oftedal et al. 2008 Oslo	2001–2002 Age 9–10 yr (lifetime residents)	SPT ≥ 3 mm to dust mite allergen: cat allergen: dog allergen: any pollen allergen:	 1.88 (1.02 to 3.47) 1.20 (0.91 to 1.58) 1.21 (0.81 to 1.66) 0.94 (0.76 to 1.16)	NO_2 from traffic (from source-specific dispersion model), per IQR 19.5 μg/m^3
Oosterlee et al. 1996 Haarlem, the Netherlands	1991 Age 0–15 yr	Doctor's diagnosis of allergy ever (245)	1.4 (0.6 to 3.4)	Living on busy street with high NO_2 (116–150 μg/m^3) and traffic density (10,000–30,000 vehicles/day) vs. rest of population
Shima et al. 2003 Chiba prefecture, Japan	1992–1995 Children from schools in urban and rural areas; residents at same home in last 3 yr Age 6-9 yr	Prevalence of history of allergic disease (1263)	Only unadjusted data available with no variance estimates	Living ≥ 50 m from trunk roads vs. living in rural areas
Van Roosbroeck et al. 2008 the Netherlands	Children from 24 schools within 400 m of motorway Age 7-12 yr Same as Janssen et al. 2003	Conjunctivitis	Prevalence ratio	Pollutants at schools adjusted for measurement error using personal exposure data
		(45)	**5.06 (1.02 to 24.96)**	Soot (BS) at school per 9.3 μg/m^3 (= 1.3 × 10^{-5}/m absorbance)[g]
		(67)	6.60 (1.33 to 32.77)	NO_2, per 17.6 μg/m^3
		Total IgE ≥ 100 IU/mL (45)	**2.98 (1.22 to 7.26)**	Soot at school per 9.3 μg/m^3 (= 1.3 × 10^{-5}/m absorbance)[g]
		(67)	4.20 (1.54 to 11.48)	NO_2, per 17.6 μg/m^3

[a] **Bold** indicates OR values plotted in Figure 4.12a and 412b.

[b] Abbreviations: EC = elemental carbon; ETS = environmental tobacco smoke; GINI = German Infant Nutrition Intervention; GIS = geographic information system; IgE = immunoglobulin E; IQR = interquartile range; ISAAC = International Study of Asthma and Allergies in Children; LISA = Influences of Lifestyle Related Factors on the Human Immune System and Development of Allergies in Children; LUR = land use regression; OR = odds ratio; PIAMA = Prevention and Incidence of Asthma and Mite Allergy study; SPT = skin prick test.

[c] Estimates at residential address unless otherwise indicated.

[d] The models explained 73%, 81%, and 85% of the variability of $PM_{2.5}$, soot, and NO_2, respectively.

[e] Measured as absorbance of $PM_{2.5}$ collected on filters; 1 × 10^{-5}/m absorbance = 1.45 μg/m^3 EC (Brauer et al. 2002 and Morgenstern et al. 2007).

[f] Pearson correlation between NO_2 concentrations and traffic volume in front of the residence of 0.70 (likely overestimated).

[g] The conversion from the measured absorbance to μg/m^3 was made using the following equation: BS = −3.633 + 9.897 × absorption (from Janssen et al. 2001) (Nicole Janssen, personal communication, October 2009).

Table 4.16. Studies of Exposure to Traffic Pollution and Birth Outcomes[a,b]

Study / Location	Year of Study (*N* = live births)	Birth Outcome	Selected Effect Estimate OR or RR (95% CI)	Effect Scale and Exposure Metric[c]
Brauer et al. 2008 Vancouver	1999–2002 (70,249)	Small for gestational age (< 10th percentile of cohort weight at same week of gestation)	OR for exposure during entire pregnancy:	Exposure estimated by IDW of concentration at nearest regulatory monitor (maximum = 10 km)
			1.14 (1.09 to 1.18)	NO_2 per 10 μg/m^3
			1.05 (1.03 to 1.08)	NO per 10 μg/m^3
			1.02 (0.98 to 1.05)	$PM_{2.5}$ per 1 μg/m^3
				Exposure estimated from LUR model (from measurements at various locations and road density variables)
			0.99 (0.96 to 1.02)	NO_2 per 10 μg/m^3
			1.02 (1.00 to 1.04)	NO per 10 μg/m^3
			1.02 (1.00 to 1.03)	$PM_{2.5}$ per 1 μg/m^3
				Distance to highway (21,000–114,000 vehicles/day) or to major road (15,000–18,000 vehicles/day)
			1.26 (1.07 to 1.49)	< 50 m to highway
			0.93 (0.83 to 1.03)	< 150 m to highway
			1.03 (0.95 to 1.12)	< 50 to major road
		Low birth weight (≥ 37 wk of gestation and < 2500 g)		IDW
			1.11 (1.01 to 1.23)	NO_2 per 10 μg/m^3
			1.03 (0.96 to 1.10)	NO per 10 μg/m^3
			0.98 (0.92 to 1.05)	$PM_{2.5}$ per 1 μg/m^3
				LUR
			0.97 (0.98 to 1.05)	NO_2 per 10 μg/m^3
			1.01 (0.96 to 1.07)	NO per 10 μg/m^3
			1.03 (0.99 to 1.07)	$PM_{2.5}$ per 1 μg/m^3

Table continues next page

[a] **Bold** indicates OR plotted in Figure 4.13.

[b] Abbreviations: IDW = inverse distance-weighted; LUR = land-use regression; OR = odds ratio; and SES = socioeconomic status.

[c] Estimated at maternal residence during gestation.

[d] SES indicator based on combined census tract and was computed at the neighborhood level for percentage below poverty, unemployed, and receiving public assistance.

[e] Results from model that includes individual covariates, indicator for freeway in residential buffer, and census-block SES variables; analysis did not account for clustering.

Table 4.16 (*Continued*). Studies of Exposure to Traffic Pollution and Birth Outcomes[a,b]

Study / Location	Year of Study (*N* = live births)	Birth Outcome	Selected Effect Estimate OR or RR (95% CI)	Effect Scale and Exposure Metric[c]
Ponce et al. 2005 Los Angeles county, Calif.	1994–1996 (37,347)	Preterm births (< 37 gestation wk completed)	OR for exposure during 3rd trimester	Exposure estimated by distance-weighted traffic density within 750-ft buffer
			Summer	≥ 80th percentile vs. < 20th percentile
			Low SES[d]: **0.93 (0.76 to 1.13)**	
			Middle SES: **1.19 (0.99 to 1.43)**	
			High SES: **0.93 (0.80 to 1.09)**	
			Winter	
			Low SES[d]: **1.30 (1.07 to 1.58)**	
			Middle SES: **1.18 (0.99 to 1.41)**	
			High SES: **1.00 (0.85 to 1.17)**	
Slama et al. 2007 Munich	1998–1999 (1016)	Low birth weight (< 3000 g at ≥ 37 wk of gestation)	OR for exposure during entire pregnancy:	Exposure estimated from LUR (including measurements at 40 sites and measures of road density) per quartile of exposure range; reference: < 24 µg/m^3 NO_2 (Q1) or < 13.5 µg/m^3 $PM_{2.5}$ (Q1)
			0.80 (0.52 to 1.28)	NO_2, 24–33 µg/m^3 (Q2)
			1.32 (0.86 to 2.09)	NO_2, 33–36 µg/m^3(Q3)
			1.16 (0.71 to 1.71)	NO_2, 39–61 µg/m^3(Q4)
			1.08 (0.63 to 1.82)	$PM_{2.5}$, 13.5–14.4 µg/m^3(Q2)
			1.34 (0.86 to 2.13)	$PM_{2.5}$, 14.5–15.4 µg/m^3(Q3)
			1.73 (1.15 to 2.69)	$PM_{2.5}$, 15.5–17.5 µg/m^3(Q4)
Wilhelm and Ritz 2003 Los Angeles county, Calif.	1994–1996 (37,433)	Preterm births (< 37 wk of gestation) or preterm plus low-weight births (< 2500 g)	RR for exposure during entire pregnancy (for those with 3rd trimester in fall or winter)[e]:	Distance-weighted traffic density (counts) for all streets within 750-ft buffer derived from dispersion model, per quintile; reference: < 20th percentile. Model adjusted for SES.
			Preterm births	
			0.97 (0.89 to 1.06)	20th to 39th
			1.04 (0.95 to 1.13)	40th to 59th
			1.08 (0.99 to 1.18)	60th to 79th
			1.15 (1.05 to 1.26)	≥ 80th
			Preterm plus low-weight births	
			0.93 (0.78 to 1.11)	20th to 39th
			0.98 (0.82 to 1.17)	40th to 59th
			1.11 (0.93 to 1.33)	60th to 79th
			1.24 (1.03 to 1.48)	≥ 80th

[a] **Bold** indicates OR plotted in Figure 4.13.

[b] Abbreviations: IDW = inverse distance-weighted; LUR = land-use regression; OR = odds ratio; and SES = socioeconomic status.

[c] Estimated at maternal residence during gestation.

[d] SES indicator based on combined census tract and was computed at the neighborhood level for percentage below poverty, unemployed, and receiving public assistance.

[e] Results from model that includes individual covariates, indicator for freeway in residential buffer, and census-block SES variables; analysis did not account for clustering.

Table 4.17. Studies of Exposure to Traffic Pollution and Cancer[a,b]

Study / Location	Years of Diagnosis/ Age	Malignancy Type (*N*)	Selected Effect Estimate OR or IR (95% CI)	Exposure Metric[c]
Childhood Cancers				
Harrison et al. 1999 West Midlands, U.K.	1990–1994 Age 0–15 yr	Leukemia (24 cases; 482,588 total population); solid tumors (31)	IR of leukemia (observed cases vs. expected cases in population, with indirect age and sex standardization)	< 100 m from source (major road or gasoline station)
			1.16 (0.74 to 1.72)	Major road (mean 23,400 vehicles/day)
			1.48 (0.65 to 2.93)	Gasoline station
			0.81 (0.16 to 2.38)	Major road and gasoline station
Pearson et al. 2000 Same subjects as Savitz and Feingold 1989	1976–1983 Age 0–14 yr	Leukemia (8 cases; 3 controls); all cancers (18 cases; 3 controls)	OR of leukemia **8.28 (2.09 to 32.80)**	Distance-weighted traffic density (< 750 ft) on street with highest traffic (≥ 20,000 vs. < 500 vehicles/day)
			OR of all cancers **5.90 (1.69 to 20.56)**	
Raaschou-Nielsen et al. 2001 Denmark	1968–1991 Age 0–15 yr	Leukemia (870 cases; 1721 controls); Hodgkin lymphomas (166 cases; 814 controls)	RR for Hodgkin lymphomas (conditional logistic match of age and birth)	Benzene and NO_2 during gestation (modeled from traffic density and speed, emission rates, vehicle type, distance to road)
			4.3 (1.5 to 12.4)	Benzene: 99th percentile (12.9 ppb) vs. 50th percentile (1.8 ppb)
			6.7 (1.7 to 28.0)	NO_2: 99th percentile (19.4 ppb, or 36.6 µg/m^3) vs. 50th percentile (5.5 ppb, or 10.3 ug/m^3)
Reynolds et al. 2004 California	1988–1997 Age < 5 yr	All cancers (4369 cases; 8596 controls); leukemia (1728 cases), brain (CNS) cancer (746 cases)	OR: All cancers **0.87 (0.75 to 1.00)** Leukemias **0.79 (0.63 to 1.00)** Brain (CNS) **1.03 (0.75 to 1.43)**	Road density: length of all roads within 500-foot radius (mi/mi^2); ≥ 90th percentile vs. < 25th percentile
			All cancers **0.92 (0.80 to 1.06)** Leukemias **0.92 (0.73 to 1.15)** Brain (CNS) **1.22 (0.87 to 1.70)**	Traffic density: VMT/mi^2 within 500-foot radius; ≥ 90th percentile vs. < 25th percentile

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[a] **Bold** indicates values plotted in Figures 4.14a and 4.14b.

[b] Abbreviations: BS = black smoke; CNS = central nervous system; IR = incidence ratio; RR = relative risk; and VMT = vehicle miles traveled.

[c] Estimates at residential address unless otherwise indicated.

Table 4.17 (*Continued*). Studies of Exposure to Traffic Pollution and Cancer[a,b]

Study / Location	Years of Diagnosis/ Age	Malignancy Type (*N*)	Selected Effect Estimate OR or IR (95% CI)	Exposure Metric[c]
Childhood Cancers (*Continued*)				
Savitz and Feingold 1989 Denver	1976–1983 Age 0–14 yr	All cancers (328 cases; 262 controls); leukemia (98 cases); brain (61 cases)	OR All cancers **1.7 (1.0 to 2.80)** Leukemia **2.1 (1.1 to 4.0)** Brain **1.7 (0.8 to 3.9)**	Traffic density (vehicles/day) on street in front residence > 500 vehicles/day vs. < 500
Adult Cancers				
Beelen et al. 2008c the Netherlands (Cohort Study on Diet and Cancer)	1986–1997 Age 59–66 yr (at recruitment), males	Lung cancer (1940 cases in full-cohort analysis; 1295 cases in case-cohort analysis)	RR (Cox proportional hazard model)	BS and NO_2 from model that included regional, urban, and local (traffic) contribution
			All cases (full cohort)	
			0.96 (0.83 to 1.11)	BS per 10 µg/m^3 (95th-5th percentile)
			0.86 (0.70 to 1.07)	NO_2 per 30 µg/m^3 (95th-5th percentile)
			All cases (case cohort)	
			1.03 (0.78 to 1.34)	BS per 10 µg/m^3
			0.86 (0.57 to 1.29)	NO_2 per 30 µg/m^3
			Never-smokers (full cohort, 252 cases)	
			1.47 (1.01 to 2.16)	BS per 10 µg/m^3
			1.11 (0.88 to 1.41)	Traffic density on nearest road (10,000 vehicles/day)
			1.36 (0.99 to 1.87)	Traffic density within 100-m buffer (335,000 vehicles/day)
			1.55 (0.98 to 2.43)	< 100 m of motorway or < 50 m of major road

Table continues next page

[a] **Bold** indicates values plotted in Figures 4.14a and 4.14b.

[b] Abbreviations: BS = black smoke; CNS = central nervous system; IR = incidence ratio; ; RR = relative risk; and VMT = vehicle miles traveled.

[c] Estimates at residential address unless otherwise indicated.

Table 4.17 (*Continued*). Studies of Exposure to Traffic Pollution and Cancer[a,b]

Study / Location	Years of Diagnosis/ Age	Malignancy Type (*N*)	Selected Effect Estimate OR or IR (95% CI)	Exposure Metric[c]
Adult Cancers (*Continued*)				
Nie et al. 2007 Erie and Niagara counties, N.Y.	1996–2001 Age 35–79 yr, females	Breast cancer (1068 cases; 1944 controls)	OR for nonsmokers	Benzo[*a*]pyrene as surrogate of PAH from dispersion model (using traffic, emissions data, and road segments), by quartile (reference = 1st quartile)
			Exposure at age of menarch	
			Premenopausal cancers (26 cases, 40 controls) **6.67 (1.74 to 25.67)**	4th quartile
			Exposure at age of 1st childbirth	4th quartile
			Premenopausal cancer (13 cases; 48 controls) **2.06 (0.44 to 9.73)**	
			Postmenopausal cancers (25 cases; 24 controls) **6.23 (1.70 to 22.82)**	4th quartile
Nyberg et al. 2000 Stockholm	1985–1990 Age 40–75 yr, males	Lung cancer (1042 cases; 2364 controls)	OR	NO_x/NO_2 and SO_2 from dispersion model (using emissions data from line and area sources); yearly estimates by source
			All cases	NO_2 from road traffic, per 10 µg/m^3
			1.05 (0.93 to 1.18)	30-year average exposure before end of follow-up
			1.10 (0.97 to 1.23)	10-year average exposure, lagged 20 yr from end of follow-up
			Never-smokers (30 cases; 629 controls) **1.68 (0.67 to 4.19)**	NO_2 > 90th percentile (29.3 µg/m^3) vs. < 90th percentile; 10-year average exposure lagged 20 yr from end of follow-up
Vineis et al. 2006 Many European cities (GenAir study)	1994–~2004 Age 35–74 yr (at recruitment, 1993–1998)	Lung cancer in never-smokers or exsmokers (197 cases and 556 controls with exposure data)	OR	Living near a major road with heavy traffic (> 10,000 cars/day) vs. light traffic (< 10,000 cars/day) (distance not specified)
			1.38 (0.87 to 2.19)	1. Regression model with matching variables
			1.46 (0.89 to 2.40)	2. Regression model (1) futher adjusted by BMI, education, type of food intake
			2.87 (1.13 to 7.35)	3. Regression model (2) futher adjusted by cotinine
			1.31 (0.82 to 2.09)	4. Regression model (3) further adjusted by occupational exposure

[a] **Bold** indicates values plotted in Figures 4.14a and 4.14b.

[b] Abbreviations: BS = black smoke; CNS = central nervous system; IR = incidence ratio; ; RR = relative risk; and VMT = vehicle miles traveled.

[c] Estimates at residential address unless otherwise indicated.

Table 4.18. Studies of Exposure to Traffic-Related Pollutants and Health Effects in Occupational Settings

Study / Location	Year(s) of Study (*N*)	Occupation /Control	Traffic Exposure Metric(s)	Comments
Atimtay et al. 2000 Ankara	1998 (85 exposed, 32 controls)	Traffic police /Police in office	Expired CO while in traffic	No adequate control for smoking age, duration of work; results could be explained by smoking during shift.
De Paula Santos et al. 2005 Sao Paulo	Summer / winter 2000 (48)	Vehicle Traffic controllers / No controls	CO, PM_{10}, NO_2, SO_2	Panel study, no control for noise or stress; BP most closely associated with SO_2, CO not NO_2; HRV associated imprecisely with SO_2.
Erdogmus et al. 2006 Kaynasli, Golyaka-Duzce region of Turkey	(61 exposed, 48 controls)	Toll-takers (sex not given) / "Healthy" controls (defined in text but source and occupations not given)	Duration of work < 10 yr, 10–20 yr, > 20 yr	Duration associated with carotid intima wall thickness (IWT). IWT associated with age, univariate strongest association in non-smoking toll-takers; no quantitative results from linear regression given (stated that only variable associated with IWT was duration of work; no model fit data given).
Evans et al. 1988 New York, N.Y.	1970–1981 (945)	Male toll takers in tunnel / Outdoors	Toll workers vs. tunnel workers	No direct measurement of exposure; adjusted only for age. Outcome: respiratory symptoms and lung function.
Herbert et al. 2000 New York, N.Y.	1993–1995 (200)	Toll takers in tunnel / Outdoors	Single CO measured as COHb	Cross-sectional; Same population as Evans et al. 1988; frequent report of limited ability to make decisions, low activity, and high job strain. No association between exposures and outcome. Outcome: parameters from exercise stress testing to evaluate risk of CHD.
Iavicoli et al. 2004 Rome	Summer 2001 (103 traffic, 58 office)	Traffic police / Police in office	Urinary Platinum	No specific traffic exposure data; could have been no difference in exposure between two groups. No difference in urine platinum level. No health outcome measured.
Jones et al. 2008 Mongkok district of Hong Kong	Roadside vendors (33), shopkeeper assistants (31), university workers (92)	Roadside vendors / Nearby shopkeeper assistants in air conditioned shops / University workers ≥ 30 yr, not near roads as control for both groups of vendors	Location of occupation, blood lead, expired CO	No direct measures of traffic presented. No meaningful differences in lung function between roadside vendors and shopkeepers; exhaled CO somewhat lower for shopkeepers, but university workers higher than vendors and shopkeepers; no difference in blood lead levels between two groups of vendors.
Kocasoy et al. 2004 Istanbul Bosphorous Bridge	Year not given (104 exposed)	Cashiers at busy bridge / Relative controls	COHb pre and post shift	Inadequate description of exposure and controls, inadequate analysis with adjustment for confounders.

Table continues next page

Table 4.18 (*Continued*). Studies of Exposure to Traffic-Related Pollutants and Health Effects in Occupational Settings

Study / Location	Year(s) of Study (*N*)	Occupation/Control	Traffic Exposure Metric(s)	Comments
Lai et al. 2005 Taipei City, Taiwan	Year not given (47 exposed, 27 controls)	Female toll takers/ Trainees in class	Vehicles/hr × shift time; urine biomarker for pyrene metabolite; five single measurements	Cross sectional; multiple confounders by questionnaire (include diet and charbroil, protective gear); inadequate data on association between number of vehicles and CO; inadequate control of confounding . Outcomes: Urine biomarkers, plasma NO.
Raaschou-Neilson et al. 1995 Copenhagen	1989 (116 exposed, 115 controls)	Street cleaners on traffic roads / Cemetery workers	NO, NO_2, CO, SO_2 at 5 streets representative of work environments	Large amount of missing data relative to target population; no summary of subject characteristics; no traffic or pollutant data to street locations of work; no confidence intervals for estimates. Outcomes: questionnaire-based asthma and chronic bronchitis.
Tamura et al. 2003 Bangkok	1998–1999 (698 heavy, 448 moderate, 457 controls)	Traffic policemen / Comparison of worker in areas with different traffic density	Pollution not based on traffic but on categories based on PM_{10} and TSP	Cross-sectional; Some overlap in traffic density and PM_{10} between areas of pollution; control for smoking, age; no other covariates explored, results from logistic regression not presented. Outcomes: asthma, dyspnea.
Tollerud et al. 1983 Boston, Mass.	1972–1975 (91 total, 84 seen twice, 73 with outcome data)	Tunnel toll takers; tunnel maintenance workers; tunnel administrators	Duration in work force (≥ 7 yr as cut-point); hair and blood lead	No associations between any exposure marker respiratory symptoms, asthma, FEV_1 or FVC; only covariates smoking, height, and weight.
Ulfvarson et al. 1987 Sweden	Year not given. (91 cross-sectional, 84 longitudinal)	Tunnel workers (toll takers, maintenance); tunnel administrators	Hair and blood lead	Only covariates smoking, heath, weight, not clear if all eligible subjects studied.
Volpino et al. 2004 Rome	Year not given (63 traffic, 62 office)	Traffic police /Police in office	Annual benzene, NO_2 from 1993–2001	Not control for any confounder — assumption groups comparable not supported by data; incomplete data analysis. Outcomes: multiple respiratory symptom and function and cardiovascular.
Watt et al. 1995 Aberdeen, Scotland	1994 (14)	Traffic wardens / No controls	Black smoke	Exposure estimates only based on personal sampling over 4 days. Outcome: no health effect estimates.
Wongsurakiat et al. 1999 Bangkok	1996–1997 (629 policemen, 303 population controls)	Policeman /Controls (farmers, gardeners, government workers, office workers, self-employed, students)	Job as policeman	All non-smokers, only other covariates, age, job title, use of respiratory protection; no specific estimates of traffic exposure controls included occupations with exposure to vehicles.

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ABBREVIATIONS AND OTHER TERMS

APHENA	Air Pollution and Health: A Combined European and North American Approach
ARIC	Atherosclerosis Risk in Communities
BMI	body mass index
C_{total}	total carbon present
CI	confidence interval
CO	carbon monoxide
COPD	chronic obstructive pulmonary disease
ECRHS	European Community Respiratory Health Survey
FEF_{25}	forced expiratory flow at 25%
FEV_1	forced expiratory volume in 1 second
FVC	forced vital capacity
GINI	German Infant Nutrition Intervention
GIS	geographic information system
HRV	heart-rate variability
ICD-9	International Classification of Diseases, 9th revision
IMPROVE	Interagency Monitoring of Protected Visual Environments
IQR	interquartile range
ISAAC	International Study of Asthma and Allergies in Children
LISA	Influences of Lifestyle Related Factors on the Human Immune System and Development of Allergies in Children
MEF	maximum expiratory flow
NAFTA	North American Free Trade Agreement
NLCS	Netherlands Cohort Study on Diet and Cancer
NMMAPS	National Morbidity, Mortality, and Air Pollution Study
NO	nitric oxide
NO_2	nitrogen dioxide
NO_3^-	nitrate
OH·	oxygen radical
OR	odds ratio
PAH	polycyclic aromatic hydrocarbon
PEF	peak expiratory flow
PIAMA	Prevention and Incidence of Asthma and Mite Allergy study
PM	particulate matter

$PM_{2.5}$	PM ≤ 2.5 μm in aerodynamic diameter
PM_{10}	PM ≤ 10 μm in aerodynamic diameter
RAP	rate advancement period
rMSSD	root mean square of successive differences in normal-to-normal intervals
RR	relative risk
SALIA	Study on the influence of Air pollution on Lung function, Inflammation, and Aging
SAPALDIA	Swiss Study on Air Pollution and Lung Disease in Adults
SAVIAH	Small Area Variations in Air pollution and Health Project
SDNN	standard deviation of normal-to-normal sinus beat intervals
SO_2	sulfur dioxide
SO_4^{2-}	sulfate
TRAPCA	Traffic Related Air Pollution and Childhood Asthma
VMT	vehicle miles traveled

Chapter 5

Health Effects: Toxicology of Traffic-Related Air Pollution

CONTENTS

Chapter 5

Health Effects: Toxicology of Traffic-Related Air Pollution

CONTENTS (*Continued*)

Chapter 5

Health Effects: Toxicology of Traffic-Related Air Pollution

5.I. INTRODUCTION

The aim of this chapter is to review the health effects of traffic-related air pollution from the perspective of toxicology. Understanding the health effects of air pollutants is a multidisciplinary endeavor, and the research approaches include epidemiology, human clinical studies, animal exposure studies, and in vitro studies. In general, understanding of the health effects of air pollution on the scale of whole populations is driven by epidemiology, which describes associations between exposure and health effects. Toxicologic studies are often designed to assess plausibility, explore mechanisms involved in the relationships observed in epidemiologic studies, and determine exposure–response relationships.

The disciplines of epidemiology and toxicology each have their own strengths and weaknesses but offer complementary approaches. Epidemiologic studies involve assessing the effects of exposures to complex mixtures of ambient air pollutants. Efforts to dissect the effects of single pollutants by mathematically adjusting for the effects of other pollutants are hampered, in part by limitations in monitoring and measurements and by imperfect exposure assessment. Toxicologic studies can evaluate the effects of single pollutants and simple mixtures in a controlled laboratory environment, using appropriate clean-air control exposures. They can also assess the effects of specific polluted environments. However, they are generally limited to assessments of relatively short-term exposures and of acute or subacute effects. Prolonged animal-exposure studies can be conducted for months and even years, but their relevance to lifelong human exposures is often uncertain. Toxicologic studies therefore have limited ability to assess the effects of chronic exposure or the ability of pollutants to initiate disease processes, such as asthma or atherosclerosis.

This chapter will review the toxicologic evidence from studies of humans, animals, and cell systems. (Chapter 6 will then integrate and discuss the coherence of the epidemiologic and toxicologic evidence for traffic-related health effects.)

Toxicologic studies have the following general objectives:

- To understand the mechanisms by which exposures cause health effects, from the initial exposure all the way to the cellular and molecular levels;
- To understand concentration–response relationships;
- To understand the specific pollutant characteristics and components and the multiple pollutant interactions that contribute to toxicity;
- To understand individual susceptibility to pollutants; and
- To inform risk assessment and strategies for risk reduction.

The toxicology of traffic-related pollution presents significant challenges. Traffic-related pollution is a complex mixture; moreover, it cannot so far be cleanly "teased out" from the broader mix of pollutants from other sources. The chemistry of traffic emissions changes as the emissions aerosol "ages" in the atmosphere, with the result that the composition and toxicology can vary over time and with distance from sources. It is difficult to envision an experimental exposure scenario for human or animal studies that would permit a comparison of exclusively traffic-related pollution with either clean air or other pollutants. We are left with studying exposure environments that are enriched in traffic pollutants, such as those near roads; creating laboratory atmospheres that replicate aspects of the traffic mix, such as gasoline or diesel exhaust; and studying specific components or their mixtures. All of these approaches will be necessary for a more adequate understanding of the role of traffic emissions in the effects being observed in epidemiologic studies.

5.I.1 DOSIMETRY ISSUES

Dosimetry and dose–response relationships, basic elements of toxicology, are particularly problematic in studying traffic pollution. As a subset of the complex mix of ambient air pollution, traffic-related pollution is itself a complex mix with components that vary in concentration depending on a variety of conditions that were explored in Chapter 2. Dosimetry in studies of traffic exposure must be considered in the context of the specific experimental objectives. The particulate-matter (PM^*) mass, PM number, nitrogen dioxide (NO_2), carbon monoxide (CO), or elemental carbon (EC) may be used as surrogates of exposure to traffic; however, the choice of exposure surrogate will likely affect the outcome, and where possible, multiple relevant metrics should be considered in characterizing the exposure. Measurements of PM mass, for example, might fail to reflect exposure to ultrafine particles (UFP), which contribute little to mass but dominate particle counts. Particles have been shown to have varying degrees of oxidative

* A list of abbreviations and other terms appears at the end of this chapter.

potential, presumably as a result of their surface chemistry, and some evidence suggests that UFP is more reactive than larger particles. Thus there is a need to consider oxidative potential as an additional exposure metric for PM in toxicologic studies. This issue is examined in more detail in Section 5.II, below.

A challenge facing researchers who study the health effects of air pollution is designing studies to investigate the relatively small excess health risks detected in epidemiologic studies using proportional or relative-risk models. This is often addressed by using exposure concentrations that are much higher than real-world ambient concentrations, in a proof-of-concept approach. However, higher concentrations of a given pollutant might bring different toxicologic pathways and mechanisms into play. Another approach is to study subjects, or animal models, that have increased susceptibility.

5.I.2 STUDY DESIGN ISSUES

Human, animal, and in vitro experimental approaches each have their strengths and weaknesses (Allen 2006; Devlin et al. 2005; Frampton et al. 2006a).

A major strength of human controlled exposure (or "clinical") studies is the involvement of the most relevant species, namely, humans. Subjects can be selected using specified criteria and characterized thoroughly. In addition, exposures in a controlled environment can provide well-defined and reproducible exposure atmospheres and conditions. Weaknesses include the difficulties and risks of studying the most susceptible subjects, such as children or people with severe respiratory or cardiovascular disease. Studies usually focus on specific components of traffic-related pollution, such as model particles, single gases, or mixtures (such as concentrated ambient particles [CAPs] or diesel exhaust [DE]). Effects from these exposures might not be representative of the pollution mix as a whole. Exposures are generally limited to several hours in duration, and the number of subjects is limited by cost and practicality.

Animal-exposure studies also use controlled and defined atmospheres and provide the opportunity to explore physiologic and pathogenic mechanisms. They are generally less costly than human studies, more prolonged exposures are possible, and experiments can be more invasive. The availability of genetically engineered and manipulated animals, especially mice, provides opportunities to explore the role of specific genes in determining pollutant effects and susceptibility. However, there are significant differences in pollutant responses among animal species and strains. Most important are the difficulties in extrapolating findings from animal studies to humans. Dosimetry is affected by differences in body size, airway structure, and metabolic pathways; pollutant responses might be affected by differences in diurnal cycles, diet, body temperature, stress responses, and disease susceptibility.

In vitro studies provide data on the responses of specific cell types and tissues to pollutants or pollutant mixtures; they have been useful in screening various pollutants for cytotoxic effects, determining specific cell responses and signaling mechanisms, and exploring dose–response relationships. However, findings and dosimetry cannot be directly extrapolated to animals or humans.

Recently developed technology permits the concentration of outdoor ambient particles for exposure in clinical and toxicologic studies. Concentrators have been developed that concentrate particle sizes from coarse to ultrafine. This review includes selected studies of exposure to CAPs because they provide insight into the health effects of complex PM exposures that include traffic emissions. Where sample size is sufficient, detailed analyses of each exposure's CAPs composition might allow estimation of the pollutant sources involved, including traffic sources. The contribution of traffic sources obviously depends on the specific location of the concentrator's air intake and the time of the exposures. However, CAPs studies cannot reliably separate the effects of traffic emissions from those of the particle mix as a whole.

A strength of CAPs studies is that their exposures are to real air-pollution particles in real time, with particle characteristics that are similar to those of ambient aerosol, rather than to surrogate particles or to particles obtained from collection filters. However, CAPs concentrations and composition vary hourly and daily, reflecting changes in ambient PM characteristics and sources, which limits statistical power for a given sample size. The process of concentration might subtly alter particle composition or surface characteristics. Particle concentrators do not concentrate gases, which may be variably "scrubbed" in the process of particle concentration. In addition, they do not concentrate all particle sizes with equal efficiency; particles smaller than about 40 nm are not efficiently concentrated with current technology.

This chapter begins with a discussion of a key hypothesis related to the health effects of air pollution in general, namely, the oxidative stress hypothesis. A discussion of traffic-emissions toxicology follows, organized by health effect, including cardiovascular, respiratory, reproductive, cancer, and neurologic effects. The chapter will focus on studies of exposure to traffic emissions or traffic-related mixtures, though there are relatively few studies in the former category. The chapter will also review studies of the toxicology of components of traffic emissions, including PM, DE, CO, nitrogen oxides (NO_x), and selected air toxics.

The literature on animal and in vitro toxicology for traffic-related components is extensive, and a comprehensive review of all relevant studies is beyond the scope of this special report. Instead, the review will provide selected examples of studies that illustrate approaches in exploring the mechanisms of health effects. Emphasis is placed on studies of health effects and outcomes for which the epidemiologic findings indicate relationships with traffic emissions. The chapter will rely in part on recent authoritative reviews and governmental reports on, for example, DE (Sydbom et al. 2001; U.S. EPA 2002), NO_2 (California Environmental Protection Agency [California EPA] 2007; U.S. EPA 2008), and air toxics (HEI Air Toxics Review Panel 2007). Tables 5.2 and 5.3 summarize the human and animal studies, respectively, that are cited in this chapter.

5.II. THE OXIDATIVE STRESS HYPOTHESIS

Exposure to a broad spectrum of particle types (from, for example, vehicle emissions, cigarette smoke, or wood smoke) elicits similar acute responses in humans, namely neutrophilic inflammation (Salvi et al. 1999; Ghio et al. 2000a,b), reduced inspiratory capacity (Salvi et al. 1999; Chen et al. 2001), and heightened bronchial reactivity (Sherman et al. 1989; Menon et al. 1992; Nordenhäll et al. 2000). The exact mechanisms by which particles have adverse effects are unknown, as particle inhalation has been associated with numerous responses, some of which might be of more consequence than others. As described in detail later in this chapter, exposure to particles also leads to alterations in vascular biology, including changes in blood viscosity, fibrinogen, and C-reactive protein. Furthermore, increases in heart rate in response to increasing air pollution have been described and are most marked in individuals who have high blood viscosity. In vitro studies have also revealed that particle contact with macrophages enhances calcium influx in these cells. It has thus been argued that diverse particle types act through common mechanisms, which might relate to the capacity of these particles to cause damaging oxidation reactions, or "oxidative stress," in the body.

Oxidative stress is a relatively new term in biology; it was introduced by Sies (1991) and is a concept that can relate to events occurring in any tissue in the body when the prooxidant–antioxidant balance is disturbed (Figure 5.1). This imbalance can occur when the generation of reactive oxygen species (ROS), or free radicals, exceeds the available antioxidant defenses. It is the damage arising from aberrant free-radical activity that is often loosely referred to as oxidative stress, and it is characterized by the presence of increased cellular concentrations of oxidized lipids, proteins, and DNA.

A strong body of evidence, utilizing in vitro and in vivo systems, has now accumulated, demonstrating disturbances in normal cellular and extracellular constituents (specifically, the degree to which they are in the oxidized state) in response to exposure to components of traffic pollution. Many of these studies have focused on DE (Bonvallot et al. 2001; Hirano et al. 2003; Pourazar et al. 2005; Li et al. 2007); only a modest number have focused on emissions from gasoline-fueled engines (Reed et al. 2008; Seagrave et al. 2008). ROS can trigger inflammation by way of activating redox-sensitive signaling pathways (Bonvallot et al. 2001; Pourazar et al. 2005) (Figure 5.2).

The capacity of traffic-related PM to elicit such a response has been explained by the delivery of surface-absorbed redox-active transition metals (Mudway et al. 2004) (see Sidebar 5.1) and organic components such as polycyclic aromatic hydrocarbons (PAHs) (Squadrito et al. 2001) (see Sidebar 5.2) into the lung, which in turn drive oxidation reactions and the generation of free radicals (Kelly 2003). With alterations in the redox state of the cell, oxidant-sensitive transcription factors are activated (Pinkus et al. 1996; Lander 1997; Cohen and Nikula 1999; MacNee and Donaldson 1999). The latter are important for the expression of many genes (including genes for cytokines, chemokines, and adhesion molecules) that participate in inflammatory reactions in the lung (Sen and Packer 1996). The resultant airway inflammation itself then leads to an increased production of oxidants by activated phagocytes recruited to the airways, perpetuating the cycle of oxidative injury.

Protective mechanisms that counteract the oxidizing effects of traffic-related pollution also exist. Laboratory-generated carbon-black nanoparticles, and diesel-exhaust

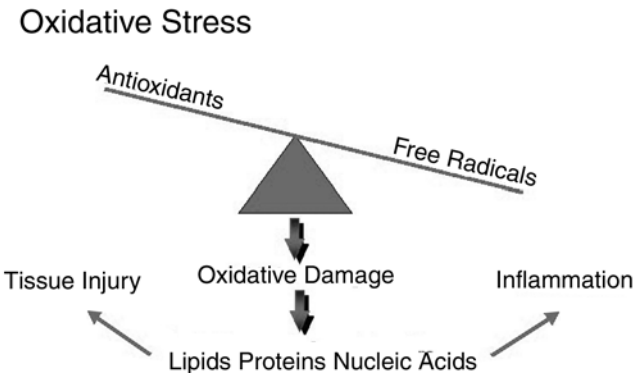

Figure 5.1. Schematic representation of the link between exposure to PM, oxidative stress, and inflammation. Oxidative stress exists when there is an excess of free radicals over antioxidant defenses. As a consequence, free radicals attack and oxidize other cell components such as lipids (particularly polyunsaturated lipids), proteins, and nucleic acids. This leads to tissue injury and in some cases the influx of inflammatory cells to the sites of injury. (Reprinted from Kelly 2003, with permission of BMJ Publishing Group Ltd.)

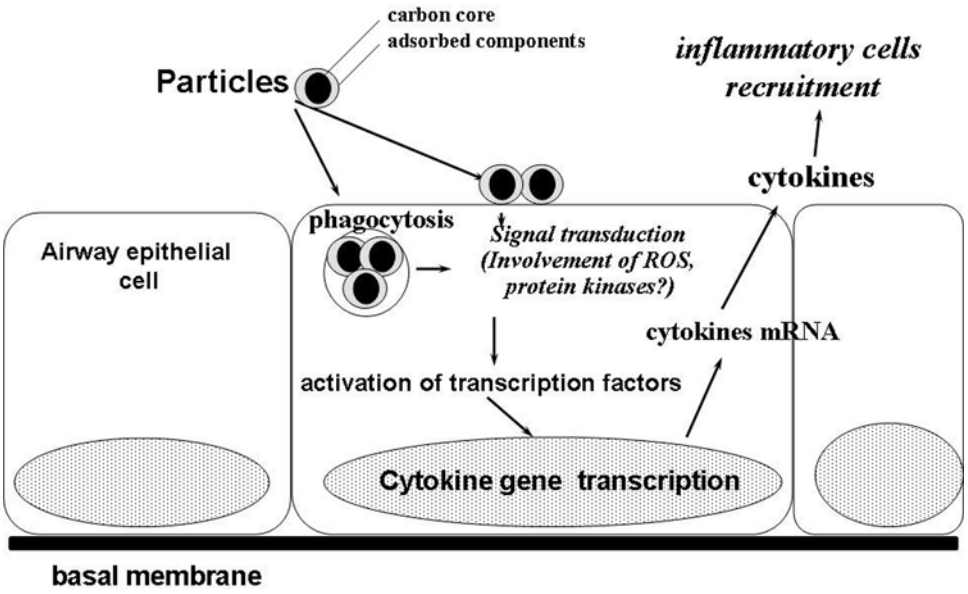

Figure 5.2. Hypothetical cellular and molecular events triggered during PM-induced inflammatory responses in airway epithelial cells. ROS = reactive oxygen species. (Reprinted from Baeza-Squiban et al. 1999, with permission of Springer Science and Business Media.)

particulate matter (DEP; also referred to as DPM), can increase expression of the oxidative-stress-response gene, heme oxygenase (HO-1) (Koike and Kobayashi 2006). In murine lungs, pretreatment with free-radical scavengers such as superoxide dismutase and rosmarinic acid inhibits lung injury induced by DEP (Sagai et al. 1993; Sanbongi et al. 2003). Furthermore, when Mudway and colleagues (2004) investigated the effect of exposing healthy subjects to DE (100 µg/m^3 PM_{10} [PM with an aerodynamic diameter $\leq$ 10 µm], 0.6 ppm NO_2 for 2 hours) or filtered air, neither airway inflammation nor antioxidant (ascorbate, urate, and reduced glutathione) depletion were seen at any level of the respiratory tract at 6 hours after exposure. Instead, an increased flux of reduced glutathione into the bronchial and nasal airways indicated that the antioxidant network at the air–lung interface in healthy subjects was capable of dealing with the oxidative challenge posed by DE at ambient concentrations.

A limited number of studies quantifying the free-radical–generating capacity of ambient and traffic-related PM have indicated that smaller PM size fractions show the highest levels of radical formation (de Kok et al. 2005; Shi et al. 2003) and that the ROS-generating capacity of curbside $PM_{2.5}$ (PM with an aerodynamic diameter $\leq$ 2.5 µm) was higher than that of $PM_{2.5}$ from an urban background location (Baulig et al. 2004). However in another study in

Sidebar 5.1 Metal-Driven Oxidative Stress

Transition metals such as iron, copper, chromium, and vanadium can generate ROS through Fenton-type reactions and catalyze the Haber–Weiss reaction (Halliwell and Gutteridge 1999):

$$O_2^{\bullet -} + H_2O_2 \xrightarrow[\text{catalyst}]{\text{metal}} OH^{\bullet} + OH^- + O_2,$$

where ferrous iron (Fe^{2+}) reduces hydrogen peroxide (H_2O_2) with the formation of hydroxyl radical (OH^-) and oxidation of ferrous iron to ferric iron (Fe^{3+}) (see also Sidebar 5.2). This reaction can recycle by way of reductants, such as superoxide anions, glutathione, and ascorbic acid, that reduce Fe^{3+} to Fe^{2+}. Indeed, several studies using diesel-exhaust particles (DEP) have shown that iron and other transition metals, either by leaching from particles or from their presence on particle surfaces, play a role in the generation of ROS in biologic systems (Ghio et al. 2000a,b and Han et al. 2001). For example, Ghio and colleagues (2000b) reported that DEP exposure influenced an accumulation of endogenous and biologically active iron in the rat lung. This accumulation of iron was associated with oxidative stress, release of oxidant-sensitive mediators, and neutrophilic lung injury. This is consistent with in vitro studies demonstrating that DEP generates superoxide anions, leading to the generation of H_2O_2 and hydroxyl radicals in the absence of additional biochemical or biologic activation (Dellinger et al. 2001; Sagai et al. 1993).

which samples were taken at various locations in one city, no correlations were found between ROS-generating capacity and traffic intensity (de Kok et al. 2005). A positive correlation has been found between PAH concentrations and the radical-generating capacity of PM_{10} and $PM_{2.5}$, but no such correlations were seen between radical formation and metal or transition-metal concentrations or between PAHs and metal concentrations (de Kok et al. 2005).

In summary, there is broad evidence supporting the oxidative stress hypothesis as an important determinant of the health effects of air pollution, including traffic-related air pollution. The increased burden of free radicals presented by ambient air pollutants, including PM and its components, may upset the balance between oxidative stress and oxidant defense mechanisms. An increased oxidant burden may also play a role in transcriptional activation of proinflammatory genes, contributing to tissue injury.

5.III. STUDIES OF CARDIOVASCULAR HEALTH EFFECTS

The consideration of possible cardiovascular effects of exposure to traffic-related air pollution must include both acute cardiac or vascular events and the chronic progression of cardiovascular disease. Table 5.1 provides a partial list of cardiovascular events or diseases for which traffic-related air pollution, especially its PM component, has been or could be implicated as a contributing factor, based on studies reviewed in this section.

Epidemiologic studies can provide evidence for associations between exposure to ambient PM and cardiovascular effects, but mechanistic pathways have only begun to be investigated using toxicologic approaches. The ambient pollutant most consistently associated with cardiovascular disease in epidemiologic studies is PM. Because PM is a complex mixture from diverse sources, including traffic as well as stationary sources, attribution of the role of traffic emissions in causing cardiovascular events is problematic.

Table 5.1. Cardiovascular Events and Diseases Possibly Associated with Traffic-Related Air Pollution

	Acute	Subacute and Chronic
Cardiac		
	Arrhythmia	Congestive heart failure
	Myocardial infarction	Cardiomyopathy
	Cardiac arrest	Atherosclerosis
	Pulmonary edema	Pulmonary hypertension
	Unstable angina	
Vascular		
	Stroke	Claudication
	Acute limb ischemia	Atherosclerosis

Potential pathogenic pathways linking PM with cardiac events have been proposed and are depicted in Figure 5.3. These pathways are relevant for traffic emissions as well. Traffic-related emissions might induce changes in cardiovascular function by way of pulmonary-mediated changes in the autonomic nervous system, through pulmonary inflammation leading to systemic inflammation and increased coagulation, or possibly by way of direct effects on endothelial cells, blood cells, or myocardium by particles or their components gaining access to the circulatory system. There is experimental support for the involvement of each of these pathways in response to PM exposures, but their relative importance in the real-world effects of traffic exposure has not been established.

Sidebar 5.2 PAH-Driven Oxidative Stress

The organic fractions of gasoline-engine exhaust (Jakober et al. 2007; Riddle et al. 2007) and diesel exhaust (Kumagai et al. 2002; Xia et al. 2006), namely, PAHs, can induce oxidative stress indirectly through biotransformation by cytochrome P450 and dihydrodiol dehydrogenase to generate quinones. Quinones are highly redox-active molecules that can generate ROS (Bolton et al. 2000; Kumagai et al. 2002). For example, as shown here, a semiquinone radical ($QH^{\bullet}$) can reduce oxygen to form superoxide; this will undergo dismutation to H_2O_2 and finally form the hydroxyl radical in the presence of "free" iron. Biologic reductants such as ascorbate, NAD(P)H, and glutathione are then able to reduce the oxidized quinoid back to the reduced state ($QH^{\bullet}$ and the hydroquinone) enabling the reaction to cycle again.

$$QH^{\bullet} + O_2 \rightarrow Q + O_2^{\bullet -} + H$$
$$2O_2^{\bullet -} + 2H^{+} \rightarrow H_2O_2 + \_O_2$$
$$H_2O_2 + Fe^{2+} \rightarrow OH^{\bullet} + OH + Fe^{3+}$$
$$Q + e^{-} + H^{+} \rightarrow QH^{\bullet}$$
$$QH^{\bullet} + e^{-} + H^{+} \rightarrow QH_2$$

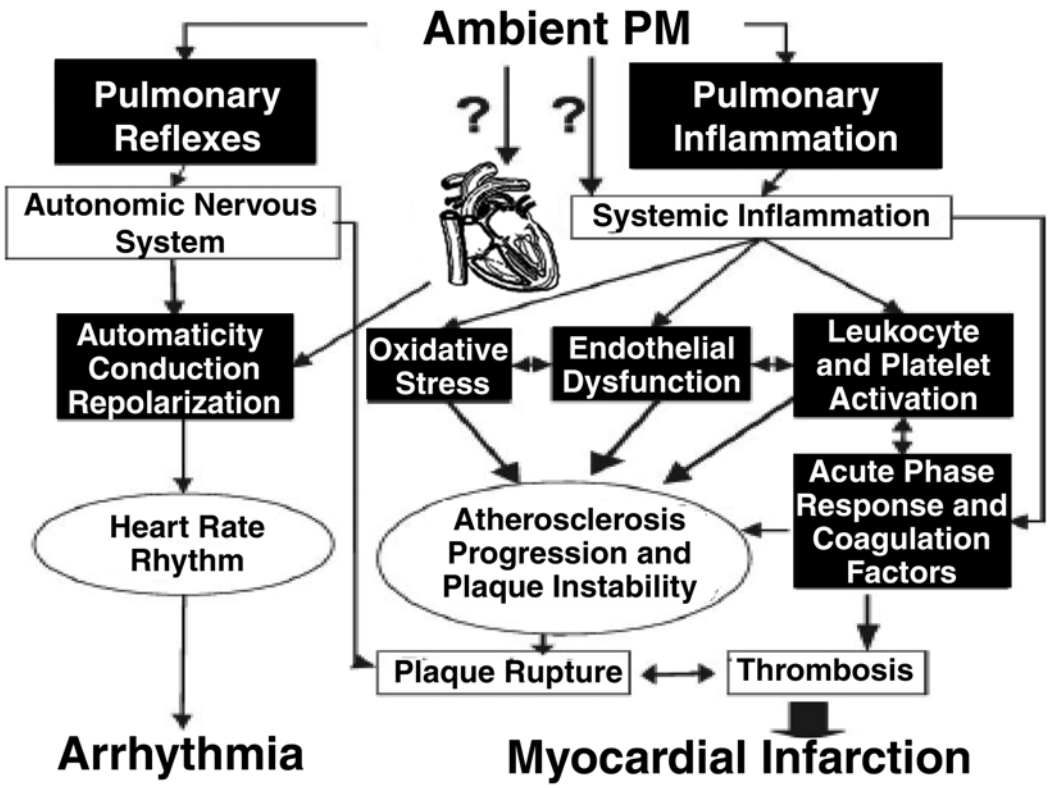

Figure 5.3. Hypothesized mechanistic pathways for cardiovascular effects of PM. (Reprinted from Brook et al. 2004, with permission of the American Heart Association, Inc.)

5.III.1 TRAFFIC MIXTURES

5.III.1.A Human Studies

There are no controlled human studies of the cardiovascular effects of exposures to the ambient pollutant mix that derives exclusively from traffic, because it is not possible, in the experimental setting, to separate traffic-related pollutants from those that derive from other sources. Recent studies examining the cardiovascular effects of diesel exhaust are considered below. There are also numerous human studies of specific components of traffic emissions, including PM, CO, and NO_2, but relatively few of these have focused on cardiovascular outcomes.

A few human studies have used a real-world exposure design in which subjects spend time in a polluted location, and the resulting effects are compared with equivalent activities in a location with relatively clean air. Rundell and colleagues (2007) described rather profound effects on vascular function in athletes exercising near a busy roadway (see Table 5.2, at the end of the chapter). Sixteen nonsmoking college athletes ran outdoors for 30 minutes, achieving 85% to 90% of maximum heart rate, on two occasions, each in a different setting: once on a soccer field adjacent to a major highway and once on campus in a low-traffic area. Exposure was assessed based on measurements of PM number taken at each location. Endothelial function was evaluated before and after each exercise period by measuring forearm flow-mediated dilatation (FMD) combined with forearm tissue oxygenation (measured by near-infrared [NIR] light absorption of oxygenated and deoxygenated hemoglobin and myoglobin). FMD measures the ability of a blood vessel (i.e., the brachial artery) to dilate in response to increased blood flow. FMD after exercise was almost completely impaired in the high-PM environment and did not change significantly in the low-PM environment. The NIR reoxygenation slope was similarly reduced after high-PM exposure.

This study supports a growing body of literature indicating that PM exposure impairs systemic vascular responsiveness. However, important weaknesses in the study design of Rundell and colleagues included the inability to blind the exposures, for either the subjects or the investigators, and obvious differences in the exposure environments other than their particle concentrations. For example, the two environments likely differed in noise level, running surface, and exposure to gaseous pollutants,

among other differences. Furthermore, complete impairment of FMD is beyond expectations and raises concerns about technical aspects of the study. Finally, the exposures included sources other than traffic that might have differed in the two locations.

Bräuner and colleagues (2008a) examined the effects of indoor particle exposure on the function of the peripheral vasculature in 21 nonsmoking elderly couples, using peripheral arterial tonometry. Particle air filters were placed in the subjects' homes. After 48 hours of breathing filtered air in their homes, peripheral arterial tone after arm ischemia (measured in the subject's finger) improved 8.1% compared with 48 hours of breathing their usual indoor air. In contrast, in another study conducted by Bräuner and colleagues (2008b), young healthy subjects exposed in a chamber to ambient air obtained near a busy street showed no change in vascular function compared with exposure to filtered air. The subjects were younger and the exposure was shorter (24 hours), compared with the study of filtered air in homes. The findings of these studies suggest that ongoing exposure to even modest concentrations of PM impairs systemic vascular function in the elderly and that short-term reductions in PM concentrations improve vascular function.

5.III.1.B Animal Studies

Very few animal-exposure studies have specifically involved traffic-related pollutant mixtures. One series of studies (Elder et al. 2004, 2007) used a model in which aged rats (21-month-old F-344) or aged, spontaneously hypertensive rats were exposed, in the bay of a truck traveling on a major highway, to the entire on-road atmosphere, to gases only, or to filtered air. In some cases, the filtered-air exposures were performed in a separate vehicle. Details of these studies are provided in Table 5.3, at the end of the chapter. Some of the rats were pretreated with a low dose of inhaled endotoxin or instilled with influenza virus to induce lung inflammation. The on-road exposures increased plasma fibrinogen, possibly reflecting a systemic acute-phase inflammatory response, and increased plasma concentrations of endothelin-2, a potent vasoconstrictor. Interactions between on-road particles and the priming agents were also found. In rats with implanted cardiac-monitoring devices, on-road exposures decreased the heart rate and altered heart-rate variability (HRV), and the effect lasted longer with endotoxin pretreatment. These results suggested that exposure to on-road particle mixtures has effects on systemic inflammation, vascular function, and autonomic control of the heart in compromised, aged rats. These are all mechanisms implicated in the cardiovascular effects of exposure to PM. However, it is also possible that noise, odor, or other stresses contributed to the effects, especially for the studies in which the clean-air exposures occurred in a different vehicle.

One proposed mechanism for the cardiovascular effects of UFP is translocation of particles from the lung to the heart by way of the blood, with direct toxic effects on the myocardium or coronary circulation. To test this hypothesis, hearts were obtained from mongrel dogs that had resided in two polluted areas of Mexico City, Mexico, and compared pathologically with hearts from dogs that had resided in less polluted areas of the country (Calderón-Garcidueñas et al. 2001). The hearts of the Mexico City dogs revealed a high prevalence of myocardial foci of inflammation, fat cells, apoptotic myocardial cells, degranulated mast cells, and capillary endothelial abnormalities compared with the hearts of the dogs from the less polluted areas. Cardiac abnormalities were associated with pulmonary epithelial and endothelial abnormalities in these animals. Weaknesses of this study included an apparent lack of blinding on the part of the pathologists and possible causes other than air pollution for the myocardial abnormalities, such as infectious diseases, nutritional status, or genetics. However, the data generally supported the hypothesis that chronic exposure to air pollution causes discrete cardiac abnormalities.

5.III.2 PARTICULATE MATTER: CONCENTRATED-AMBIENT-PARTICLE STUDIES

5.III.2.A Human Studies

Studies of human subjects inhaling CAPs (see Table 5.2, at the end of this chapter) have provided variable evidence for cardiovascular effects. Studies at the Gage Institute in Toronto, Canada (Brook et al. 2002), found that exposure to a mixture of CAPs (150 $\mu g/m^3$) and ozone (0.12 ppm) caused constriction of the brachial (forearm) artery 10 minutes after exposure, with no change in systolic or diastolic blood pressure measured at the same time. Analysis of the day-to-day variability in PM composition in relation to this effect suggested a role for both organic and EC (Urch et al. 2004). There was surprisingly no CAPs-related effect on FMD in the study, despite the observed vasoconstriction. The investigators subsequently reported an increase in diastolic blood pressure at the end of the 2-hour exposure to CAPs and ozone in the 20 original subjects, as well as in 3 additional subjects added from another study with the same exposure protocol (Urch et al. 2005).

Studies in other laboratories of exposures to CAPs, DE, and ultrafine carbon particles (summarized in Table 5.2) have not found effects on blood pressure, although transient

changes might have been missed if the measurements were not taken immediately after exposure. This is an important unresolved issue. If traffic-related pollutant exposure increases blood pressure even transiently, the resulting increase in myocardial oxygen demand could worsen ischemia in patients with critical coronary-artery disease.

A recent CAPs-exposure study in Edinburgh, Scotland (Mills et al. 2008), investigated 12 healthy subjects and 12 patients with stable coronary-artery disease, all males. Two-hour exposures to fine and ultrafine CAPs did not alter systemic vascular function, measured using forearm plethysmography, in response to brachial-artery infusion of vasoactive agents. Analysis using aerosol time-of-flight mass spectrometry revealed that the concentrated particles consisted of about 92% sodium chloride, or sea salt. The absence of vascular effects in this study might reflect the relative absence of combustion products in the concentrated aerosol, in contrast with the group's positive findings in response to DE exposure (Mills et al. 2005). However, the mean PM-mass exposure concentration was also lower than that of the previous DE exposures (190 $\mu g/m^3$ compared with 300 $\mu g/m^3$, respectively).

Several human CAPs-exposure studies have assessed effects on HRV. The healthy heartbeat is variable when analyzed in terms of either time or frequency domains. Reduced measures of HRV are associated with heart disease and are predictive of adverse cardiovascular events in patients with heart disease (Lombardi 2001). However, the significance of transient changes in HRV in response to pollutant exposure in terms of general health has not been established.

The effects of CAPs exposures on HRV have varied. Gong and colleagues (2003), for example, conducted a series of studies in Los Angeles, Calif., where traffic and road dust contribute substantially to ambient fine and coarse PM. In a study of 12 healthy subjects and 12 subjects with asthma who inhaled concentrated fine particles (~175 $\mu g/m^3$) and air for 2 hours with intermittent exercise, PM exposure was associated with reductions in the low-frequency/high-frequency power ratio, suggesting an increase in parasympathetic influence. In general, the changes were quite small and were not always consistent across the various measures of HRV. In another study (Gong et al. 2004a), 6 healthy elderly subjects and 13 patients with chronic obstructive pulmonary disease (COPD) inhaled air and fine CAPs (~200 $\mu g/m^3$) for 2 hours with intermittent exercise. In comparison with air, CAPs exposure increased the frequency of ectopic heartbeats in the healthy subjects but decreased ectopic beats in the subjects with COPD. HRV decreased in the healthy subjects but not in the subjects with COPD. Overall, the effects were modest, and the subjects with COPD appeared to be less susceptible than the healthy subjects. Gong and colleagues (2004b) also found that, in healthy volunteers and volunteers with asthma exposed to coarse CAPs for 2 hours with intermittent exercise, heart rate increased and HRV decreased, without effects on cardiac ectopy. The effects were generally greater in the healthy subjects than in the subjects with asthma. Finally, 17 healthy subjects and 14 subjects with asthma in another study by Gong and colleagues (2008) inhaled concentrated UFP for 2 hours with intermittent exercise. There were small, marginally significant reductions in low-frequency HRV, indicating reduced sympathetic influence. In this study, there were respiratory effects, with a 0.5% reduction in oxygen saturation and a 2% decrease in the forced expiratory volume in 1 second (FEV_1). There were no differences between the healthy subjects and the subjects with asthma.

A study in Chapel Hill, N.C. (Devlin et al. 2003), of healthy elderly subjects (60 to 80 years of age) inhaling concentrated ambient fine particles for 2 hours at rest, showed particle-associated reductions in the fraction of consecutive normal sinus electrocardiogram (ECG) intervals that differ by more than 50 milliseconds as well as reductions in high-frequency power, consistent with a reduction in parasympathetic influence on the heart. The investigators did not find changes in HRV with younger healthy subjects (18 to 40 years of age) who exercised intermittently during exposure.

Samet and colleagues (2007) published a summary of findings in healthy subjects exposed to concentrated coarse, fine, and ultrafine PM in Chapel Hill. These studies found reductions in HRV after exposure to coarse and ultrafine particles but not to fine particles.

Other findings from CAPs studies also lack consistency, possibly attributable in part to differing locations (and thus differing PM sources and CAPs characteristics) and subjects. In the study by Samet and colleagues (2007), fine and ultrafine, but not coarse, particles induced changes in measures of blood clotting, suggesting increased potential for blood coagulation. However, only a few selected measurements were statistically significant, and final publications of these studies were not yet available at the time of this writing. Inhalation of fine CAPs for 2 hours in healthy subjects increased plasma fibrinogen (Ghio et al. 2000a), but this did not occur in similar exposures of elderly subjects (Devlin et al. 2003). No effects of CAPs were found on blood or lung immune cells (Harder et al. 2001). In one of the studies by Gong and colleagues (2003), systolic blood pressure decreased in subjects with asthma and increased in healthy subjects upon exposure to CAPs compared with exposure to air. Plasma concentrations of intercellular adhesion molecule-1 (ICAM-1), a marker of systemic inflammation, increased 4 hours after CAPs exposure.

Taken together, the human CAPs studies showed variable findings, possibly attributable to the relatively small numbers of subjects, differences in subject selection criteria, varying pollutant mixes and concentrations, and varying experimental protocols. It is also possible that CAPs exposures are less toxic than exposures to ambient air when compared on a particle-mass basis, because gaseous pollutants are not concentrated. In spite of the variability in the findings, the CAPs studies generally provided support for existence of PM effects on vascular and cardiac function and suggested that these effects might differ according to particle size fraction and subject susceptibility.

5.III.2.B Animal and In Vitro Studies

Particle-concentrator technology has been used to expose both healthy and diseased animals. A number of studies using susceptible animal models have provided support for cardiac and vascular effects of both acute and chronic exposures. Exposures in healthy animals have generally shown minimal if any effects, even at relatively high exposure concentrations, and some studies with susceptible animals have also failed to show major effects. For example, Kooter and colleagues (2006) exposed spontaneously hypertensive rats in two settings, each controlled with a clean-air exposure: (1) fine CAPs at an urban background location and (2) combined ultrafine and fine CAPs in a traffic tunnel. Exposure concentrations ranged from 399 to 3,613 μg/m^3 for the fine CAPs and from 269 to 556 μg/m^3 for the combined ultrafine and fine CAPs. Exposures were 6 hr/day for 2 days; the animals were killed after 18 hours of recovery. Ammonium, nitrate, and sulfate ions accounted for 56 ± 16% of the total fine-CAPs mass concentrations but only 17 ± 6% of the mass concentrations of combined ultrafine and fine CAPs, emphasizing the difference between urban background exposures and high-density traffic exposures. Notably, neither the fine CAPs nor the combined ultrafine and fine CAPs induced significant systemic inflammatory effects, despite the fact that exposure concentrations were quite high. Plasma fibrinogen levels did not increase, contrasting with a previous study conducted by this laboratory (Cassee et al. 2005). However, markers of oxidative stress (heme oxygenase-1 and malondialdehyde) were affected by both types of CAPs exposure.

Examples of other CAPs studies using animal models that reported few cardiovascular or systemic effects are summarized in Table 5.3, at the end of the chapter (Gordon et al. 1998; Kodavanti et al. 2005).

Other CAPs-exposure studies, however, do provide evidence for cardiovascular effects of PM exposure. Wellenius and colleagues (2003) used a canine model of coronary-artery occlusion to assess PM effects on myocardial ischemia. Six-hour exposures of dogs to fine CAPs (median concentration 285.7 μg/m^3) enhanced ST elevation induced by coronary-artery occlusion in comparison with exposure to clean air. The degree of ischemia was not related to particle mass concentration but to the silicon content of the particles, suggesting crustal material might contribute to myocardial ischemia. In previous studies of dogs exposed to CAPs, lung lavage and blood analyses (Clarke et al. 2000) showed increases in circulating leukocytes were associated with the aluminum and silicon content of the particles but not with the particle mass. This again supported the possibility of a contribution by crustal materials to the systemic effects of exposure to CAPs. Crustal materials would be expected in wind-blown dust or road dust but not in tailpipe emissions.

Exposure to fine CAPs might increase oxidative stress to the heart as a whole, as measured by whole-organ chemiluminescence in rats (Gurgueira et al. 2002). This increase is prevented by pretreatment with atenolol (a β-adrenergic blocker) or glycopyrrolate (a cholinergic inhibitor) (Rhoden et al. 2005), indicating that the PM-associated increase in cardiac oxidative stress is mediated by the autonomic nervous system.

There is an emerging coherence among a variety of animal and in vitro studies suggesting that exposure to ambient PM alters systemic endothelial function, in part through endothelial mechanisms that depend on endogenous nitric oxide (NO). Several panel studies (see Chapter 4) and human clinical studies (see Table 5.2, at the end of the chapter) also provide support for the existence of acute vascular effects of PM. Endothelial dysfunction is considered to be a marker of early vascular events that lead to atherosclerosis. Vasoconstrictive responses after PM exposure might be related in part to the endothelins, potent mediators of vasoconstriction. Vincent and colleagues have shown in a series of studies in rats (Vincent et al. 2001; Thomson et al. 2004, 2005, 2006) that exposures to high concentrations of ozone and urban PM increase plasma levels of endothelin-1, with increases in both endothelin-1 mRNA (messenger RNA) and protein expression in the lung.

One of the circulating endogenous inhibitors of NO synthase is asymmetric dimethylarginine (ADMA). Dvonch and colleagues (2004) found that exposure to CAPs in Detroit, Mich., 8 hr/day for 3 days, increased plasma ADMA levels in rats. ADMA is produced through the activation of dimethylarginine dimethylaminohydrolase, which is regulated in part by oxidative stress. Thus one hypothesis for the vascular effects of PM exposure is that PM-induced oxidative stress increases levels of ADMA, which inhibits NO synthase, reducing NO production and allowing vasoconstrictors such as the endothelins to predominate (Rajagopalan et al. 2005).

Animal studies have also provided support for increased coagulation as a mechanism for the triggering of myocardial infarctions after exposure to PM. Nemmar and colleagues (2002), using a model of arterial injury and thrombosis in hamsters, demonstrated that UF and fine polystyrene particles enhanced thrombosis when instilled intratracheally and that this effect depended on particle size (Nemmar et al. 2003a). Similar effects were seen with instillation of DEP (Nemmar et al. 2003b). Silva and colleagues (2005) found similar effects of instilled polystyrene particles in rats, using an ear-vein model of vascular injury and thrombosis. In the diesel studies, vascular thrombotic effects were linked with a pulmonary inflammatory response that was generally more pronounced with particle instillation than with inhalation.

Karoly and colleagues (2007) exposed human pulmonary-artery endothelial cells to ultrafine CAPs for 4 hours and then measured changes in gene expression using microarrays. Ultrafine CAPs increased the expression of genes related to coagulation, including genes involved in tissue-factor expression. It remains unclear whether enhancement of thrombosis is in fact a mechanism contributing to the association between traffic-related pollutant exposure and myocardial infarction (Chapter 4). However, the findings described above are consistent with findings in human clinical exposures to DE, discussed in section 5.III.4.A.

Most toxicologic studies involve short-term exposures and acute effects, and studies of the cardiovascular effects of air pollution are no different. However, atherosclerotic vascular disease in humans takes years to develop. Experimental models testing the hypothesis that traffic emissions or other pollutants worsen atherosclerotic vascular disease require prolonged exposures in susceptible animal models; difficulty and cost limit this approach. Nevertheless, inhalation studies in genetically atherosclerosis-prone mice fed a high-fat diet showed that prolonged exposures to CAPs accelerated the development of atherosclerotic vascular disease (Sun et al. 2005) and had effects on heart rate (Hwang et al. 2005) and HRV (Chen and Hwang 2005). These studies provided validation of a previous model using Watanabe hyperlipidemic rabbits (Suwa et al. 2002). Instillation of PM_{10} collected in Ottawa, Canada, twice weekly for 4 weeks, resulted in more rapid progression of atherosclerotic plaques compared with instillation of saline.

CAPs exposure might also alter pulmonary vascular function. Rats exposed to fine CAPs for 5 hr/day for 3 days showed evidence of constriction of small pulmonary arteries (Batalha et al. 2002). In contrast, chronic (24-month) exposures of rats to high concentrations of DEP (2 mg/m^3) did not affect the weight of the heart, the thickness of the right or left ventricles, or the thickness of the pulmonary artery (Vallyathan et al. 1986), all of which are indicators that the animals did not develop pulmonary hypertension. Li and colleagues (2006b) found that incubation of human pulmonary-artery endothelial cells (HPAEC) with ambient air particles collected in St. Louis, Mo., increased cell production of H_2O_2 from mitochondria and from activation of nicotinamide adenosine dinucleotide phosphate (NADPH) oxidase. PM also caused contraction of rat pulmonary-artery rings in vitro, which was prevented with an inhibitor of the NADPH oxidase. As described below, human studies of exposure to EC UFP provided indirect evidence of transient effects on pulmonary vascular function (Pietropaoli et al. 2004a).

Taken together, these studies indicated that at least some types of ambient-PM exposure acutely altered pulmonary vascular function, possibly through a mechanism that involved oxidative stress. Whether chronic exposures contribute to the development of pulmonary vascular remodeling and pulmonary hypertension is unclear. The specific role of vascular effects of PM from traffic emissions, compared with PM from other sources, remains speculative.

5.III.3 PARTICULATE MATTER: LABORATORY-GENERATED ULTRAFINE PARTICULATE MATTER

A series of human studies has examined the cardiovascular effects of exposure to laboratory-generated EC UFP (see Table 5.2; Pietropaoli et al. 2004a,b; Frampton 2006b, 2007; Shah et al. 2008). Healthy subjects and subjects with asthma inhaled 10- or 25-μg/m^3 UFP for 2 hours with intermittent exercise. There were no respiratory effects or changes in heart rate, blood pressure, or oxygenation and no effects on blood levels of coagulation factors or inflammation markers (Pietropaoli et al. 2004a,b). Peripheral blood leukocyte expression of adhesion molecules decreased 3 to 4 hours after exposure compared with air exposure (Frampton et al. 2006b). The authors hypothesized that the exposure to UFP delayed transit of activated leukocytes through the pulmonary capillary bed, indicating a pulmonary vascular effect. Exposure to 50-μg/m^3 UFP for 2 hours decreased the diffusing capacity for CO in healthy subjects, providing further support for a pulmonary vascular effect of UFP exposure (Pietropaoli et al. 2004a). Inhalation of UFP also altered forearm reactive hyperemia, a measure of systemic vascular responsiveness, and reduced plasma nitrate concentrations, findings consistent with reduced endogenous NO availability and subtle systemic vascular effects of UFP exposure (Shah et al. 2008). There were no effects on heart rate or rhythm and only minor effects on HRV (Zareba et al. 2008).

In general, these findings supported the hypothesis that acute exposures to UFP alter pulmonary and systemic vascular function in humans, in the absence of significant pulmonary inflammation. Furthermore, organic chemicals and metals are not necessary components in eliciting these effects.

5.III.4 DIESEL EXHAUST

5.III.4.A Human Studies

A series of human DE-exposure studies have provided evidence for effects on systemic and possibly coronary vascular function and on blood coagulation. In a study from Sweden and the United Kingdom in healthy male subjects (Mills et al. 2005), 1-hour exposures to DE containing ~300 μg/m^3 PM impaired forearm dilatation (i.e., blood flow) responses to acetylcholine, bradykinin, and sodium nitroprusside 2 and 6 hours after exposure, indicating effects of DE on the regulation of systemic vascular-dilatation responses. Exposure to DE also impaired the increase in plasma tissue plasminogen activator induced by bradykinin, a response that favors coagulation. A separate study in a similar group of subjects (Törnqvist et al. 2007) found that these effects persisted 24 hours after exposure. The same group of investigators found that exposure of healthy subjects to DE containing ~350 μg/m^3 PM for 2 hours with intermittent exercise increased blood-thrombus formation and platelet activation 2 and 6 hours after exposure (Lucking et al. 2008). No effects on plasma concentrations of fibrinogen or other clotting factors were found in these studies. Finally, in patients with previous myocardial infarction, 2-hour exposures to ~300 μg/m^3 DEP increased cardiac ischemia during exercise (i.e., increased ST-segment depression) and impaired acute endothelial release of tissue plasminogen activator in plasma (Mills et al. 2007). In contrast to the previous study in healthy subjects (Mills et al. 2005), no effect was seen on the forearm dilatation response perhaps because these patients already had impaired vascular function.

A series of studies in Seattle, Wash., also addressed the cardiovascular effects of exposure to DE. Two-hour exposures of healthy subjects and subjects with metabolic syndrome to 100- or 200-μg/m^3 DE (Peretz et al. 2008b) induced constriction of the brachial artery and increased plasma levels of the potent vasoconstrictor endothelin-1 without effects on FMD. This finding of major-artery constriction is similar to that reported by Brooks and colleagues (2002) after exposure of subjects to a mixture of fine CAPs and ozone. In the Seattle study, analysis of changes in gene expression in peripheral blood mononuclear cells was performed in a subset of subjects exposed to 200-μg/m^3 DE, which elicited greater than 1.5-fold changes in 1290 out of 54,675 gene-probe sets (Peretz et al. 2007), consistent with systemic or vascular effects. There were few significant effects on heart rate or HRV (Peretz et al. 2008a) and no effects on plasma fibrinogen or markers of blood coagulation (Carlsten et al. 2007).

In all of the human DE-exposure studies, the DEP concentrations used were well above those encountered in typical ambient traffic-related exposures to DE, and neither the specific mechanisms nor the most active chemical components are known. However, the DE-exposure data convincingly demonstrated effects on systemic vascular endothelial function, a physiologic endpoint with relevance to both acute and long-term adverse cardiovascular effects. The finding of systemic vascular effects at both 2 and 24 hours after exposure (Törnqvist et al. 2007) fits with epidemiologic data indicating increased myocardial infarction associated with exposure to traffic (Peters et al. 2004; 2005) and exposure to $PM_{2.5}$ in the preceding hours (Peters et al. 2001). There is a need for additional studies at lower exposures at more relevant ambient concentrations.

5.III.4.B Animal Studies

A number of animal studies have provided support for the existence of both acute and chronic vascular effects of exposure to DE or its chemical components. Often these studies involved exposure methods (such as intravenous or peritoneal injection or intratracheal instillation) or high concentrations that have limited relevance to the inhalation of ambient traffic-related pollution. However, a few studies have supported cardiovascular effects at reasonably relevant concentration ranges. Spontaneously hypertensive rats exposed to DEP (at PM concentrations of 0, 30, 100, 300, or 1000 μg/m^3) 6 hr/day for 7 days had elevated heart rates throughout the exposure and significantly prolonged PQ intervals in the ECG, which might indicate risk of arrhythmia (Campen et al. 2003). More recently, this group of investigators (Campen et al. 2005) reported that gaseous (filtered) DE as well as whole DE (at PM concentrations of 500 or 3,600 μg/m^3) altered cardiac function in apolipoprotein-E-knockout mice (ApoE$^{-/-}$, a mouse strain used to study atherosclerotic vascular disease). The results showed dose-related effects of filtered and whole DE on T-wave depression on the ECG, suggestive of myocardial ischemia. However, the filtered DE did not induce airway inflammation, as was observed after exposure to the highest concentration of whole DE, suggesting different roles for the gaseous and particulate exhaust components. In another study, the incidence of ventricular arrhythmia was evaluated after 3 hours of exposure to DE (PM ~500 μg/m^3) in both healthy rats and rats with heart failure from a previous

myocardial infarction (Anselme et al. 2007). Cardiac ventricular arrhythmias increased after DE exposure in the rats with heart failure but not in the healthy rats.

These findings of cardiovascular effects in susceptible animal models support the findings in the human studies and suggest that exposure to DE, at concentrations considerably higher than ambient concentrations, exacerbate cardiac ischemia by way of effects on coronary artery function. The relative role of gaseous and particulate components remains unresolved.

5.III.4.C In Vitro Studies

A number of studies have provided evidence for direct effects of PM on cultured endothelial cells. One recent study (Gong et al. 2007) exposed human vascular endothelial cells to an organic extract of particles from DE and to an oxidized phospholipid implicated in the development of atherosclerosis. Gene-expression microarray profiles showed evidence for effects of DEP extracts on genes involved in vascular inflammation and atherosclerosis and provided evidence for interactive effects on gene expression between exposure to DEP extracts and to the oxidized phospholipid. Although these findings support the plausibility of endothelial injury by organic extracts of DEP, caution must be exercised in interpreting the findings because the relevance of the dosimetry is unclear, and findings in isolated cell cultures might differ from findings in vivo.

In another study (Yamawaki and Iwai 2006), incubation of cultured human umbilical-vein endothelial cells with carbon-black particles (laboratory-generated particles often used to reproduce the EC core of DEP) caused cytotoxicity, increased expression of monocyte chemotactic protein-1, and reduced expression of endothelial NO synthase. Bai and colleagues (2001) found that organic extracts of DEP caused cytotoxicity in HPAEC, which was partially prevented by inhibitors of ROS and NO synthase. This supports the involvement of ROS, including peroxynitrite, in injury of endothelial cells by PM. DEP has been shown to inhibit acetylcholine-induced relaxation of rat thoracic aorta in vitro (Ikeda et al. 1995), possibly by scavenging NO (Ikeda et al. 1998).

These in vitro studies of DEP generally supported the human clinical and animal studies of systemic vascular effects and have helped to elucidate possible active components and pathways. However, the specific mechanisms and active components of the vascular effects of DE remain unknown.

5.III.5 GASOLINE-ENGINE EXHAUST

Findings from animal and in vitro studies on the cardiovascular effects of exposure to exhaust from a gasoline-fueled engine vary. Lund and colleagues (2007) exposed groups of genetically susceptible mice to gasoline-engine exhaust at PM concentrations ranging from 0 to 60 $\mu g/m^3$, 6 hr/day, 7 days/wk, for 7 weeks. Aortic tissue from exposed mice showed a concentration-related increase in expression of mRNA for a number of proteins important in atherosclerosis, vascular function, and oxidative stress. Surprisingly, filtering the engine exhaust to remove particles did not change the effect, indicating that the gaseous components were responsible. There was no significant lung inflammation with these exposures, indicating that the vascular effects were not induced by lung inflammation. The findings indicated that the gaseous component of gasoline-engine exhaust enhanced pathways to atherosclerosis in this susceptible animal model.

On the other hand, extensive animal-exposure studies at the National Environmental Respiratory Center provided little evidence for cardiovascular effects of gasoline-engine exhaust (Reed et al. 2008). Rats (F344 and spontaneously hypertensive) were exposed to filtered air and various dilutions (undiluted, 1:10, 1:15, or 1:90) of gasoline-fueled-engine exhaust for one week to six months. In spontaneously hypertensive rats with implanted ECG monitoring, there was no change in heart rate or ECG after six months of exposure. There was a dose-related increase in blood hemoglobin in F344 rats, also seen in rats exposed to filtered exhaust, that was attributed to CO exposure.

Tzeng and colleagues (2003) demonstrated that organic extracts of particles collected from motorcycle exhaust enhanced the contraction of rat aorta induced by phenylephrine. This effect occurred in aortas with and without removal of the endothelium, indicating the effect was not dependent on the endothelium. The effect was inhibited by N-acetylcysteine, a scavenger of ROS. The study supported effects of PM from gasoline-engine exhaust, in contrast with Lund and colleagues (2007), who found that the gaseous component of gasoline exhaust alone reproduced their findings for the whole exhaust. Additional studies are needed to sort out the relative roles of PM and gases in the vascular effects of gasoline-engine emissions.

5.III.6 OTHER COMPONENTS

5.III.6.A Nitrogen Oxides

Some epidemiologic studies have found relationships between changes in ambient NO_2 concentrations and cardiovascular health, and in this context NO_2 has been considered

a marker for traffic-related pollution rather than the responsible agent. However, NO_x atmospheric chemistry includes NO, which serves as a key intercellular signaling molecule with immunoregulatory functions and potent vasodilator properties. Inhalation of NO gas causes pulmonary vasodilatation and is used therapeutically in patients with acute respiratory failure to lower pulmonary vascular pressures and improve the matching of ventilation and perfusion. It is possible that inhalation of NO_2 could influence airway or pulmonary vascular availability of NO, with consequences for the regulation of pulmonary or systemic vascular function. However, few studies have examined the cardiovascular effects of NO_2 exposure, and there is no convincing evidence that exposure to ambient concentrations of NO_2 alters cardiovascular function.

Folinsbee and colleagues (1978) found no significant effects of 2-hour exposures to 0.62-ppm NO_2 on cardiac output, using the CO_2-rebreathing technique, in healthy subjects. Drechsler-Parks (1995), using noninvasive impedance cardiography in eight healthy subjects, observed a relative reduction in cardiac output during exercise with exposure to 0.60-ppm NO_2 with 0.45-ppm ozone for 2 hours, compared with exposure to air. No effects of NO_2 or ozone alone were found. Frampton and colleagues (2002) found small reductions in hematocrit and hemoglobin in healthy subjects exposed to 0.6- and 1.5-ppm NO_2 for 3 hours. Reductions in hemoglobin could have indirect adverse cardiovascular effects in patients with cardiac disease by reducing the oxygen-carrying capacity of the blood.

These few studies suggest that NO_2 exposure at concentrations below 2.0 ppm, either alone or in combination with ozone, causes some systemic effects. They raise the question of whether ambient NO_2 contributes directly to the cardiovascular effects of traffic-related pollution rather than serving simply as a marker of traffic exposure. A combination of subtle NO_2-induced reductions in cardiac output, along with small reductions in blood hemoglobin, could further worsen myocardial oxygen delivery during critical ischemia in patients with coronary artery disease. However, these experimental observations require confirmation, and it remains unknown whether effects occur at outdoor ambient concentrations of NO_2, which are well below 1 ppm.

5.III.6.B Carbon Monoxide

CO emissions from motor vehicles increase ambient concentrations of CO, especially on and near highways. It is possible that CO exposure contributes to the observed association between exposure to traffic-related pollution and acute myocardial infarction (Peters et al. 2004). CO reduces oxygen delivery by binding avidly to hemoglobin, displacing oxygen. In healthy people, exposure to concentrations as low as 100 to 200 ppm for 2 to 3 hours can cause headache and lightheadedness. Much higher concentrations can impair consciousness and cause brain injury. The primary mechanism is reduced oxygen delivery with tissue hypoxemia, although CO also impairs cellular function. Concentrations of CO (~100 to ~250 ppm), sufficient to induce relatively low carboxyhemoglobin concentrations of 2% to 4%, have been shown to reduce the time to onset of ischemia in exercising men with coronary artery disease (Allred et al. 1989). These concentrations are well above typical ambient concentrations, even on roadways (see Chapter 3) and are above the current 1-hour U.S. EPA National Ambient Air Quality Standard for CO (35 ppm). It is less clear whether exposure to low concentrations of CO increases cardiac arrhythmias in the context of coronary artery disease. Wellenius and colleagues (2004), using a rat model of acute myocardial infarction, found that 1-hour exposures to 35 ppm CO actually reduced the frequency of ventricular premature beats, possibly by acting as a coronary vasodilator.

5.III.6.C Air Toxics

The Health Effects Institute recently published a comprehensive review of toxic air pollutants from mobile sources (HEI Air Toxics Review Panel 2007). Most toxicologic data on toxic air pollutants are derived from animal-exposure studies, and there has been little focus on cardiovascular endpoints. The most studied air toxic is benzene, an important component of gasoline. Animals exposed to benzene in high concentrations, many orders of magnitude above ambient concentrations, develop ventricular fibrillation. Workers exposed to benzene at concentrations as low as 0.82 mg/m^3 have shown reductions in bone-marrow production of blood cells, including red blood cells (Qu et al. 2002). Anemia reduces the oxygen-carrying capacity of the blood and could worsen cardiac ischemia in patients with severe coronary artery disease. However, there is no evidence that exposures to the concentrations of benzene observed in ambient air have cardiovascular effects. Epidemiologic data from workplace exposures in the asphalt industry suggest that long-term exposure to benzo[*a*]-pyrene increases the risk of death from coronary artery disease (Burstyn et al. 2005). However, there are no toxicologic data addressing this issue.

Traffic-related ambient PM contains polycyclic organic molecules and other air toxics, but the degree to which the air-toxics component is responsible for the cardiovascular effects of PM is unknown. Overall, there is little or no evidence supporting the cardiovascular toxicity of toxic air pollutants at concentrations relevant to ambient exposure.

5.III.7 SUMMARY

There remains a dearth of toxicologic studies examining the cardiovascular effects of traffic emissions specifically.

However, the recent toxicology literature provides suggestive evidence that exposure to pollutants that are components of traffic emissions, including ambient and laboratory-generated PM and exhaust from diesel and gasoline-fueled engines, alters cardiovascular function. Toxicologic studies provide plausible mechanisms and pathways for cardiovascular effects. There is evidence for acute effects on vascular homeostasis and suggestive evidence in animal models that repeated or chronic PM exposure enhances the development of atherosclerosis. However, there remains substantial inconsistency among the studies. More important, the specific PM components, cellular responses, and signaling pathways responsible for these effects have not been identified. Increasing evidence supports the involvement of oxidative stress, but whether the oxidants come from the pollutants themselves or from the inflammatory response they initiate is unknown. In addition, the cardiovascular effects investigated in toxicologic studies have generally been demonstrated at exposure concentrations substantially above, but often still relevant to, ambient concentrations. Therefore, whether traffic-related emissions other than PM have cardiovascular effects or contribute to the cardiovascular effects associated with PM exposure is unclear.

5.IV. STUDIES OF RESPIRATORY HEALTH EFFECTS

The epidemiologic data reviewed in Chapter 4 indicated that the respiratory health effects of traffic-pollution exposure include both allergic and non-allergic diseases. At present, there is a paucity of toxicologic studies focusing specifically on traffic-derived pollution and its effects on the respiratory tract. Because traffic-derived PM is a component of ambient PM in general, the much larger literature on the respiratory toxicology of PM is a model for future studies of traffic-specific toxicity. Similarly, DE is an important component of traffic-pollution exposure in many, but not all, settings. Moreover, the epidemiology and toxicology of DE exposures has been extensively studied and reviewed. Hence, key points from studies of PM and DE toxicology will be included in our survey of the available data on the toxicology of traffic pollutants.

5.IV.1 TRAFFIC MIXTURES

5.IV.1.A Human Studies

The epidemiologic data on the respiratory effects of traffic exposures were reviewed in Chapter 4. In contrast to these data, which are observational, the data in toxicologic studies are based on controlled, intentional exposures. Only a small number of such studies have been reported, but they offer important data on traffic-exposure effects. These studies are summarized in Table 5.2, at the end of the chapter.

Svartengren and colleagues (2000) sought to assess whether air pollution in traffic tunnels would promote asthmatic reactions in subjects with mild allergic asthma. Twenty volunteers with mild allergic asthma were exposed, inside a car, for 30 minutes in a Stockholm traffic tunnel. Control subjects were exposed to much lower pollution concentrations in a suburban area. Four hours after the exposure, the subjects inhaled a low dose of allergen. Although subjective symptoms during the tunnel exposure (which included NO_2 concentrations of ~300 μg/m^3) were not pronounced, the subjects exposed to the tunnel air had a significantly greater early reaction to the allergen, as well as lower lung function and more asthma symptoms during the late reaction phase, compared with the controls. These data suggested that exposure to air pollution in traffic tunnels might significantly enhance asthmatic reactions to subsequently inhaled allergens.

McCreanor and colleagues (2007) also studied the effects of short-term exposure to traffic-related pollution in persons with asthma. They evaluated 60 adults with either mild or moderate asthma in a randomized, crossover study during and after walking on a street in London (Oxford Street) with heavy traffic (primarily of diesel-fueled vehicles) and in a city park (Hyde Park). Concentrations of $PM_{2.5}$, UFP, EC, and NO_2 were elevated on the street relative to the park. Detailed physiologic and immunologic measurements showed that after walking on the heavy-traffic street the subjects experienced asymptomatic but consistent reductions in FEV_1 (up to 6.1%; see Figure 5.4) and

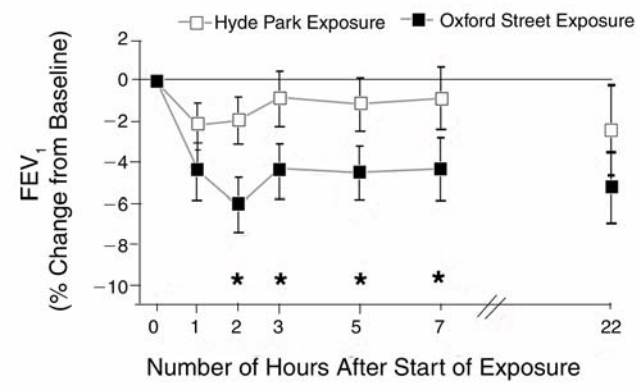

Figure 5.4. Change in FEV_1 in asthmatic subjects after walking on Oxford Street (DE pollution) and in Hyde Park (control). Asterisks denote $P < 0.05$ for the difference in values between Oxford Street and Hyde Park exposures. *I* bars represent 95% CI. (Reprinted from McCreanor et al. 2007, with permission of the Massachusetts Medical Society. All rights reserved.)

forced vital capacity (FVC) (up to 5.4%) that were statistically significantly larger than those after walking in the park. Subjects with moderate asthma showed greater effects than those with mild asthma. These changes were accompanied by increases in biomarkers of neutrophilic inflammation and airway acidification. The changes were associated most consistently with exposures to UFP, EC, and NO_2. The data provided a demonstration of the effects of exposure in an environment enriched with DE on respiratory function and also served as an example of how human exposure studies can be conducted in an ethical and productive manner.

A similar approach has recently provided a useful counterpoint. Normal, healthy volunteers exposed to air from a heavy-traffic street in Copenhagen showed no effects on tests of pulmonary function, lung permeability, or plasma markers of inflammation (Bräuner et al. 2008b, 2009). These results were consistent with epidemiologic findings that air-pollution effects are most prominent in susceptible populations. Another study of healthy subjects found a mild pulmonary-cellular response without evidence of acute injury (Larsson et al. 2007). Larsson and colleagues investigated whether exposure to air pollution in a traffic tunnel caused airway inflammation and blood coagulation in healthy volunteers. In bronchoalveolar lavage fluid, significantly higher numbers of cells (total cell number), lymphocytes, and alveolar macrophages were present after the traffic-tunnel exposure compared with control. Notably, no increase in neutrophils was observed.

These studies indicated that short-term exposures to traffic-related pollution have adverse respiratory effects in people with asthma.

5.IV.1.B Animal Studies

As with human exposure studies, only a few investigators have reported results for animal exposures to traffic-related air pollution. These include studies of susceptible (developing, aged, or hypertensive) or allergic rodents. These studies and the state of in vitro studies of traffic pollutants are reviewed in the next section of this chapter. The animal studies are summarized in Table 5.3, at the end of the chapter.

The on-road rat exposure studies reported by Elder and colleagues (2004) were summarized above, in Section 5.III.1.B. In addition to findings indicating effects of traffic-related aerosols on systemic inflammation, the combination of traffic-pollution exposure and prior lipopolysaccharide stimulation increased the expression of ICAM-1 on lung alveolar macrophages. However, there was no effect of aerosol exposure on inflammatory-cell recovery in bronchoalveolar lavage fluid, suggesting minimal enhancement of lung inflammation by traffic-pollutant exposure.

Fernvik and colleagues (2002) investigated the potential role of PM collected from tunnel air (referred to as traffic PM) or pure carbon-black particles in the initiation and persistence of experimental allergic inflammation. Mice were immunized with birch pollen alone or in combination with traffic PM, carbon, or alum adjuvants. Specific immunoglobulin E (IgE) titers, airway responsiveness, the number of recruited eosinophils, and levels of fibronectin and lactate dehydrogenase in bronchoalveolar lavage fluid were increased in the mice immunized and challenged with a mixture of birch pollen and traffic PM. This study suggested the potential of exposure to a combination of PM and allergens to enhance induction of allergic disease, a possibility consistent with data from a study using DEP (Riedl and Diaz-Sanchez 2005). In a separate parallel study, Fernvik and colleagues (2002) fractionated the traffic PM and identified two specific fractions — one rich in organic acids and one rich in highly polar compounds — that seemed to enhance the allergen-mediated response. Mice exposed to air from a heavy-traffic street in São Paulo, Brazil, showed significant alterations of lung structure and elastic properties, consistent with a potentially harmful effect of traffic-related pollution on lung growth (Mauad et al. 2008).

5.IV.1.C In Vitro Studies

The only study to evaluate in vitro effects of particles explicitly stated to have been collected from a heavy-traffic site was reported by Karlsson and colleagues (2006). They used particles collected from an urban street, as well as a panel of other particle types, to measure effects on pro-inflammatory cytokine release by a lung epithelial-cell line. Inflammatory effects were measured as induction of IL-6, IL-8, and TNF-α after exposure of human macrophages. The particles collected from an urban street were most potent in inducing inflammatory cytokines.

5.IV.2 PARTICULATE MATTER: CONCENTRATED AMBIENT PARTICLE STUDIES

5.IV.2.A Human Studies

Ghio and colleagues (2000a) found that 2-hour exposure of healthy volunteers to CAPS from Chapel Hill, N.C., (ranging from 23 to 311 $\mu g/m^3$) was associated with an influx of inflammatory cells (i.e., neutrophils) into the lower respiratory tract 18 hours after the end of exposure. No symptoms were reported by volunteers after the exposure. Similarly, there were no decrements in pulmonary function. The data indicated that ambient air particles are capable of inducing mild inflammation in the lower respiratory tract. A similar study in healthy and asthmatic subjects

exposed to CAPS from Downey, Calif., (Gong et al. 2003) found no effects on lung inflammation and function. These studies, as well as studies in nonrespiratory systems, are reviewed in Ghio and Huang (2004).

In a subsequent study, Gong and colleagues (2005) found small but statistically significant decrements in maximal mid-expiratory flow and arterial O_2 saturation (measured by pulse oximetry) associated with exposure to CAPs from a site on a highway close to other highways. The effects were greater in healthy subjects than in subjects with COPD. Other lung-function and cell endpoints showed no effects. Two additional studies are noteworthy for their finding of an absence of pulmonary effects. Healthy subjects and subjects with asthma were exposed to concentrated air from a Los Angeles suburb with heavy motor-vehicle traffic. After exposures to either concentrated UFP (Gong et al. 2008) or coarse particles (Gong et al. 2004b), no effects on spirometry, exhaled NO, or cell counts in induced sputum were noted.

Direct extrapolation to traffic-related effects remains problematic because the CAPs exposures included both traffic and non-traffic sources, and the relative contribution of the traffic components to the observed effects is unknown.

5.IV.2.B Animal Studies

There is an abundant literature analyzing respiratory effects of PM exposure in animal models. In general, these data reveal the ability of elevated PM concentrations both to cause acute inflammatory responses and to exacerbate allergic processes. These studies are well reviewed by Ghio and Huang (2004), and two of the them are presented below.

The study by Kooter and colleagues (2006) in spontaneously hypertensive rats was summarized in section 5.III.2.B. Exposures to relatively high concentrations of concentrated fine and ultrafine ambient PM failed to induce significant changes in cytotoxicity or inflammation in the lung. The study found only relatively minor pulmonary effects after exposure, possibly due to the brief duration of exposures (6 hours on 2 consecutive days).

Kleinman and colleagues (2005) studied the effect of traffic exposures in a murine model of asthma. A particle concentrator and mobile exposure facility were used to expose ovalbumin-sensitized BALB/c mice to clean air and CAPs and concentrated UFP from a roadway that was heavily affected by emissions from heavy-duty diesel-powered vehicles. Exposure to these traffic-related CAPs increased the biomarkers associated with airway allergies (IL-5, IgE, IgG1, and eosinophils). In addition, mice exposed to CAPs 50 m downwind of the roadway had, on average, greater allergic responses and showed greater indications of inflammation than did mice exposed to CAPs 150 m downwind. This study provided direct experimental support for the postulate that exposure to pollutants found near a heavily trafficked roadway can increase allergic airway responses.

5.IV.3 DIESEL EXHAUST

5.IV.3.A Human Studies

Controlled exposure of human subjects to DE allows analysis of a major component of traffic pollution found in many, but not all, settings. It must be noted that these studies used concentrations that were substantially higher than those typically encountered in real-world situations, a characteristic shared by inhalation toxicologic studies of DE in animal models, as reviewed by Mauderly and Garshick (2009; U.S. EPA 2002). DE-inhalation studies showed some evidence of inflammatory and airway effects in healthy subjects at elevated exposure concentrations (300 µg/m^3 or greater) (Rudell et al. 1999a; Salvi et al. 1999). These studies have demonstrated, for example, increases in inflammatory measures (i.e., a significant increase in neutrophils and in CD4+ and CD8+ lymphocytes) in bronchoalveolar lavage several hours after exposure (Rudell et al. 1994; 1996; 1999a,b). Both airway resistance and specific airway resistance increased significantly during exposures to DE, compared with exposures to filtered air (Rudell et al 1996). Studies using a lower exposure concentration (100 µg/m^3) also found inflammatory responses in healthy subjects (Stenfors et al. 2004). However, among subjects with mild asthma, DE at this concentration did not induce any significant change in airway neutrophils, eosinophils, or other inflammatory cells; cytokines; or mediators of inflammation (Stenfors et al. 2004). It is also noteworthy that ozone exposure magnified the neutrophilia in induced sputum that was produced by exposure to DE (Bosson et al. 2007).

Additional studies of healthy subjects have identified potential molecular mechanisms for the acute inflammatory response of the human airway to inhaled DE. The response was characterized by neutrophil, mast-cell, and lymphocyte infiltration into the bronchial mucosa with enhanced epithelial expression of IL-8, GRO-α, and IL-13 (Salvi et al. 2000; Holgate et al. 2003). Also, redox-sensitive transcription factors were activated as a consequence of DE exposure, consistent with the triggering of airway-inflammation oxidative stress (Pourazar et al. 2005). In archived biopsies from 15 healthy subjects exposed to DE (PM_{10} at ~300 µg/m^3) and air, immunohistochemical staining revealed that DE induced a significant increase in

the nuclear translocation of nuclear factor NF-κB (P = 0.02), AP-1 (P = 0.02), phosphorylated JNK (P = 0.04), and phosphorylated p38 (P = 0.01) as well as an increase in total (cytoplasmic plus nuclear) immunostaining of phosphorylated p38 (P = 0.03) (Pourazar et al. 2005). These observations are consistent with oxidative stress triggering the increased synthesis of proinflammatory cytokines. The potential of inhaled oxidants to enhance DE effects was supported by observations of increased inflammation in subjects exposed to both DE and ozone (0.2 ppm) (Bosson et al. 2007).

Controlled exposure to DE has been used to investigate the effects of short-term exposure in people with asthma by specifically addressing the effects on airway hyperresponsiveness, lung function, and airway inflammation. Nordenhall and colleagues (2001) studied 14 nonsmokers with stable atopic asthma on continuous treatment with inhaled corticosteroids. Exposure to DE was associated with a significant increase in the degree of hyperresponsiveness, compared with exposure to air, at 24 hours after exposure ($P < 0.001$). DE also induced a significant increase in airway resistance (P = 0.004) and in sputum levels of IL-6 (P = 0.048). The study indicated that short-term exposure to DE, at concentrations well above typical ambient concentrations, is associated with adverse effects in asthmatic airways even with inhaled-corticosteroid therapy. Curiously, in contrast with healthy controls, among subjects with mild asthma, DE at a relatively lower PM concentration (100 $\mu g/m^3$) did not induce any significant change in airway neutrophils, eosinophils, or other inflammatory cells; cytokines; or mediators of inflammation (Stenfors et al. 2004), although epithelial staining for the cytokine IL-10 increased after DE exposure in the group with asthma. The basis for these differences in healthy subjects compared with subjects with asthma is unclear.

In addition to exposure by inhalation, experimental instillation of DEP into the nasal cavity of healthy subjects or subjects with allergy has provided a powerful model for the effects of DEP on human allergy, as reviewed in Riedl and Diaz-Sanchez (2005). Effects in the nose were observed in all phases of the allergic response, from early to late, including increases in allergen-induced histamine release and symptoms, cellular inflammation, altered immune responses related to increased Th2 cell and the cytokines they produce (such as IL-4), and production of IgE. Diaz-Sanchez and colleagues (1999) hypothesized that DEP might also increase the rate of primary allergic sensitization and contribute to a higher prevalence of allergy related to traffic pollution. These changes were accompanied by depletion of Th1 cells (and a consequent decrease in the cytokines they produce, such as interferon γ) in nasal lavage (Diaz Sanchez et al. 1997). These findings have been replicated in a recent study by Gilliland and colleagues (2004) in which 19 allergic subjects were exposed to the same dose of DEP plus allergen intranasally (0.3 mg) as in the earlier study by Diaz-Sanchez and colleagues. The results showed that DEP increased the allergic response by increasing ragweed-specific IgE, IL-4, and histamine and by decreasing interferon γ in nasal lavage. The authors reported that subjects with certain variant genotypes were more susceptible to DEP. The data from these studies suggested that DEP might exacerbate allergic responses. However, nasal administration of DEP represents an artificially high bolus dose compared with realistic aerosol exposures.

5.IV.3.B Animal Studies

A number of studies have investigated the effects of repeated exposure to DE on the respiratory system in animals (primarily rodents) (for a review see U.S. EPA 2002; Hesterberg et al. 2009). The changes that have been reported include increases in inflammatory cells (such as neutrophils) and inflammatory mediators and decreases in lung biochemical defenses (such as glutathione). These effects were accompanied by gradual changes in lung structure, including fibrotic or emphysematous lesions. Impairment in pulmonary function has also been reported after chronic exposures. These effects have been observed only after exposure to concentrations of DE that are orders of magnitude higher than ambient concentrations; the findings therefore have questionable relevance to human ambient exposures.

There is an abundant literature analyzing respiratory effects of DE in animal models. In general, these data show that exposures to DE or DEP cause acute inflammatory responses and exacerbate allergic processes. These studies are well reviewed by Gilmour and colleagues (2006).

5.IV.4 OTHER COMPONENTS

5.IV.4.A Nitrogen Dioxide

NO_2 is an important component of air pollution generated by combustion sources, including motor vehicles. The potential for human health effects has been extensively studied, including substantial and detailed analyses using controlled human exposures. Excellent reviews of NO_2 toxicity are available (Greim 2005; California EPA 2007; U.S. EPA 2008). Short-term exposures to NO_2 concentrations greater than ambient concentrations caused little or no physiologic effects in healthy human volunteers. In contrast, similar studies have found some evidence of enhanced

late-phase responses to allergens in subjects with asthma (Strand et al. 1997). NO_2 also diminished lung macrophage-defense function against viral infections (Frampton et al. 1989). These data suggest that NO_2 as part of traffic exposures could have toxic effects in certain susceptible populations, but this possibility needs to be explored through more direct experimentation before any conclusions can be reached.

5.IV.4.B Air Toxics

Combustion emissions also include numerous complex volatile organic compounds (VOCs). As with NO_2, the potential for VOCs to contribute to traffic-related health effects is suggested by the toxicity of certain components (such as the PAHs studied in DE). However, experimental toxicologic studies of traffic-related VOCs, either alone or in combination with other components, have not been performed. Barriers to progress include incomplete characterization of the composition and concentration of traffic-related VOCs as well as technologies for their generation for use in controlled-exposure studies. Certain components of air toxics (such as benzene and formaldehyde) have known carcinogenic potential, as detailed below and in the recent comprehensive review of mobile-source air toxics (HEI Air Toxics Review Panel 2007).

5.IV.5 SUMMARY

The small number of studies that directly investigate the effects of intentional exposure to real-world traffic-related pollution show decrements in lung function and enhanced response to allergens in subjects with asthma. Exposure to components of traffic pollution resulted in mild acute inflammatory responses in healthy individuals and enhanced allergic responses in asthmatic allergic individuals and animal models. The paucity of direct studies of traffic particles or components does not yet allow identification of specific components or pathogenic pathways for exposure effects. Data from studies of PM or DE are instructive and provide strong clues to traffic-pollution toxicity because many of the same mechanisms likely apply to traffic-related effects (e.g., oxidative stress, synergy with other inhaled oxidants, and pre-existing lung disease). However, PM and DE are not perfect surrogates for traffic-pollutant mixtures. Hence, future research should be guided by the rich literature developed in studies of PM and DE, but it should include more direct analysis of actual traffic-mixture exposures in vivo and in vitro.

5.V. STUDIES OF CANCERS AND MUTAGENICITY

Mechanisms by which exposure to traffic-related air pollution might be associated with an increased risk of cancer involve damage to DNA (such as the formation of bulky DNA adducts, base oxidations and deletions, and chromosomal aberrations), which in turn might lead to a broad spectrum of mutations. Among DNA base oxidations (a consequence of oxidative stress), 8-oxo-7,8-dihydro-2′-deoxyguanosine (8-oxo-dG; also reported as 8-hydroxy-2′-deoxyguanosine, or 8-OHdG) is probably the most studied product owing to its relative ease of measurement and premutagenic potential (Kasai 1997). Indeed, the accumulation of 8-oxo-dG is considered an important factor in enhancing the mutation rate leading to lung cancer. Oxidative DNA-base damage (with 8-oxo-dG generation) and strand breaks after exposure to DE and DEP have been widely reported in cell-free systems (Nagashima et al. 1995; Iwai et al. 2000; Greenwell et al. 2002; Pan et al. 2004), cell cultures (Don Porto Carero et al. 2001; Prahalad et al. 2001; Dybdahl et al. 2004; Karlsson et al. 2005), and in animals (Nagashima et al. 1995; Tokiwa et al. 1999; Iwai et al. 2000; Moller et al. 2003; Risom et al. 2003; Dybdahl et al. 2004; Saber et al. 2005). Although an association between 8-oxo-dG in DNA levels and tumor development has been demonstrated in DEP-treated mice (Ichinose et al. 1997) and rats (Iwai et al. 2000), a definitive contribution of oxidative damage to DNA (and other cellular components, such as proteins and lipids) to a risk of cancer has not yet been established. Figure 5.5 illustrates possible mechanisms by which air-pollution particles could lead to cancer via oxidative stress and DNA damage.

The toxicologic research summarized in this section includes in vitro mutagenicity studies after exposure to a traffic mix, diesel or biodiesel, and organic components as well as animal tumorigenicity studies after exposures to exhaust from diesel and gasoline-fueled engines.

5.V.1 TRAFFIC MIXTURES

The relationship between traffic intensity or density and mutagenicity has been investigated in a limited number of in vitro studies (Bronzetti et al. 1997; Ducatti and Vargas 2003; Vargas 2003; de Kok et al. 2005). While Ducatti and Vargas (2003) demonstrated a positive effect of motor-vehicle density on the mutagenicity of PM, Bronzetti and colleagues (1997) observed higher mutagenicity of total suspended particulates from an area of high traffic intensity compared with that of total suspended particulates from an area of low traffic intensity. A positive relationship has also been reported between mutagenicity and PAH concentration as well as nitro-PAH concentration (Vargas 2003). In

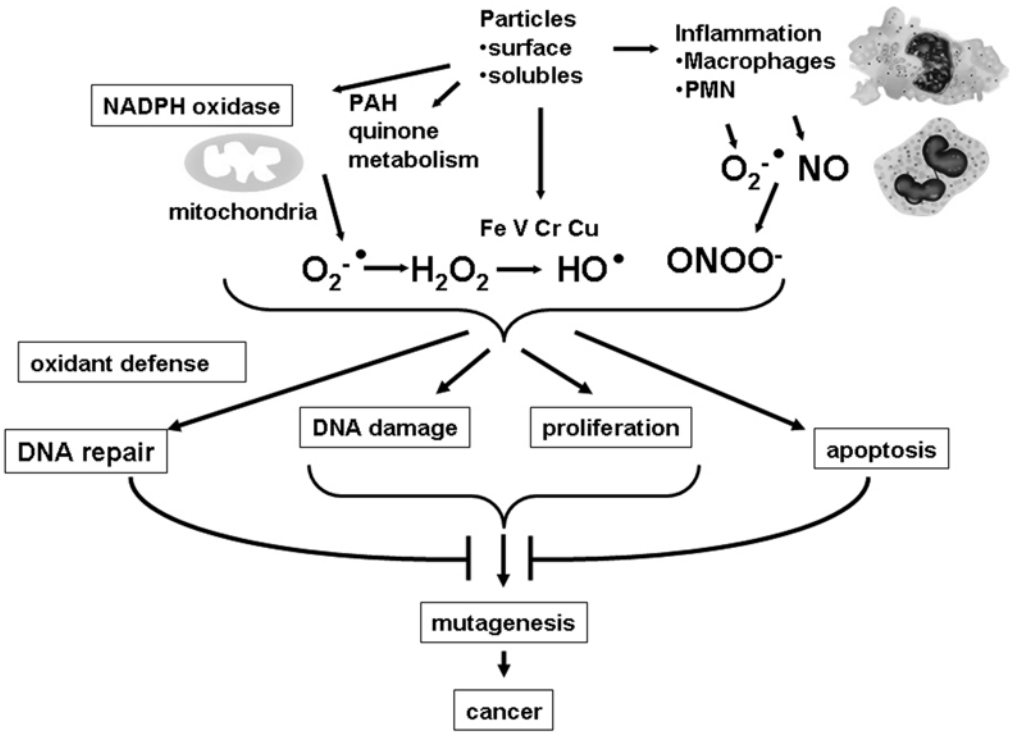

Figure 5.5. Possible mechanisms for induction of oxidative stress and DNA damage by air pollution particles and their roles in carcinogenesis. (Reprinted from Risom et al. 2005, with permission of Elsevier.)

addition, the analysis of specific traffic-related VOCs in PM confirmed the positive association of these compounds with traffic intensity. In contrast, others have failed to find a clear correlation between traffic intensity and mutagenicity per microgram of PM (de Kok et al. 2005. A recent study in human volunteers exposed in a chamber to UFP sampled near a busy road or filtered air for 24 hours found increased levels of DNA-strand breaks in peripheral mononuclear blood cells after exposure to UFP (Bräuner et al. 2007).

5.V.2 DIESEL EXHAUST

5.V.2.A Animal Studies

A long series of animal inhalation studies have reported that DE, at sufficiently high concentrations, is a pulmonary carcinogen in rats chronically exposed by inhalation, as demonstrated by a dose-related increase in lung tumors (Iwai et al. 1986, 1997, 2000; Mauderly et al. 1987, 1994; Heinrich et al. 1995, 1986; Nikula et al. 1995). Hesterberg and colleagues (2006) have recently reviewed the work in this field. However, these laboratory studies must be interpreted with caution with respect to predicting the carcinogenic potential of DE in humans. Of species chronically exposed to DE by inhalation (rats, hamsters, mice, monkeys, and cats), only rats consistently developed lung tumors, and only after exposure to high concentrations of DE (> 2.0 mg/m^3 DEP). Although no increased incidence of lung tumors was observed in hamsters exposed to DE at very high concentrations (Brightwell et al. 1989; Heinrich et al. 1995), both positive and negative responses in mice to equivalent concentrations have been reported (Heinrich et al. 1986, 1995). As such, a consensus exists that the tumorigenic effects of high-dose DE observed in the rat studies were primarily caused by a species-specific impairment of lung clearance and particle accumulation, known as "lung overload," that is not generally applicable to exposure to the low concentrations that humans are exposed to (Heinrich et al. 1986; Stöber 1986; Mauderly et al. 1996; International Life Sciences Institute [ILSI] 2000). The mechanism by which lung overload induces cancer is believed to involve a progressive series of cellular responses (i.e., inflammation, alveolar epithelial proliferation, and fibrosis) rather than the typical mechanisms that involve DNA damage and mutation (McClellan 1996). This was supported by a recent chronic-inhalation study in rats in which lung tumors were observed after exposures to DE, without formation of DNA adducts (Stinn et al. 2005). Furthermore, a meta-analysis of the data at a lower exposure

concentration (0.2 to 0.6 mg/m^3) in rats did not support a risk of lung cancer for DE exposure in non-overload conditions (Valberg and Crouch 1999). In reviewing the literature on bioassay data for DE in rodents, Nikula (2000) has reported that filtering out the particles to leave only the gases abolished the carcinogenicity of DE, indicating a role for the particles.

It appears from these studies that only very high concentrations of DE, sufficient to induce lung-clearance overload, were carcinogenic. These findings are of questionable relevance to ambient exposure concentrations.

5.V.2.B In Vitro Studies

Evidence exists that in vitro exposure of cells to DEP causes DNA and chromosomal damage, including bulky DNA adducts, oxidized bases, deletions, and chromosomal aberrations, which might lead to a broad spectrum of mutations (Tsurudome et al. 1999; DeMarini et al. 2004; Muller et al. 2004). For example, DEP and their extracts are highly mutagenic (in a dose-dependent manner) to strains TA98 and TA100 in the Ames test (DeMarini et al. 2004); more recently, the dose-dependent mutagenicity (but minimal cytotoxicity) of DEP in mammalian cells, namely, the human–hamster hybrid (A_L), has been documented (Bao et al. 2007).

Information about the mutagenic potential of biodiesel emissions is limited and requires further investigation before any firm conclusions can be drawn. Using in vitro bacterial assays, Mauderly (1997) attributed most of the mutagenic activity in biodiesel exhaust to a minority of the solvent-extractable organic fraction mass, particularly PAHs. In another study, the mutagenicity of the soluble organic fraction of biodiesel was investigated using rat hepatocytes in addition to the traditional Ames test (Eckl et al. 1997). In the Ames test, higher mutagenic potential was observed in DE than in the rapeseed-oil methylester biodiesel fuel; however, the results were less dramatic in the rat hepatocyte model, a difference attributed by the author to the differences in metabolic capacities between the models. Compared with conventional diesel fuel, in a study by Bünger and colleagues (2000; 2006), DEP from two biodiesel fuels (rapeseed-oil methylesters and soybean-oil methylesters) and a fossil diesel with low sulfur content were found to be significantly less mutagenic (using the *Salmonella typhimurium*–mammalian-microsome assay with strains TA98 and TA100). In particular, the increased mutagenicity of DEP was associated with high sulfur content and high engine speeds and loads. The researchers went on to investigate the effects of an oxidation catalytic converter on the mutagenic effects of the fuels (Bünger et al. 2006). Interestingly, a consistent but not significant increase in direct mutagenicity was observed for conventional diesel fuel and the low-sulfur diesel fuel at two of the load modes tested when emissions were treated with the oxidation catalytic converter. In interpreting these results, the authors hypothesized that the catalytic converter increased the formation of mutagens under certain conditions by the reaction of NO_x with PAHs, resulting in the formation of nitrated-PAHs (Bünger et al. 2006).

The applicability of in vitro mutagenicity studies to human risk assessment has, however, been questioned on a number of counts. The extracts reported to exhibit mutagenicity can be obtained from DEP only by using strong organic solvents, agitation, and heat. In contrast, biologic fluids in vivo are far less efficient at extracting potentially mutagenic organic compounds (Brooks et al. 1984). In addition, not only are mutagenic chemicals tightly adhered to diesel PM and not likely to be bioactive in vivo (Borm et al. 2005), but biologic fluids (such as serum and surfactants) might even mitigate the activity of extracted compounds such as PAHs (McClellan et al. 1982). Although some evidence does exist that DEP coated with surfactant might have mutagenic activity, the interpretation of these results is unclear (Wallace et al. 1987; Keane et al. 1991).

5.V.3 GASOLINE-ENGINE EXHAUST

Unlike DE, which is among the most studied anthropogenic emissions, there are very few carcinogenicity studies of exhaust from gasoline-fueled engines even though the early studies of Kotin and colleagues (1954) found that extracts from emissions samples of both diesel and gasoline-fueled engines caused tumors in a mouse-skin-painting assay. The appearance of tumors has also been studied in male rats exposed for 2 years to emissions (23 ppm NO_x, 0.92 ppm NO_2, 0.3% CO_2, 2.0 ppm aldehydes, and 50 ppm CO) from a 33-hp engine from a typical French car burning premium gasoline at 2000 to 2500 rpm (Stupfel et al. 1973). Although the incidence of tumors was increased by exposure (29% compared with 11% for controls), the distributions were similar in the exposed and control groups, and no tumors were found in the lungs.

5.V.4 OTHER COMPONENTS

5.V.4.A Organic Compounds

Benzene and formaldehyde, together with other volatile organic molecules such as acetaldehyde and 1,3-butadiene, are all (1) considered to be carcinogenic in some animals and (2) classified by the International Agency for Research on Cancer as carcinogenic for humans, albeit with varying

degrees of certainty (Krzyzanowski et al. 2005; Huff 2007). As a consequence, an enormous amount of toxicology literature exists on the carcinogenicity of these compounds. Organic-carbon compounds, extracted and concentrated from diesel and gasoline PM, can induce gene mutations in *Salmonella* bacteria and in mammalian cells (Liu et al. 2005). Some interesting observations include the requirement of aliphatic and aromatic fractions of diesel fuel to undergo a reaction with NO_2 before mutagenic activity is demonstrated (Henderson et al. 1981) and the much higher toxicity of semivolatile organic compounds from gasoline-fueled engine exhaust compared with diesel exhaust (Liu et al. 2005). Nitrated PAHs and benzo[*a*]pyrene form DNA adducts in human lymphocytes (Gallagher et al. 1993), and benz[*l*]aceanthrylene, benz[*j*]aceanthrylene, and benzo[*a*]pyrene have been reported to produce DNA adducts in rat and rabbit primary lung cells, Clara cells, type-2 cells, and macrophages (Holme et al. 1993; Johnsen et al. 1997). When one extrapolates ambient concentrations of volatile organic molecules to concentrations required to induce cancer, however, risk is believed to be low (Krzyzanowski et al. 2005). A recent review on the carcinogenic potential of benzene, for example, concluded that "the toxicologic and epidemiologic literature on chronic exposure to unleaded gasoline indicates that the benzene exposures required to induce a measurable carcinogenic response are substantially greater than exposures likely to be encountered from exposure to gasoline at contaminated properties" (Jamall and Willhite 2008).

5.V.5 SUMMARY

Research examining the effects of traffic-related pollutants on mutagenicity and cancer is an extensive and complicated area. The in vitro studies into the relationship between traffic intensity and mutagenicity have generated a mix of positive and negative results. Although studies in cells demonstrating the capacity of DEP to induce DNA-strand breaks, base oxidation, and mutagenicity provide a possible mechanism for the induction of carcinogenicity by traffic-related pollution, the applicability of in vitro mutagenicity studies to human risk assessment has been questioned. Animal studies have demonstrated the ability of high concentrations of exhaust components from both diesel and gasoline-fueled engines to cause cancer in animals. However, caution must be exercised in extrapolating these data to ambient concentrations and the risks to humans. Finally, as with all health effects, continued research is needed to assess the risk of mutagenesis and carcinogenesis of exhaust from new-technology diesel engines and biodiesel fuels.

5.VI. STUDIES OF REPRODUCTIVE HEALTH

The toxicologic outcomes reviewed in this section include effects on reproductive endocrine function; sperm production, motility, and viability; fertility; and birth outcomes. Selected occupational-exposure studies are included.

5.VI.1 TRAFFIC MIXTURES

5.VI.1.A Human Studies

Investigations into the semen quality of men occupationally exposed to traffic have included small numbers of subjects, and therefore, the results should be interpreted with caution. De Rosa and colleagues (2003) compared several measures of male fertility in 85 men employed at highway toll booths with 85 age-matched controls living in the same area. Sperm count and serum concentrations of follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone were normal in both groups, although sperm total motility, forward progression, functional-test performance, and kinetics were significantly lower in the tollgate workers. In a subset of the workers with below-normal sperm motility, this measure was inversely correlated with both blood methemoglobin and lead, indicating a role for NO_2 and lead in contributing to lower semen quality. Other occupational hazards associated with working at toll booths that might contribute to altered sperm characteristics include being seated in cramped positions for prolonged periods and placing the contents of the scrotum in a tight position, which can increase scrotal temperatures (Mayo Clinic 2007). Another study examined lead exposure ($N = 43$) and semen quality ($N = 18$) among traffic policemen in Arequipa, Peru, where leaded gasoline was in use (Eibensteiner et al. 2005). Although higher blood levels of lead (> 40 µg/dL) were associated with declines in some semen parameters (sperm morphology, concentration, and total number), a significant correlation was found only with sperm motility and viability.

5.VI.2 DIESEL EXHAUST

5.VI.2.A Animal Studies

Watanabe and Oonuki (1999) exposed rats from birth to 3 months of age to whole DE (containing 5.63 mg/m^3 PM, 4.1 ppm NO_2, and 8.10 ppm NO) and also to filtered DE (i.e., without PM). In both groups, serum testosterone and estradiol were significantly higher and FSH was significantly suppressed; significant declines in LH, however,

were evident only in the group exposed to the whole DE. Although testis weight did not differ significantly between the groups, sperm production and the activity of testicular hyaluronidase were significantly reduced in both. In interpreting these results, the authors suggested that, in rats, DE stimulates hormone secretion by way of the adrenal cortex, depresses gonadotropin-releasing hormone, and inhibits spermatogenesis. Furthermore, because these effects were not inhibited by filtration, the gaseous phase of the exhaust appears to be more responsible than PM for disrupting the endocrine system. In a study in which 13-month-old male rats were exposed to lower concentrations of DE (0.3, 1.0, or 3.0 mg/m^3 PM for 8 months), no changes in sperm counts were reported, but the authors did observe effects on the accessory glands (i.e., the prostate, coagulating thymus, and adrenal) as well as increased serum LH and testosterone at 0.3 and 1.0 mg/m^3 DEP and an increase in testicular testosterone at 3.0 mg/m^3 DEP (Tsukue et al. 2001). Exposure of mice to DEP (containing 0.3 to 3.0 mg particles/m^3) led to ultrastructural changes and reduced LH-receptor mRNA expression in Leydig cells in addition to a dose-dependent decrease in daily sperm production per gram of testis (Yoshida et al. 1999). Mori and colleagues (2007) identified several genes that were differentially expressed in the testis of mice after a subcutaneous injection of DEP. Furthermore, some of these genes seemed to be associated with spermatogenesis, suggesting that constituents of DEP, either directly or indirectly, affect gene expression in testis.

The effect of in utero exposure to DE on the male reproductive system has also been investigated. Mature rats exposed to either total DE (1.71 mg/m^3 PM and 0.80 ppm NO_2 or 0.17 mg/m^3 PM and 0.10 ppm NO_2) or filtered DE (0.80 or 0.10 ppm NO_2) during fetal development (from gestational day 7 to delivery) exhibited decreased daily sperm production because of an insufficient number of Sertoli cells, suggesting again that the gaseous phase was at least partly responsible (Watanabe 2005). In male mice whose pregnant mothers had inhaled DEP at soot concentrations of 0.3, 1.0, or 3.0 mg/m^3 for 2 to 16 days postcoitum, endocrine disruption after birth, accelerated male puberty (Yoshida et al. 2006), and detrimental effects on spermatogenesis (Ono et al. 2007) have been reported.

Studies focusing more generally on pregnancy outcomes have, using high concentrations of DE or filtered DE, reported delayed and disturbed differentiation of the testis, ovary, and thymus in the offspring of rats exposed to total DE (5.63 mg/m^3 PM, 4.10 ppm NO_2, and 8.10 ppm NO) or filtered DE (i.e., without PM) from day 7 to day 20 of pregnancy (Watanabe and Kurita 2001). In the same study, maternal testosterone and progesterone levels, which increased because of pregnancy whether or not the rats were exposed to DE, were significantly higher and lower, respectively, in rats exposed to the whole DE and filtered DE. A study in mice has reported that DE exposure (0.3, 1.0, or 3.0 mg/m^3 DEP) at 14 days postcoitum affected fetal absorption and congestion in histologic sections of placentas by modifying the expression of immune- and endocrine-related genes during gestation (Fujimoto et al. 2005). Female mice have also been exposed to DEP (0.1, 1.0, or 3.0 mg/m^3) and then either examined by necropsy or mated with unexposed males (Tsukue et al. 2002). Estrous females had significantly lower uterine weights. In the mated females, 0.3, 1.0, and 3.0 mg/m^3 DEP led to abnormal deliveries in 9.1%, 10.0%, or 25.0% of the pregnancies, respectively. Body weights of the offspring were significantly lower at 6 and 8 weeks, and sexual maturation was delayed.

5.VI.2.B In Vitro Studies

In vitro work on the reproductive health effects of traffic-related pollution is limited. A study using human spermatozoa exposed to DEP extracts reported interference with sperm motility in a dose–response fashion (Fredricsson et al. 1993).

5.VI.3 GASOLINE-ENGINE EXHAUST

5.VI.3.A Animal Studies

The reproductive-health hazards of emissions from gasoline-fueled engines have undergone little research compared with those of diesel engines. A study on the effects of gasoline-fueled-engine emissions (irradiated to simulate solar irradiation) on reproduction in LAF1-strain mice found that exposure, prior to mating, of the males but not the females was associated with reduced fertility. The cause of the effect was not determined (Lewis et al. 1967). More recently, the effects on the sexual activity of rats of three types of automotive exhaust gases (i.e., from engines of the same power running on leaded gasoline, unleaded gasoline, and diesel fuel) were studied (el Feki et al. 2000). Emissions from the leaded gasoline had no effect on female rats but caused atrophy of the testicle, seminal vesicle, and epididymis in male rats in addition to pathologic changes in spermatogenesis and a decrease in serum testosterone.

5.VI.4 OTHER COMPONENTS

5.VI.4.A 1-Nitropyrene, 3-Methyl-4-nitrophenol, and 4-Nitro-3-phenylphenol

Investigators have also evaluated the effects of the components of total traffic mix on the male reproductive

system. For example, 1-Nitropyrene, a by-product of combustion and the predominant nitrated PAH emitted in diesel-engine exhaust, has also been tested in rodents. After exposure of the rodents to 0.5 to 50 mg/m^3 1-nitropyrene aerosol, no treatment-related effects on sperm motility or vaginal cytology were noted. Testicular atrophy was observed in all male rats (control and test groups) but was considered a secondary effect resulting from daily confinement in the exposure tubes (Chan 1996). Another component of DE, 3-methyl-4-nitrophenol (at 78, 103, or 135 mg/kg administered by intramuscular injection), has been reported to cause testicular atrophy associated with reduced sperm formation, plasma LH, and testosterone in adult male Japanese quail (Li et al. 2006a). Lowered plasma LH was detected as early as one hour after in vivo exposure, along with a significant reduction in testosterone secretion, in a time- and dose-dependent manner, from exposed cultured interstitial cells containing Leydig cells, indicating that 3-methyl-4-nitrophenol induces reproductive toxicity at both the central and testicular levels.

The estrogenic activity of 3-methyl-4-nitrophenol and 4-nitro-3-phenylphenol have been demonstrated in ovariectomized female rats, which when injected subcutaneously with 3-methyl-4-nitrophenol (100 mg/kg) and 4-nitro-3-phenylphenol (0.1 and 1.0 mg/kg) for 2 days showed significant increases in uterine weight (Furuta et al. 2004). This activity has also been demonstrated in vitro, using both rat uterine horns and recombinant yeast screens (Furuta et al. 2004).

5.VI.4.B Benzene–Hydrocarbon Mix

Studies investigating the effects hydrocarbons on the human male reproductive system are limited to occupational exposure studies. In 24 men working in environments (i.e., in shoemaking, spray painting, paint-manufacturing factories) where ambient concentrations of benzene, toluene, and xylene exceeded the maximum allowable concentrations, sperm vitality, sperm motility, acrosin activity, gamma-GT activity, and LDH-C4 relative activity all decreased (Xiao et al. 1999; Xiao et al. 2001). Another group of 48 men working in the rubber industry and exposed to hydrocarbons (such as ethyl benzene, benzene, toluene, and xylene) for 2 to 24 years exhibited abnormal ejaculate characteristics such as alterations in viscosity, liquefaction capacity, sperm count, sperm motility, and sperm morphology (De Celis et al. 2000).

Benzene (500–1000 mg/m^3) and ethylbenzene (600–2400 mg/m^3) have been reported to induce skeletal anomalies and retardation of fetal development in rats and mice and spontaneous abortion in rabbits when administered for 24 hr/day for up to 9 days during pregnancy; yet they have not proved to be teratogenic in any of the species tested (Hudák and Ungváry 1978; Ungváry and Tátrai 1985).

5.VI.4.C Formaldehyde

Formaldehyde administered to rats has been reported to induce abnormal sperms (without affecting testis weight or sperm count) at 100 and 200 mg/kg (Cassidy et al. 1983); a fall in sperm motility, viability, and count and lowered DNA content in the testis and prostate at 10 mg/kg for 30 days (Majumder and Kumar 1995); and an increase in sperm-head abnormalities at 0.125 to 0.500 mg/kg for 5 days (Odeigah 1997). In the latter study, there was a reduction of fertile matings in females mated 1 to 7 days after males were treated with formaldehyde. The destruction of testicular structure and sperm quantity and quality in rats exposed to formaldehyde (10 mg/m^3 for 2 weeks) was partially reversed by vitamin E, prompting the suggestion that oxidative stress played a role in the damage and that there was a direct free radical–scavenging effect of the vitamin (Zhou et al. 2006).

The teratogenic effects of formaldehyde in rodents have been reviewed by Thrasher and Kilburn (2001). Various exposure regimens (i.e., prior to mating, during mating, or during the entire gestation period) led to a host of effects on the embryo, including increased mortality and anomalies and decreased concentrations of ascorbic acid, and caused abnormalities in enzymes of the mitochondria, lysosomes, and endoplasmic reticulum (Ulsamer et al. 1984; Saillenfait et al. 1989; U.S. Department of Health and Human Services 1999). Newborn rodents exposed to formaldehyde in utero have also been reported to exhibit abnormal performance in open-field tests.

5.VI.5 SUMMARY

Among the challenges in assessing, from the toxicologic viewpoint, the risk of traffic-related pollution adversely affecting human-reproductive health are the data limitations and the almost-universal use of very high exposure concentrations that have questionable relevance to actual ambient concentrations. The findings currently available must therefore be interpreted with caution. Further research is needed using other components of traffic pollution, including exhaust from gasoline-fueled engines, at more relevant concentrations.

5.VII. STUDIES OF NEUROTOXICITY

To elicit neurotoxicity, inhaled pollutants must reach the central nervous system. Although entry by way of the circulatory system is likely to be limited by the tight junctions of

the blood–brain barrier, the effectiveness of this barrier in controlling the influx of neurotoxins can be compromised by factors that include, among others, oxidative stress. Indeed, DEP has been shown to affect the function of the blood–brain barrier through oxidative stress and proinflammatory cytokine production (Hartz et al. 2008). In addition, studies have shown that the olfactory mucosa allows direct access to the olfactory bulb and even other areas of the brain to some inhaled pollutants — including some organic solvents (e.g., toluene and xylene) (Ghantous et al. 1990) and metals (e.g., manganese, cadmium, and aluminum) found in hydrocarbon fuels (Tjalve and Henriksson 1999). Particles, especially those in the ultrafine size range, also might gain access to the olfactory bulb by way of the nose and olfactory nerve (Elder et al. 2006).

The toxicologic outcomes reviewed in this section reflect the disparity of research in the area and include in vivo effects of the traffic mix on neuropathologic markers and of CAPs on markers of inflammation in some regions of the brain. Outcomes of in vivo exposures to diesel and gasoline range from effects on neuropathology and neurotransmitters to effects on coordination, headache, and nausea; in vitro studies have focused on neurodegeneration and transmitter perturbations. Neurologic outcomes studied after in vivo exposure to components of the traffic mix pertain to learning, memory, and motor activity.

5.VII.1 TRAFFIC MIXTURES

An association between ambient PM and neuropathology was supported by the findings in the brains of 32 dogs exposed to high concentrations of PM in Mexico City (Calderón-Garcidueñas et al. 2002). Compared with the brains of 8 control dogs from less polluted cities, several neuropathologic markers (including expression of NF-κB and inducible NO synthase in cortical endothelial cells) were found in the dogs exposed to the higher PM concentrations. In addition, physical damage to the blood–brain barrier and neurodegenerative pathology were reported.

5.VII.2 PARTICULATE MATTER: CONCENTRATED-AMBIENT-PARTICLE STUDIES

Animal studies have examined the effects of exposure to airborne PM on inflammation and immune function in the brain. Investigators exposed ovalbumin-sensitized BALB/c mice and $ApoE^{-/-}$ mice to concentrated (4- to 20-fold) fine and ultrafine airborne particulates at sites of high-traffic density in Los Angeles (Campbell et al. 2005; Kleinman et al. 2008). Exposure (4 hours, 5 days/wk, for 2 weeks) was found to increase concentrations of IL-1α, TNF-α, and the transcription factor NF-κB in brain tissue compared with that of control animals (Campbell et al. 2005). Further evidence of inflammatory activation in the brains of exposed animals (5 hr/day, 3 days/wk, for 6 weeks) was another dose-related increase in nuclear translocation of NF-κB, as well as increased concentrations of another transcription factor, AP-1, and the glial fibrillary acidic protein (Kleinman et al. 2008).

5.VII.3 DIESEL EXHAUST

5.VII.3.A Animal Studies

To learn about the effects of traditional DE on the brain, work has been undertaken using various components of the diesel mix. A systemic (i.e., intraperitoneal) injection of the PAH benzo[*a*]pyrene (0, 5, 25, and 100 mg/kg) into mice twice a week for 3 weeks resulted in increased metabolism of monoamines in the brain (Jayasekara et al. 1992). To identify the neurotoxic effects of various DE fractions, Andersson and colleagues (1998) studied exhaust emissions from a heavy-duty diesel vehicle separated into particulate and semivolatile phases and then fractionated according to polarity. The fractions were evaluated in the adult rat brain by injection into the striatum or hippocampus, two brain regions involved in locomotor function, memory, and cognition and in which pathology is correlated with common neurodegenerative diseases. Intrastriatal as well as intrahippocampal injections of particulate fractions (containing mononitro-PAHs, dinitro-PAHs, quinones, and polar material) and of semivolatile fractions, in amounts corresponding to their emissions from a vehicle driven 19.5 m, caused major lesions with tissue loss and disappearance of tissue staining for glial fibrillary acidic protein, tyrosine hydroxylase, and acetylcholine esterase. Particulate fractions containing "light" aliphatic hydrocarbons, "heavy" aliphatic hydrocarbons, PAH, and a semivolatile fractions produced smaller lesions. The damage seemed to be the consequence of general toxicity, resulting in the loss of glial cells, nerve cells, and nerve fibers in the lesions. The use of non-inhalation routes of exposure, in both this study and the work of Jayasekara and colleagues (1992), compromised the relevance of the neurotoxicity observed to human exposure to traffic-related pollution.

The health effects of alternative diesel fuels have also been investigated to rule out the possibility that the new fuels might present new health hazards. One type of fuel shown to reduce NO_x and PM emissions compared with traditional diesel fuels is the diesel–water emulsion PuriNOx (Barnes et al. 2000; Langer et al. 2000; Park et al. 2001). In rats exposed to combustion emissions of PuriNOx (100, 200, and 400 µg total PM/m^3, 6 hr/day, 5 days/wk for the first 11 weeks and 7 days/wk thereafter),

no evidence of neurotoxicity, reproductive or developmental toxicity, or in vivo genotoxicity was found (Reed et al. 2005). Noteworthy observations were limited to small decreases in serum cholesterol and small increases in platelet values in some groups of exposed animals.

5.VII.3.B In Vitro Studies

With the aim of elucidating the mechanism by which environmental toxins might trigger neurodegenerative diseases, Block and colleagues (2004) investigated the selective toxicity DEP might have for dopaminergic neurons. As hypothesized, cultures of mesencephalic neurons and glia treated with DEP (0.22 µM; 5–50 µg/mL) underwent a selective and dose-dependent decrease in dopaminergic neurons through the activation of microglial NADPH oxidase and consequent oxidative insult. Of interest, dopaminergic neurons possess reduced antioxidant capacity, as evidenced by low intracellular glutathione concentrations, which render dopaminergic neurons more vulnerable to oxidative stress and microglial activation, compared with other cell types (Loeffler et al. 1994). It was also observed that the mobility of the microglial cytoskeleton is mandatory for the generation of DEP-induced superoxide, supporting the role of phagocytosis as one of the contributing mechanisms to microglial-derived oxidative damage (Figure 5.6).

5.VII.4 OTHER COMPONENTS

5.VII.4.A Methylcyclopentadienyl Manganese Tricarbonyl

The manganese fuel additive methylcyclopentadienyl manganese tricarbonyl (MMT) is a gasoline-octane enhancer that was developed to replace lead in gasoline. For a review of MMT usage and regulation see Appendix B of Chapter 2. Unlike lead, manganese is an essential nutrient and is important for cellular functioning; however, when inhaled (in the workplace) or ingested (occasionally via drinking water) at high concentrations it has been implicated in oxidative stress in the brain (Desole et al. 1997; Stokes et al. 2000) as well as in alterations in neurotransmitter metabolism with concurrent neurobehavioral deficits (Miele et al. 2000; Montes et al. 2001). Because a much larger percentage of inhaled manganese is taken up into the body compared with ingested manganese, and accumulates in the brain more readily, exposure via the inhalation route is of more concern. When combusted, the manganese from MMT is in the form of several aerosolized salts, the most abundant being phosphate and sulfate (Lynam et al. 1999; Zayed et al. 1999). Pharmacokinetic studies have shown that the particular manganese salt determines the rate of transport into the brain, such that $MnCl_2 > MnSO_4 > MnPO_4$ (Drown et al. 1986; Dorman et al. 2001), prompting further work to determine the salt-specific neurotoxicity of these species. Much research has focused on the mechanism of transport into the brain, which may occur via transporter molecules or via the olfactory nerve, in which case the protective blood–brain barrier gets bypassed. In cultured rat primary astrocytes exposed to 500 µM $MnCl_2$, it was reported that the uptake of glutamate (a common brain neurotransmitter) was suppressed by nearly 40% in association with a 48% decrease in the glutamate–aspartate transporter (GLAST), the most prevalent glutamate transporter in cultured astrocytes, responsible for regulating glutamate in the extracellular space. High extracellular glutamate levels are toxic to the cells (Erikson and Aschner 2002). $MnCl_2$ exposure caused a significant overall decrease in astrocytic GLAST mRNA concentrations, $MnSO_4$ caused only a moderate decrease, and $MnPO_4$ did not alter GLAST mRNA in astrocytes (Erikson et al. 2002). A study by Yokel and Crossgrove (2004) showed that manganese was actively transported into the brain, but that no transporters were involved in removing manganese from the brain, which would indicate

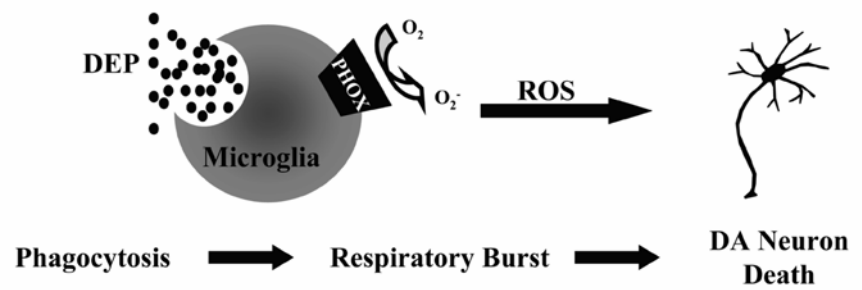

Figure 5.6. Phagocytosis-mediated dopamine neurotoxicity. DEP are phagocytized by microglia, which results in activation of NADPH oxidase (PHOX) and the neurotoxic respiratory burst. Dopaminergic (DA) neurons are particularly vulnerable to oxidative damage (ROS) and may have an increased sensitivity to ongoing phagocytosis from neighboring microglia compared with other neuronal cell types. (Reprinted from Block et al. 2004, with permission of the FASEB Journal.)

that manganese in the brain is subject to accumulation over time. A review of the health effects of manganese can be found in U.S. EPA 2003.

However, it is unclear whether manganese concentrations in ambient air from its use as a fuel additive will be high enough to pose a risk. In a review by Abbott (1987), the observation was made that the small increase in airborne manganese from the use of MMT in gasoline was three to four orders of magnitude smaller, even in areas of high traffic density, than the concentrations assumed to produce symptoms of toxic manganese exposure. A study in Toronto after the introduction of MMT into the gasoline supply showed that car emissions increased the level of manganese in ambient air initially, but that the effect was diminished by subsequent dilution. In addition, personal exposure levels of manganese in particulate matter for the general population in Toronto did not exceed 0.05 μg/m^3 (Clayton et al 1999).

A risk assessment conducted by Health Canada (Wood and Egyed 1994) concluded that addition of MMT to the Canadian gasoline supply had not substantially increased manganese levels in ambient air above previous levels resulting from industrial sources and motor-vehicle sources other than exhaust emissions (for example, brake wear). However, the U.S. EPA concluded that "to support an improved health risk characterization for MMT, further investigation is needed in the areas of health effects, emission characterization, and exposure analysis" (Davis 1998). It remains possible that accumulation of low-level manganese exposure over a lifetime could contribute to neurologic diseases, especially in the elderly.

5.VII.4.B Benzene

Animal studies investigating the neurotoxicity of benzene have reported significant increases in mouse milk-licking responses on inhaling 100 and 300 ppm (Dempster et al. 1984), increased spontaneous motor activity and decreased response to d-amphetamine challenge after 550 mg/kg on days 9, 11, and 13 postpartum (Tilson et al. 1980), and increased concentrations of catecholamines in the brain after exposure in drinking water at 8 mg/kg/day (Hsieh et al. 1988). A more recent study reported long-lasting changes in motor behavior and cognitive processes in the offspring of rats injected subcutaneously with 0.1 mg/kg benzene on day 15 of gestation (Lo Pumo et al. 2006).

In a review of the neurotoxic effects of a number of compounds that are present in or added to gasoline (i.e., methyl tertiary butyl ether [MTBE], ethyl tertiary butyl ether, tertiary amyl methyl ether, xylene, toluene, methyl alcohol, ethyl alcohol, and benzene), Burbacher (1993) concluded that "there is a substantial margin of safety between the current permissible exposure levels and levels that would be expected to cause overt signs of neurotoxicity in humans."

5.VII.4.C Formaldehyde

There have been few animal studies on the neurotoxicologic effects of formaldehyde. Rats trained to find food in a maze and then exposed to 2.6 ppm or 4.6 ppm formaldehyde (10 min/day, 7 days/wk, for 90 days) needed more time and made more mistakes than the control group while negotiating the maze (Pitten et al. 2000). Negative effects on learning and memory in mice have also been reported after exposure to 3 mg/m^3 but not to 1 mg/m^3 (Lu et al. 2008).

5.VII.4.D Gasoline Vapors

Although the neurologic effects of gasoline-fueled-engine exhaust have not been evaluated, the few studies investigating acute and long-term neurologic effects of gasoline itself were reviewed by Ritchie and colleagues (2001). Brief (6-hour) exposure to high concentrations (1000 ppm; 5500 mg/m^3) of gasoline vapor induced loss of coordination in rats (Dutch Expert Committee for Occupational Standards 1992); the same dose in human volunteers led to dizziness, nausea, and headache (Drinker et al. 1979). Still higher concentrations in humans (2600 ppm; 14,300 mg/m^3) caused intoxication and partial anesthesia. Chronic exposures (8 hr/day, 5 days/wk, for 60 days) of rats to 2000 mg/m^3 (364 ppm) resulted in significant increases in adrenal catecholamines and serum corticosterone (Vyskocil et al. 1988). A more intensive chronic-exposure regimen in rats (1500 ppm; 8250 mg/m^3 for 6 hr/day, for up to 18 months) resulted in axonal dystrophy in the spinal cord and cell abnormalities in the anterior horn (Spencer 1984).

5.VII.5 SUMMARY

It is difficult to analyze and compare in detail the available data on the neurotoxicity of traffic-related pollutants. Of the few published studies available for review, a diverse collection of protocols (with respect to both agents and routes of exposure), animal models (in vivo and in vitro), and endpoints have been investigated. The study most relevant to human ambient exposures identified neuropathologic markers, physical damage to the blood–brain barrier, and neurodegenerative pathology in a small number of dogs exposed to high PM concentrations in Mexico City (N = 32) when compared with only 8 dogs from a less polluted control city. Toxicologic studies must be interpreted with caution, owing to the use of irrelevant routes of exposure or the use of elevated pollutant concentrations.

Although the CAPs-exposure studies reporting increased markers of inflammation in the brains of mice are of interest, data are not yet available to determine whether such a biologic response translates into an adverse health outcome.

5.VIII. CONCLUSIONS

There is broad evidence supporting the role of oxidative stress in the health effects associated with air pollution, including traffic-related pollution. The increased burden of ROS presented by ambient air pollutants, including PM and its components, might upset the balance between oxidative-stress and oxidant-defense mechanisms. An increased oxidant burden might also play a role in the transcriptional activation of proinflammatory genes, contributing to tissue injury.

There is toxicologic evidence for adverse cardiovascular effects of exposure to PM, both acute and chronic, at exposure concentrations that are higher than, but still relevant to, ambient concentrations. DE at elevated concentrations, as a component of the traffic-emissions mix, has been shown in a few recent studies to alter vascular function in healthy people and to increase myocardial ischemia during exercise in men with coronary artery disease. However, the specific mechanisms and PM components responsible for these effects have not been identified, and the relative contribution of traffic-related emissions in cardiovascular health effects has not been determined.

Nevertheless, the recent toxicologic literature provides suggestive evidence that exposure to pollutants that are components of traffic emissions, including ambient and laboratory-generated PM and exhaust from diesel and gasoline-fueled engines, alters cardiovascular function. Toxicologic studies provide plausible mechanisms and pathways for cardiovascular effects. There is evidence for acute effects on vascular homeostasis and suggestive evidence in animal models that repeated or chronic PM exposure enhances the development of atherosclerosis. However, there remains substantial inconsistency among studies. More important, the specific PM components, cellular responses, and signaling pathways responsible for these effects have not been identified. Increasing evidence supports the involvement of oxidative stress, but whether the oxidants come from the pollutants themselves or the inflammatory response they initiate is unknown. In addition, cardiovascular effects in toxicologic studies have generally been demonstrated at exposures substantially above ambient concentrations. Whether traffic-related emissions other than PM have cardiovascular effects or contribute to the cardiovascular effects associated with PM exposure is unclear.

There is also evidence for respiratory effects of components of traffic-related air pollution, especially PM and DE. These effects include exacerbation of both allergic and non-allergic diseases. The small number of studies that directly investigated the effects of intentional (real-world) exposure to traffic-related pollution showed decrements in lung function and enhanced response to allergens in asthmatic allergic subjects. Exposure to components of traffic pollution resulted in mild acute inflammatory responses in healthy individuals and enhanced allergic responses in asthmatic allergic individuals and in animal models. As is the case for cardiovascular effects, the paucity of direct studies of traffic-related mixtures has not allowed identification of specific components or pathogenic pathways for traffic-related respiratory effects.

Other possible health effects of traffic-related pollutants include malignancy, reproductive effects, and neurotoxicity. DE can cause DNA strand breaks and mutations, and DE might be carcinogenic. Animal studies and some human studies have suggested that DE exposure at high concentrations might alter male reproductive function. Animal toxicologic studies have suggested that exposure during early development might affect reproductive and pregnancy outcomes. Overall, the toxicologic data are not sufficient to determine whether exposures to traffic-related pollution or its components, at ambient concentrations, cause malignancy, reproductive effects, or neurotoxicity.

5.VIII.1 RESEARCH GAPS

In understanding the toxicology of traffic emissions, there are the following major gaps:

- Few studies have focused specifically on traffic-related exposures and their health effects. There is a need to compare the toxicity of traffic-related pollution to that from other sources.
- The specific components of traffic pollution that are most responsible for health effects remain unknown.
- Little is known about the health effects of traffic-emissions mixtures and pollutant interactions. Although much has been learned about the cardiac and respiratory effects of DE exposure, toxicologic studies need to further address the effects of exposure to emissions from gasoline-fueled engines, gaseous versus particulate components of traffic emissions, and road dust. Studies are also needed to address potential pollutant interactions in inducing health effects.

- Emissions related to new-technology diesel engines and new fuel formulations require study. Changes in fuel and energy sources change emissions and will likely alter health risks associated with traffic exposure. There is a need to study the toxicology of emissions related to ethanol and biodiesel fuels, whose use is increasing, and to anticipate the potential health risks of new fuels as they emerge.

- There is a need for additional dose–response and concentration–response studies. Studies are needed that use exposure concentrations relevant to ambient air in order to understand concentration–response relationships and to identify no-effect concentrations.

- Measurements of the oxidant potential of exposure atmospheres are needed to test the hypothesis that health effects are related in part to the oxidative capacity of traffic emissions. Given the strong evidence of a role for oxidative stress in mediating air pollution's health effects, there is a need to know the degree to which this stress comes from the exposure itself.

Table 5.2. Summary of Human Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Subjects	Exposure Conditions (Concentration, Time)	Findings
Traffic Mixture				
Bräuner et al. 2007	DNA damage and oxidative stress	29 healthy adults (20–40 yr)	Exposure in large chamber to filtered air (91–542 particles/cm^3) or unfiltered air from a busy roadway in Copenhagen (6,169–15,362 particles/cm^3) for 24 hr, with two 90-min episodes of exercise	UFP exposure associated with increased strand breaks and oxidized purines. Dose–response relation between particle number and DNA damage.
Bräuner et al. 2008a	Microvascular function, markers of systemic inflammation and coagulation	41 healthy adults (60–75 yr)	Exposure in homes within 350 m of major roads in Copenhagen to unfiltered air (7,718–12,988 particles/cm^3) or filtered air (2,533–4,058 particles/cm^3) for two consecutive 48-hr exposures	8.1% improvement in peripheral arterial tone following ischemia after particle filtration, compared with no filtration. No differences in blood markers.
Bräuner et al. 2008b	Microvascular function, markers of systemic inflammation and coagulation	29 healthy adults (20–40 yr) (same as Bräuner et al. 2007)	Exposure in a room to filtered air (~555 particles/cm^3) or unfiltered air from a busy roadway (~11,600 particles/cm^3) for 24 hr with two 90-min periods of exercise	No significant effects on peripheral vascular function or blood markers.
Larsson et al. 2007	Pulmonary cellular inflammation response	16 healthy adults (19–59 yr)	Road tunnel air (median concentrations of $PM_{2.5}$ 64 µg/m^3, PM_{10} 176 µg/m^3, NO_2 230 µg/m^3) or urban air for 2 hr on a day of normal activity	Significantly higher numbers of bronchoalveolar lavage fluid total cells, lymphocytes, alveolar macrophages, and nuclear expression of transcription factor component c-Jun; no increase in neutrophils.
McCreanor et al. 2007	Lung function	60 adults with mild or moderate asthma (19–55 yr)	Exposure while walking on no-traffic street (median concentration of $PM_{2.5}$ 11.9 µg/m^3, PM_{10} 72 µg/m^3, NO_2 21.7 µg/m^3) or high-traffic street (median concentrations of $PM_{2.5}$ 28.3 µg/m^3, PM_{10} 125 µg/m^3, NO_2 142 µg/m^3) in London	High-traffic group had significant reductions in FEV_1 and FVC compared to low-traffic group and increases in neutrophilic inflammation and airway acidification.
Rundell et al. 2007	FMD and forearm tissue oxygenation	16 male collegiate athletes (18–22 yr)	Exposure while running adjacent to highway (PM_{10} 143,501 ± 58,565 particles/cm^3) or low traffic area (PM_{10} 5,309 ± 1,942 particles/cm^3) for 30 min at 85–90% of maximum heart rate	FMD and tissue oxygenation were impaired after exercise near high traffic, and were unchanged near low traffic.

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Table 5.2 (*Continued*). Summary of Human Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Subjects	Exposure Conditions (Concentration, Time)	Findings
Traffic Mixture (*Continued*)				
Svartengren et al. 2000	Asthmatic reactions	20 adults with mild allergic asthma	Exposure inside a car in a Stockholm city road tunnel for 30 min (NO_2 ~300 µg/m^3) or in a suburban area, inhalation of a low-dose allergen 4 hr after exposure	Tunnel-exposed subjects had a significantly greater early reaction to allergen, lower lung function, and more asthma symptoms during the late phase.
Concentrated Ambient Particles (CAPs)				
Brook et al. 2002	FMD	25 healthy adults (18–50 yr)	Filtered air (zero $PM_{2.5}$, low O_3) or a mixture of CAPs (in Toronto, $PM_{2.5}$ ~150 µg/m^3) and O_3 (0.12 ppm) for 2 hr at rest	Brachial artery constriction 10 min after exposure to pollutants, not after exposure to air. No change in FMD or blood pressure measured at the same time.
Devlin et al. 2003	HRV	10 healthy adults (60–80 yr)	Filtered air or fine CAPs (Chapel Hill, N.C.; 0.1–2.5 µm, mean mass 40.5 µg/m^3, range of 21.2–80.3 µg/m^3) for 2 hr at rest	Particle-associated reductions in pNN50 and high frequency HRV.
Ghio et al. 2000a	Lung function, airway inflammation, blood markers	38 healthy adults (18–40 yr) (36 males and 2 females)	Filtered air or fine CAPs (Chapel Hill, N.C., 0.1–2.5 µm, mean mass 120 µg/m^3, range 23.1–311.1 µg/m^3) for 2 hr with intermittent exercise	Mild airway inflammation, increased plasma fibrinogen. No symptoms noted by volunteers or decrements in pulmonary function, mild increase in neutrophils in bronchial and alveolar fractions taken 18 hr after exposure.
Gong Jr. et al. 2003	Lung function, airway and systemic inflammation, HRV	12 healthy and 12 asthmatic adults with COPD (18–45 yr)	Filtered air or fine CAPs (Los Angeles, < 2.5 µm in diameter, mean mass 174 µg/m^3, range 99–224 µg/m^3) for 2 hr with intermittent exercise	Systolic blood pressure decreased in asthmatics and increased in healthy subjects during particle exposure, compared with air. Plasma levels of ICAM-1 increased 4 hr post-exposure. PM exposure was associated with HRV effects. Overall changes observed were small and not always consistent across different parameters.

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Table 5.2 (*Continued*). Summary of Human Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Subjects	Exposure Conditions (Concentration, Time)	Findings
Concentrated Ambient Particles (CAPs) (*Continued*)				
Gong Jr. et al. 2004a	Lung function, airway and systemic inflammation, HRV	13 elderly patients with COPD (54–85 yr) 6 age-matched healthy adults	Filtered air or fine CAPs (Los Angeles, < 2.5 µm in diameter, mean mass 194 ± 26 µg/m^3) for 2 hr with intermittent exercise	Ectopic heart beats increased with particles in the healthy subjects, but decreased in the COPD subjects. HRV decreased with PM in the healthy but not in the COPD subjects. The COPD subjects appeared to be less susceptible than the healthy subjects, although effects were modest.
Gong Jr. et al. 2004b	Lung function, airway and systemic inflammation, HRV	4 healthy and 12 mildly asthmatic adults (19–51 yr)	Filtered air or coarse CAPs (Los Angeles, 2.5–10 µm in diameter, mean mass 157 µg/m^3, range 56–218 µg/m^3) for 2 hr with intermittent exercise	Heart rate increased and HRV decreased, without effects on cardiac ectopy; effects were generally larger in the healthy subjects compared to the asthmatics.
Gong Jr. et al. 2008	Lung function, exhaled nitric oxide, airway inflammation, Holter electrocardiography	17 healthy and 14 asthmatic adults (18–50 yr)	Filtered air or UFP CAPs (Los Angeles, 0.1–2.5 µm in diameter, mean counts 145,000 particles/cm^3, range 39,000–312,000, mean mass 100 µg/m^3, range 13–277, for 2 hr with intermittent exercise	UFP exposures were associated with some mild acute cardiopulmonary responses (0.5% mean decrease in arterial O_2 saturation, 2% mean decrease in FEV_1 the morning after exposure, slight decrease in low frequency power in Holter readings during rest periods).
Harder et al. 2001	Airway and blood immune cell function	38 healthy adults (18–40 yr) (36 males, 2 females)	Filtered air or fine CAPs (Chapel Hill, N.C., 0.1–2.5 µm in diameter, mean mass 120.5 ± 14.0 µg/m^3, range 23.1 to 311.1 µg/m^3) for 2 hr with intermittent exercise	CAPs did not alter distribution or function of immune cells in lung or blood.
Mills et al. 2008	Peripheral vascular vasomotor and fibrinolytic function, inflammation	12 male adults with stable coronary heart disease and 12 age-matched healthy adults	Filtered air or fine CAPs (Edinburgh, U.K., mean mass 190 ± 37 µg/m^3, range 50–682 µg/m^3) for 2 hr with intermittent exercise; CAPs were 92% sodium chloride	No effect on vascular function or markers of systemic inflammation, dose-dependent significant increase in blood flow and plasma tissue plasminogen activator release.
Samet et al. 2007	Lung function, airway inflammation, blood markers, HRV measured with an ECG	72 healthy adults (18–35 yr) (38 adults exposed to fine, 14 to coarse, and 20 to ultrafine)	Filtered air or CAPs (Chapel Hill, NC): fine (mean mass 120 µg/m^3); course (mean mass 89 µg/m^3); UFP (mean number 151.8 × 10^3/mL)	Mild airway inflammation with fine and coarse, but not ultrafine CAPs. Reductions in HRV with coarse and ultrafine CAPs. Changes in measures of blood clotting with fine and ultrafine CAPs.

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Table 5.2 (*Continued*). Summary of Human Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Subjects	Exposure Conditions (Concentration, Time)	Findings
Concentrated Ambient Particles (CAPs) (*Continued*)				
Urch et al. 2004	FMD and brachial artery diameter	24 healthy adults (35 ± 10 yr) (same subjects as Brook et al. 2002 study)	Filtered air or a mixture of CAPs (Toronto, median mass 147.4 μg/m^3, range 101.5–257.3 μg/m^3) and O_3 (0.12 ppm) for 2 hr at rest	Analysis of day-to-day variability in PM composition in relation to this effect suggested a role for both organic and inorganic elemental carbon. There was no pollutant effect on FMD.
Urch et al. 2005	Blood pressure and heart rate	23 healthy adults (19–50 yr) (same subjects as the Brook et al. 2002 study with 3+ subjects)	Filtered air or a mixture of fine CAPs (Toronto, < 2.5 μm in diameter, mean concentrations 147 ± 27μg/m^3) and O_3 (0.121 ppm) for 2 hr at rest	Increased diastolic blood pressure at the end of the 2-hour CAPs + O_3 exposures. No changes in heart rate.
Particulate Matter (Laboratory-Generated UFP)				
Frampton et al. 2006b	Blood leukocytes	40 healthy and 16 asthmatic adults (18–40 yr) (same subjects as Pietropaoli et al. 2004a)	Filtered air or EC UFP (~25 nm) for 2 hr (healthy: 10, 25, and 50 μg/m^3; asthmatics: 10 μg/m^3) with intermittent exercise	Decreased peripheral blood leukocyte expression of adhesion molecules 3–4 hr after exposure.
Pietropaoli et al. 2004a, 2004b	Blood markers of coagulation, inflammation, lung function	40 healthy and asthmatic adults (18–40 yr)	Filtered air or EC UFP (~25 nm) (healthy: 25 and 50 μg/m^3; asthmatics: 10 μg/m^3) for 2 hr with intermittent exercise	No changes in blood markers of coagulation or airway inflammation. Decrease in diffusing capacity for CO.
Shah et al. 2008	Forearm reactive hyperemia (vascular responsiveness), plasma nitrate levels, vital signs	16 healthy adults (18–40 yr)	Filtered air or 50 μg/m^3 EC UFP (~25 nm) for 2 hr with intermittent exercise	Inhalation of UFP altered forearm reactive hyperemia and reduced plasma nitrate levels.
Zareba et al. 2009	HRV measured with a Holter ECG	24 healthy and asthmatic young adults	Filtered air or 10–25 μg/m^3 EC UFP for 2 hr; one study at rest and one study with intermittent exercise	No marked changes; trends toward increased parasympathetic tone.
Diesel-Engine Exhaust (DE)				
Bosson et al. 2007	Inflammatory responses	16 healthy adults (20–28 yr)	Diluted DE (PM 300 μg/m^3) for 1 hr; then after 5 hr, filtered air or O_3 (0.2 ppm) for 2 hr with intermittent exercise	Increased inflammation when exposed to DE and O_3.

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Table 5.2 (*Continued*). Summary of Human Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Subjects	Exposure Conditions (Concentration, Time)	Findings
Diesel-Engine Exhaust (DE) (*Continued*)				
Carlsten et al. 2007	Markers of coagulation and endothelial injury	13 healthy adults (18–49 yr)	Filtered air or diluted DE containing 100 and 200 µg/m^3 PM for 2 hr	No effects on plasma fibrinogen or markers of coagulation.
De Celis et al. 2000	Male reproductive system health	48 male workers in the rubber industry	Exposed to hydrocarbons (ethyl benzene, benzene, toluene, and xylene) for 2–24 yr	Abnormal ejaculate characteristics observed, such as alterations in viscosity, liquefaction capacity, sperm count, sperm motility, and sperm morphology.
De Rosa et al. 2003	Several parameters of male fertility	85 men (23–62 yr) employed at motorway tollgates, 85 age-matched male controls	Exposure at tollgates (NO_x, SO_x, and lead concentrations exceeded the maximum permitted by law and were significantly higher than those for controls living in the same area)	Sperm count and serum levels of FSH, LH, and testosterone were normal in both groups. Sperm total motility, forward progression, functional test performance and kinetics were significantly lower in the tollgate workers. Of the workers with below normal sperm motility, this parameter was inversely correlated to both blood methemoglobin and lead.
Diaz-Sanchez et al. 1999	Nasal fluid IgE, IgG, and IgA humoral responses, cytokines	25 atopic adults (21–55 yr) (10 controls and 15 subjects)	DEP (0.3 mg) instilled in the nose with keyhole limpet hemocyanin (KLH) immunization	DEPs enhanced production of IgE responses to antigen (KLH) and also was associated with an IL-4 cytokine response.
Eibensteiner et al. 2005	Semen quality	18 traffic police officers in Arequipa, Peru (leaded gasoline is used)	Mean concentration of lead in blood was 48.5 µg/dL	Levels of lead in blood were associated with lower sperm morphology, concentration, and total number. A significant correlation was only found with sperm motility and viability.
Gilliland et al. 2004	Nasal allergic responses—allergen-specific IgE, histamine, IL-4, and interferon-γ	19 patients sensitive to the ragweed allergen and history of allergic rhinitis	Challenge with intranasal doses of ragweed; then ragweed plus DEP (0.3 mg)	DEPs increased the allergic response after nasal challenge. IgE increased more than 10-fold for all participants. Histamine and IL- 4 levels also increased with exposure to DEP compared to allergen alone.
Holgate et al. 2003	Inflammatory responses	25 healthy adults (19–42 yr) 15 adults with mild atopic asthma (23–52 yr)	Filtered air or diluted DE (100 µg/m^3) for 2 hr with intermittent exercise	Neutrophil, mast cell, and lymphocyte infiltration into the bronchial mucosa with enhanced epithelial expression of IL-8, GRO-α, and IL-13.

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Table 5.2 (*Continued*). Summary of Human Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Subjects	Exposure Conditions (Concentration, Time)	Findings
Diesel-Engine Exhaust (DE) (*Continued*)				
Lucking et al. 2008	Thrombus formation (using the Badimon ex vivo perfusion chamber), platelet activation	20 healthy adults (21–44 yr)	Filtered air or diluted DE (PM 350 μg/m^3) for 2 hr with intermittent exercise	Increased ex vivo thrombus formation 2 and 6 hr after exposure, and increased platelet activation 2 hr after exposure.
Mills et al. 2005	Systemic vascular function (forearm vascular dilation in response to infused dilators: acetylcholine, bradykinin, and sodium nitroprusside), marker of fibrinolysis (plasma tissue plasminogen activator in response to bradykinin)	30 healthy males (20–38 yr)	Filtered air or diluted DE (PM 300 μg/m^3) for 1 hr with intermittent exercise	Attenuation of induced vasodilation 2 and 6 hr after exposure. Suppression of bradykinin-induced tissue plasminogen activator level in plasma 6 hr after exposure.
Mills et al. 2007	Cardiac ischemia measured by S-T segment depression in ECG, systemic vascular function, marker of fibrinolysis (as in Mills et al. 2005)	20 males with stable coronary artery disease (prior myocardial infarction > 6 months before enrollment) (mean age 60 yr)	Filtered air or diluted DE (PM 300 μg/m^3) for 1 hr with intermittent moderate exercise	Cardiac ischemia and suppression of bradykinin-induced tissue plasminogen activator level in plasma in exposed subjects. No effect on vascular dilation.
Nordenhäll et al. 2001	Airway hyperresponsiveness, lung function, and airway inflammation	14 atopic asthmatic adults (22–57 yr) on continuous treatment with inhaled corticosteroids	Filtered air or diluted DE (PM_{10} 300 μg/m^3, NO_2 1.2 ppm) for 1 hr with intermittent exercise	Significant increase in degree of hyperresponsiveness, as compared with exposure to air, at 24 hr after exposure, and significant increase in airway resistance and in sputum levels of IL-6.

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Table 5.2 (*Continued*). Summary of Human Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Subjects	Exposure Conditions (Concentration, Time)	Findings
Diesel-Engine Exhaust (DE) (*Continued*)				
Peretz et al. 2007	Gene transcription in blood mononuclear cells	5 healthy adults	Filtered air or diluted DE (PM 200 μg/m^3) for 2 hr	Significant changes in 1,290 of 54,675 gene-probe sets, suggesting changes in inflammation and oxidative stress.
Peretz et al. 2008a	HRV	16 adults (24–48 yr) (3 healthy and 13 with metabolic syndrome)	Filtered air or diluted DE (PM 100 or 200 μg/m^3) for 2 hr at rest	Increased high-frequency HRV 3 hr after start of exposure, but not at later time points.
Peretz et al. 2008b	Systemic vascular function (forearm FMD)	27 adults (20–48 yr) (10 healthy and 17 with metabolic syndrome)	Filtered air or diluted DE (PM 100 and 200 μg/m^3) for 2 hr at rest	Reduced brachial artery diameter with 200 μg/m^3 DE, and increased plasma endothelin-1. No effects on flow-mediated dilatation.
Pourazar et al. 2005	Activation of redox-sensitive transcription factors	15 healthy adults (21–28 yr)	Filtered air or diluted DE (PM_{10} ~300 μg/m^3, NO_2 1.6 ppm) for 1 hr with intermittent exercise	Significant increase in the nuclear translocation of NF-κB, AP-1, phosphorylated JNK, and phosphorylated p38, as well as an increase in total (cytoplasmic + nuclear) immunostaining of phosphorylated p38.
Rudell et al. 1999a	Inflammatory responses	32 healthy adults (21–53 yr)	Filtered air or diluted DE (PM 300 μg/m^3) for 1 hr	Significant increases in neutrophils and CD4+ and CD8+ lymphocytes in bronchoalveolar lavage after exposure and airway resistance.
Salvi et al. 2000	Inflammatory responses	15 healthy adults (21–28 yr)	Filtered air or diluted DE (PM_{10} 300 μg/m^3, NO_2 1.6 ppm) for 1 hr	Neutrophil, mast cell, and lymphocyte infiltration into the bronchial mucosa with enhanced epithelial expression of IL-8, GRO-α, and IL-13.
Stenfors et al. 2004	Inflammatory responses	25 healthy adults (mean age 24 yr) 15 mildly asthmatic adults (mean age 30 yr)	Filtered air or diluted DE (PM_{10} 100 μg/m^3, NO_2 0.7 ppm) for 2 hr	Inflammatory responses found in healthy subjects but not in mildly asthmatic subjects.
Törnqvist et al 2007	Systemic vascular function, markers of fibrinolysis	15 healthy adults males (18–38 yr) (same as Mills et al. 2005)	Filtered air or diluted DE (PM 300 μg/m^3) for 1 hr with intermittent exercise	Impairment in endothelium-dependent vasodilatation persisted at 24 hr after exposure.

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Table 5.2 (*Continued*). Summary of Human Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Subjects	Exposure Conditions (Concentration, Time)	Findings
NO_2				
Drechsler-Parks 1995	Cardiac output using impedance plethysmography	8 healthy adults (56–85 yr)	Filtered air or NO_2 (0.60 ppm) or O_3 (0.45 ppm) or $NO_2 + O_3$ for 2 hr with intermittent exercise	Reduction in cardiac output during exercise with $NO_2 + O_3$.
Folinsbee et al. 1978	Cardiac output using CO_2 rebreathing method	5 healthy male adults	Filtered air or NO_2 (0.62 ppm) for 2 hr with intermittent exercise	No effect on cardiac output.
Frampton et al. 1989	Lung macrophage anti-viral function	19 healthy adults (19–37 yr)	NO_2 (continuous 0.60 ppm or background 0.05 ppm with three 15-min peaks of 2.0 ppm) for 3 hr	Alveolar macrophages from subjects exposed to NO_2 inactivated influenza virus in vitro less effectively.
Frampton et al. 2002	Airway inflammation, epithelial cell injury, and blood hemoglobin	21 healthy adults (18–40 yr)	Filtered air or NO_2 (0.6 and 1.5 ppm) for 3 hr with intermittent exercise	Dose-related decrease in hemoglobin. Mild increase in neutrophils recovered in bronchial lavage fluid. In vitro viral challenge of bronchial epithelial cells showed increased cytotoxicity after 1.5 ppm NO_2. No effects on symptoms or pulmonary function.
Strand et al. 1997	Airway hyperresponsivenes, lung function, and airway inflammation	18 asthmatic adults with allergy to pollen	Filtered air or NO_2 (490 μg/m^3) for 30 min followed by an allergen-inhalation challenge 4 hr later	Short-term exposure to NO_2 had little to no effect on healthy subjects but enhanced reaction to allergens in asthmatic subjects.
Carbon Monoxide				
Allred et al. 1989	Cardiac ischemia	63 male adults with stable coronary artery disease	CO (117 ppm or 253 ppm) during symptom-limited treadmill exercise	Concentration-related decrease in time to angina and time to ischemia on ECG.

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Table 5.3. Summary of Animal Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Animal Model	Exposure Conditions (Concentration, Time)	Findings
Traffic Mixture				
Calderón-Garcidueñas et al. 2001	Myocardial injury	Mongrel dogs (109 in Mexico City and 43 in less-polluted cities)	Air in Mexico City and in less-polluted cities (Cuernavaca, Tlaxcala, Tuxpam)	Increased foci of myocardial inflammation, apoptosis, and capillary endothelial abnormalities as well as neuropathologic abnormalities in dogs from Mexico City.
Elder et al. 2004	Plasma endothelins, acute phase proteins, airway inflammation	F344 rats (21 mo), some pretreated with LPS or infected with influenza virus	Highway air sampled from a moving truck for 6 hr/day for 1 or 3 days; clean-air and gases-only controls	Increased lung inflammation, lavage cell activation, and plasma endothelin-2. Interactions between on-road exposures and priming agents.
Elder et al. 2007	Heart rate and HRV	Spontaneously hypertensive rats (9–12 mo) pretreated with LPS; implanted radio-telemetry	Highway air sampled from a moving truck for 6 hr; clean-air controls	Decreased heart rate and changes in HRV (elevation in high-frequency power).
Mauad et al. 2008	Lung morphometry and elastic properties	BALB/c mice	São Paulo air 24 hr/day for 4 mo	Altered alveolar structure and elastic properties.
Particulate Matter (PM)				
Batalha et al. 2002	Pulmonary circulation	Male Sprague-Dawley rats (healthy rats and rats with chronic bronchitis)	Filtered air or fine CAPs (Boston; median mass: 182.75 μg/m^3; range: 73.50–733.00 μg/m^3) 5 hr/day for 3 consecutive days	Constriction of small pulmonary arteries; chronic exposure did not affect the weight of the heart or the thickness of the ventricles or pulmonary artery.
Calderón-Garcidueñas et al. 2002	Neuropathologic markers	Mongrel dogs (32 in Mexico City and 8 in Tlaxcala)	Air in Mexico City and less-polluted Tlaxcala	Expression of NF-κB and inducible NO synthase in cortical endothelial cells. Damage to the blood–brain barrier and neuro-degenerative pathology in dogs living in Mexico City.
Campbell et al. 2005	Inflammatory indices in brain	BALB/c mice	Filtered air or fine or UF CAPs, 4 hr, 5 days/wk for 2 wk	Increased levels of IL-1, TNF-α, and NF-κB in brain tissue of exposed mice.

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Table 5.3 (*Continued*). Summary of Animal Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Animal Model	Exposure Conditions (Concentration, Time)	Findings
Particulate Matter (PM) (*Continued*)				
Cassee et al. 2005	Airway and systemic inflammation, changes in blood factors	Spontaneously hypertensive male rats (7–12 wk) exposed to ozone	Filtered air and CAPs (Utrecht, Netherlands; industrial and suburban locations, 270–3700 μg/m^3) for 6 hr	Mild airway inflammation and increased plasma fibrinogen in spontaneously hypertensive rats.
Chen and Hwang 2005	HRV	C57 and ApoE$^{-/-}$ mice (same as Hwang et al. 2005)	Filtered air and fine CAPs (Tuxedo, N.Y.; mean mass 133 μg/m^3) 6 hr/day, 5 days/wk for more than 5 mo	Initial increase and subsequent decrease in HRV.
Clarke et al. 2000	Cells in blood and bronchoalveolar lavage fluid	Female dogs (< 5 yr)	Filtered air or fine CAPs (Boston; ~200–360 μg/m^3) for 6 hr/day on 3 consecutive days; exposed via tracheostomy	No effects related to particle mass. Airway inflammation and increased blood leukocytes associated with aluminum and silicon content, reduced blood hemoglobin associated with sulfur.
Dvonch et al. 2004	Endothelial function	Brown Norway male rats	Filtered air or CAPs (Detroit; mean mass 354 μg/m^3) for 8 hr/day on 3 consecutive days	Plasma asymmetric dimethylarginine (an inhibitor of NO synthase and associated with impaired vascular function) levels increased.
Fernvik et al. 2002	Airway inflammation and allergic response	Male mice (7–8 wk) immunized with allergen	Extract fractions from traffic PM (Prague); birch pollen for immunization	Mice immunized with birch pollen and traffic PM had increased specific IgE titers, airway responsiveness, number of recruited eosinophils, and levels of fibronectin and LDH in bronchoalveolar lavage fluid.
Gordon et al. 1998	Blood leukocyte counts, heart rate	Rats (normal and treated with monocrotaline)	Air and fine CAPs (Tuxedo, N.Y.; mass range 110–350 μg/m^3) for 3 hr	Healthy and monocrotaline-treated rats showed increased blood leukocyte counts and small heart rate changes after exposure to CAPs.
Gurgueira et al. 2002	Whole-organ oxidative stress	Healthy male Sprague-Dawley rats	Filtered air or fine CAPs (Boston; mean mass 300 ± 60 μg/m^3) for 1–5 hr	Cardiac oxidative stress increased, as measured by chemiluminescence in the lung and heart.
Hwang et al. 2005	Heart rate, heart rate fluctuation, body temperature	Normal mice (C57) and mice prone to develop atherosclerosis (ApoE$^{-/-}$)	Air and fine CAPs (Tuxedo, N.Y.; mean mass 133 μg/m^3) 6 hr/day, 5 days/wk for more than 5 mo	Decreasing patterns of heart rate, body temperature, and physical activity for ApoE$^{-/-}$mice.

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Table 5.3 (*Continued*). Summary of Animal Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Animal Model	Exposure Conditions (Concentration, Time)	Findings
Particulate Matter (PM) (*Continued*)				
Kleinman et al. 2005	Allergic responses and inflammation	Ovalbumin-sensitized BALB/c mice	Filtered air or fine or UF CAPs at 50 m and 150 m downwind from a roadway with diesel vehicles	Increased levels of IL-5, ovalbumin-specific IgE and IgG1, and eosinophils, greater inflammation.
Kleinman et al. 2008	Inflammatory indices in brain	$ApoE^{-/-}$ mice	Filtered air and fine and UF CAPs (4- and 15-fold), 5 hr/day, 3 days/wk for 6 wk	Dose-related increase in NF-κB, AP-1, and glial fibrillary acidic protein.
Kodavanti et al. 2005	Lung function, airway inflammation, pathology, markers of systemic effects	Healthy male rats (10–12 wk) (normotensive WKY and spontaneously hypertensive [SHR.NCrlBR])	Filtered air and fine CAPs (Chapel Hill, N.C.; range: 144–2,758 μg/m^3) for 4 hr/day for 1 or 2 days	No effects of 1-day exposure to CAPs; subtle effects, including increased plasma fibrinogen, with multiday exposure; mass concentrations of particles did not correlate with any health effect.
Kooter et al. 2006	Pathological and blood markers of pulmonary and cardiovascular inflammation and injury	Spontaneously hypertensive rats	Fine CAPs at a city location (range: 399–3,613 μg/m^3) or UF and fine CAPs in a traffic tunnel (269–556 μg/m^3) for 6 hr/day for 2 days, sacrificed after 18 hr of recovery	Markers of oxidative stress affected by both exposures. Otherwise no significant cytotoxicity or inflammation with either atmosphere.
Nemmar et al. 2002 and 2003a	Peripheral thrombosis and airway inflammation	Hamsters	UF and fine polystyrene particles (60 nm), instilled intratracheally	UFPs enhanced thrombosis, while fine PM induced inflammation.
Reed et al. 2005	General toxicity, neurotoxicity, genotoxicity, reproduction and development	Male and female F344 rats	Emissions of PuriNOx (PM 100, 200, and 400 μg/m^3) for 6 hr/day, 5 days/wk for the first 11 wk and 7 days/wk thereafter	No neurotoxicity, reproductive/developmental toxicity, or in vivo genotoxicity. Small decreases in serum cholesterol and small increases in platelets.
Rhoden et al. 2005	Myocardial oxidative stress	Adult Sprague-Dawley rats	Fine CAPs (Boston; 750 μg instilled or 700 ± 180 μg/m^3) inhaled for 5 hr	PM-associated increase in cardiac oxidative stress was prevented by pretreatment with atenolol (a β-adrenergic blocker) or glycopyrrolate (a cholinergic inhibitor).
Silva et al. 2005	Vascular injury and thrombosis	Male F344 rats (ear-vein Rose Bengal thrombosis model)	Instilled polystyrene UFPs (60 nm) positively or negatively charged	Positively charged particles enhanced thrombosis in a dose-dependent manner, both intravenous and instilled intratracheally.

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Table 5.3 (*Continued*). Summary of Animal Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Animal Model	Exposure Conditions (Concentration, Time)	Findings
Particulate Matter (PM) (*Continued*)				
Sun et al. 2005	Atherosclerosis	$ApoE^{-/-}$ mice (6 wk) fed low- and high-fat diets	Filtered air or fine CAPs (Tuxedo, N.Y.; mean concentration 85 µg/m^3) 6 hr/day, 5 days/wk for 6 mo	Increased atherosclerotic plaque formation, vascular inflammation, altered vasomotor responses, and increased oxidative stress in animals fed a high-fat diet.
Suwa et al. 2002	Atherosclerosis	Female Watanabe hyperlipidemic rabbits	Intrapharyngeal instillation of PM_{10} (Ottawa; 5 mg saline) 2/wk for 4 wk	More rapid progression of atherosclerotic plaques with PM_{10} compared with saline instillation.
Thomson et al. 2004, 2005, 2006; and Vincent et al. 2001	Vasoconstrictive responses	Healthy F344 rats	O_3 (0, 0.4, and 0.8 ppm) and urban PM (0, 5, and 50 mg/m^3 Ottawa dust) for 4 hr	Increased plasma levels of endothelin-1, with increases in both endothelin-1 mRNA and protein expression in the lung.
Ulrich et al. 2002	Expression of genes involved in cardiovascular and pulmonary diseases	Rats with ozone-induced airway inflammation	Intratracheally instilled urban PM (Ottawa [EHC-93]; 0.5, 1.5, 5 mg)	Increased plasma endothelin-1 and fibrinogen, and increased expression of inducible NO synthase.
Wellenius et al. 2003	Cardiac ischemia (S-T segment elevation)	Female mongrel dogs	Air and fine CAPs (median: 285.7 µg/m^3, range 161.3–957.3 µg/m^3) for 6 hr/day on 3 or 4 consecutive days followed by a 5-min coronary artery occlusion	CAPs enhanced coronary-artery occlusion-induced S-T elevation. The degree of ischemia was not related to particle mass concentration, but was related to silicon content of the particles.
Wellenius et al. 2004	ECG changes	Adult male Sprague-Dawley rats (model of acute myocardial infarction)	Filtered air, fine CAPs (Chapel Hill, N.C.; 350.5 µg/m^3), CO (35 ppm) or fine CAPS + CO (318.2 µg/m^3) for 1 hr	Reduced the frequency of ventricular premature beats with CO, no significant change with CAPs.

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Table 5.3 (*Continued*). Summary of Animal Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Animal Model	Exposure Conditions (Concentration, Time)	Findings
Engine Exhaust				
Andersson et al. 1998	Acute neurotoxicologic lesions	Female adult Sprague-Dawley rats	Injection of fractioned PM from a heavy-duty diesel vehicle into the striatum or hippocampus; amount corresponded to that in emissions from a driven length of 19.5 m	Major lesions with tissue loss and disappearance of immunoreactivity for glial fibrillary acidic protein, tyrosine hydroxylase, and acetylcholine esterase. PM fractions containing "light" and "heavy" aliphatic hydrocarbons, PAHs, and a semi-volatile fraction produced smaller lesions. The damage seemed to be the consequence of general toxicity, resulting in loss of glial cells, nerve cells, and nerve fibers within the lesions.
Anselme et al. 2007	HRV and arrhythmia	Rats with and without heart failure from experimental myocardial infarction	Filtered air or diluted DE (PM ~ 500 µg/m^3) for 3 hr	Reduced HRV in both healthy and heart failure rats. Increased ventricular premature beats in heart failure rats.
Bond et al. 1990	DNA adduct formation	F344/N rats (male and female)	Filtered air, carbon black (6.2 mg/m^3) or diluted DE (6.2 mg/m^3) 16 hr/day, 5 days/wk for 12 wk	Significant increase in the level of total adducts in type II cells of rats exposed to DE and carbon black.
Brightwell et al. 1989	Cancer	Hamsters and rats (some hamsters with induced respiratory tract tumors)	Diluted gasoline-engine exhaust or DE for 16 h/day, 5 days/wk for 2 yr	No increased incidence of respiratory-tract tumors in hamsters; significant increase in lung tumors in rats exposed to DE but not gasoline-engine exhaust.
Dasenbrock et al. 1996	Cancer	Female Wistar rats (7 wk)	Instilled carbon black and diesel soot (total particle dose 15 mg subdivided into 16–17 weekly intratracheal applications)	PAHs had a carcinogenic role in the lungs of rats instilled with carbon black and two types of diesel soot.
Dybdahl et al. 2004; Risom et al. 2003; Saber et al. 2005; Tokiwa et al. 1999	DNA damage	Mice	DEP (20 and 80 mg/m^3 for 90 min, or 5 and 20 mg/m^3 for 90 min/day for 4 d)	Elevated oxidative DNA damage (8-OHdG), DNA strand breaks, and bulky DNA adducts in the lungs of exposed animals, depending on exposure regimen.

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Table 5.3 (*Continued*). Summary of Animal Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Animal Model	Exposure Conditions (Concentration, Time)	Findings
Engine Exhaust (*Continued*)				
el Feki et al. 2000	Sexual activity	Rats	Leaded gasoline-engine exhaust	No effect on females. In males, effects noted were atrophy of testicle, seminal vesicle and epididymis, pathological changes in spermatogenesis, and decreased serum testosterone.
Fujimoto et al. 2005	Pregnancy and fetal development	Pregnant mice	Filtered air or diluted DE (0.3, 1.0, or 3.0 mg/m^3) at 2 days postcoitum until 13 days postcoitum	Total fetal weight, fetal absorption, and congestion in histological sections of placentas were affected by exposure.
Heinrich et al. 1986	Cancer	Hamsters, mice, and Wistar rats	Filtered and whole DE (~4 mg/m^3) for 19 hr/day 5 days/wk for 26–32 mo	In hamsters, no lung tumors detected. In mice, increased incidence of adenocarcinomas in the lungs with both whole and filtered exhaust. In rats, increased incidence of lung tumors, mortality, and impaired lung function from exposure to whole exhaust only.
Heinrich et al. 1995	Cancer	Wistar rats and NMRI mice	Diluted DE (0, 4.5, or 7.0 mg/m^3) for 18 hr/day, 5 days/wk for 13.5–24 mo	In mice, increased lung weight and PM lung burden; no difference in tumor incidence at either concentration. In rats, decreased body weight, increased lung weight and PM lung burden, impaired alveolar clearance, increased lung tumor incidence at higher concentration.
Ichinose et al. 1997	DNA damage and cancer	480 male ICR mice (4 wk)	DEP (intratracheally injected with 0.05, 0.1, and 0.2 mg) 1/wk for 10 wk; basal fat, high fat, and β-carotene–supplemented diets	An association was found between 8-OHdG levels and tumor development in mice treated with DEP.
Iwai et al. 2000	DNA damage and cancer	F344 female rats (8 wk), pathogen-free	Diluted exhaust from a light-duty engine (PM 3.5 ± 1.4 mg/m^3) for 1 to 12 mo (17 hr/day, 3 day/wk)	An association was found between 8-OHdG levels and tumor development in rats treated with DEP.
Kotin et al. 1954	Cancer	Mice	Extracts of both DE and gasoline-engine exhaust	Tumors in a mouse-skin-painting assay.
Lewis et al. 1967	Reproduction	LAF1 mice	Irradiated gasoline emissions	Reduced fertility in males but not females.
Lund et al. 2007	Histopathology, gene expression, and markers of oxidative stress in aorta and plasma	ApoE$^{-/-}$ mice (susceptible to atherosclerosis)	Filtered air, diluted gasoline-engine exhaust (PM 8, 40, or 60 µg/m^3), or filtered exhaust for 7 wk (6 hr/day, 7 days/wk)	Increased expression of factors associated with vascular remodeling and markers of oxidative stress in aortas with both whole DE and filtered DE.

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Table 5.3 (*Continued*). Summary of Animal Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Animal Model	Exposure Conditions (Concentration, Time)	Findings
Engine Exhaust (*Continued*)				
Mauderly et al. 1994b, 1996	Cancer	F344 rats and CD-1 mice	Diluted DE (0–7.0 mg/m^3) for 7–16 hr/day, 5 days/wk for 24 mo	In mice, no exposure-related increase in primary neoplasms, increase in lung burden, no effect on survival or body weight. In rats, increased incidence of tumors at high levels of DE (rat-specific lung clearance overload mechanism).
Moller et al. 2003	DNA damage	Guinea pigs	DEP (0, 0.7, and 2.1 mg) administered intratracheally	Elevated oxidative DNA damage (8-oxo-dG) and DNA strand breaks in the lungs of exposed animals. No increase in bulky DNA adducts.
Mori et al. 2007	Gene expression	Male C57/BL mice (6 wk)	DEP (subcutaneous 0.2-mL injection of 0.37 or 1.1 mg/mL DEP suspension) twice/wk for 5 wk	Several genes were differentially expressed in the testis following treatment.
Nagashima et al. 1995 and Tokiwa et al. 1999	DNA damage	Mice	DEP (after removal of organic compounds), benzo[*a*]pyrene, 1,8-dinitropyrene, and 1-nitropyrene; administered intratracheally	Elevated lung oxidative DNA damage (8-OHdG) after exposure to DEP only
Nemmar et al. 2003b	Perpheral thrombosis and lung inflammation	Hamsters	DEP (5–500 µg, instillation)	Enhanced thrombosis and inflammation. Similar effects Nemmar et al 2003a.
Nikula et al. 1995	Cancer	Male and female rats	Diluted DE or aerosolized carbon black (both 2.5 or 6.5 mg/m^3) 16 hr/day, 5 days/wk	Soot-associated organic components of DE are important in inducing carcinogenesis.
Ono et al. 2007 and Yoshida et al. 2006	Male puberty Spermatogenesis	Male mice exposed in utero	Pregnant mothers inhaled diluted DE (PM 0.3, 1.0, or 3.0 mg/m^3) from gestational day 2–16	Endocrine disruption after birth and accelerated male puberty. Detrimental effects on spermatogenesis (observed at 12 wk).
Reed et al. 2008	F344 rats: hematology, oxidant production, inflammation; SH rats: cardiovascular effects	F344 and SH rats	Diluted gasoline-engine exhaust (dilution ratios 1:10, 1:15, 1:90; PM 60 µg/m^3 at 1:10 dilution) or filtered exhaust (1:10), 6 hr/day, 7 days/wk for 1 wk to 6 mo	F344 rats: Increased red blood cells, mild lung inflammation, depression of oxidant production by alveolar macrophages, no significant effects from the most diluted exposure. SH rats: no effects on heartrate and ECG.
Spencer 1984	Neurologic effects	Rats	Gasoline vapor (8250 mg/m^3) for 6 hr/day for up to 18 mo	Axonal dystrophy within spinal cord and cell abnormalities in anterior horn.

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Table 5.3 (*Continued*). Summary of Animal Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Animal Model	Exposure Conditions (Concentration, Time)	Findings
Engine Exhaust (*Continued*)				
Stinn et al. 2005	Cancer	Male and female rats	Diluted DE (PM 3 or 10 mg/m^3), 6 hr/day, 7 days/wk for 2 yr; also sidestream smoke	Dose-related increase in inflammation; similar increase in lung tumor in the absence of DNA adducts at two DE concentrations.
Stupfel et al. 1973	Cancer	Male rats	Diluted gasoline-engine exhaust (23 ppm NO_x, 0.92 ppm NO_2, 0.3% CO_2, 2.0 ppm aldehydes, and 50 ppm CO)	Slight increase in appearance of tumors on increasing exposure but distributions similar in exposed and control groups and none found in lung.
Tsukue et al. 2001	Several parameters of fertility	Male rats (13 mo)	Diluted DE (PM 0.3, 1.0, 3.0 mg/m^3) for 8 mo	No changes in sperm counts were observed but effects on the accessory glands, increased serum LH and testosterone at 0.3 and 1.0 mg/m^3 DEP and a rise in testicular testosterone with 3.0 mg/m^3 were reported.
Tsukue et al. 2002	Fetal delivery and growth of the young	Young, C57BI-strain female mice	Filtered air or diluted DE (PM 0.3, 1.0, or 3.0 mg/m^3) 12 hr/day, 7 days/wk for 4 mo	Estrous females had significantly lower uterine weights, while in the mated females, 0.3, 1.0, and 3.0 mg/m^3 DEP led to abnormal deliveries in 9.1, 10.0, or 25.0% of the pregnancies. Body weights of the offspring were significantly lower at 6 and 8 wk, and sexual maturation was delayed.
Tsurudome et al. 1999	DNA damage and repair	Rats	DEP (2 and 4 mg) by intratracheal administration	Increased 8-hydroxyguanine in lung DNA, decreased 8-hydroxyguanine repair activities.
Vallyathan et al. 1986	Pulmonary circulation	F344 (SPF) rats	DEP (PM 2 mg/m^3) or air for 7 hr/day, 5 days/wk for 24 mo	No pulmonary hypertension, increased pulmonary arterial wall thickness, and dust-laden macrophages.
Vyskocil et al. 1988	Neurologic effects	Rats	Gasoline vapor (650 ppm) for 8 hr/day, 5 days/wk for 60 days	Significant increases in adrenal catecholamines and serum corticosterone; decreased hypothalamic noradrenaline; no changes in serum thyroxine. Observations suggest a non-specific stress response.

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Table 5.3 (*Continued*). Summary of Animal Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Animal Model	Exposure Conditions (Concentration, Time)	Findings
Watanabe 2005	Sperm production	36 pregnant rats exposed, testicular function tested on male offspring (96 days)	Filtered air, whole DE (PM 1.71 mg/m^3 and NO_2 0.80 ppm, or PM 0.17 mg/m^3 and NO_2 0.10 ppm), or filtered DE (NO_2 0.80 or 0.10 ppm) (gestational day 7 to delivery)	Exposed rats exhibited decreased daily sperm production.
Watanabe and Kurita 2001	Fetal outcomes	72 pregnant rats and 19 nonpregnant rats	Filtered air, whole DE (PM 5.6 mg/m^3, NO_2 4 ppm, NO 8 ppm) or filtered DE (gestational day 7 to delivery)	Delayed and disturbed differentiation of the testis, ovary, and thymus in the offspring of rats exposed; maternal testosterone and progesterone levels were significantly higher and lower, respectively, in rats exposed to total exhaust and filtered exhaust.
Watanabe and Oonuki 1999	Several parameters of fertility	Young male rats	Filtered air, whole DE (PM 5.63 mg/m^3, NO_2 4.1 ppm, NO 8.10 ppm), or filtered DE from birth to 3 mo (6 hr/day for 5 days/wk)	Serum testosterone and estradiol were significantly higher and FSH was significantly suppressed in both exhaust groups. Significant declines in LH were seen in the total exhaust group. No difference in testis weight was observed but sperm production and activity of testicular hyaluronidase were significantly reduced in both exhaust-exposed groups.
Yoshida et al. 1999	Several parameters of fertility	Male mice	DEP (PM 0.3 to 3.0 mg/m^3) for up to 6 mo (12 hr/day)	Exposure to DEP led to ultrastructural changes and reduced LH receptor mRNA expression in Leydig cells and sperm production.
Other				
Cassidy et al. 1983	Sperm effects	Male Wistar rats (10 wk)	Formaldehyde (100 and 200 mg/kg) administered orally	Increases in the incidence of abnormal sperm but no effect on testis weight or sperm count.
Chan 1996	General toxicity reproductive effects	Male and female rats	1-nitropyrene aerosol (0.5 to 50 mg/m^3)	No effects on sperm motility or vaginal cytology.
Dempster et al. 1984	Behavioral and hematologic changes	C57BL mice	Benzene (100, 300, 1000, or 3000 ppm) for 6 hr/day for number of days to achieve a minimum of 3000 ppm days	Significant increases in milk-licking responses during first wk of exposure to 100 and 300 ppm, food intake and body weight reduced at high dose; decrease in circulating lymphocytes and anemia.

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Table 5.3 (*Continued*). Summary of Animal Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Animal Model	Exposure Conditions (Concentration, Time)	Findings
Other (*Continued*)				
Dorman et al. 2001	Delivery of inhaled manganese into the brain, lung, and liver	Adult male CD rats	Soluble sulfate ($MnSO_4$) or insoluble tetroxide (Mn_3O_4) (0, 0.03, 0.3, or 3.0 mg/m^3) 6 hr/day; 7 days/wk	Soluble form of Mn ($\geq$ 0.3 mg/m^3) results in elevated concentrations in the brain and lung.
Drinker et al. 1979	Neurological effects	Humans	Gasoline vapor (5,500–14,300 mg/m^3) for 6 hr	Dizziness, nausea, and headache; intoxication and partial anesthesia at highest concentration.
Drown et al. 1986	Manganese uptake into major organs	Adult male Sprague-Dawley rats	Soluble $MnCl_2$ or insoluble Mn_3O_4 (1 µmol) labeled with ^{54}Mn (8 µCi) by instilled intratracheally	More rapid uptake of Mn in the chloride form, rapid clearance from the lungs and slow clearance from the brain (high levels for several weeks).
Dutch Expert Committee for Occupational Standards 1992	Neurological effects	Rats	Gasoline (5500 mg/m^3) for 6 hr	Loss of coordination.
Furuta et al. 2004	Estrogenic activity	Ovariectomized female rats (25 day) (also in vitro using uterine horns and recombinant yeast screens)	3-Methyl-4-nitrophenol (100 mg/kg) and 4-nitro-3-phenylphenol (0.1 and 1.0 mg/kg) injected subcutaneously for 2 days	Significant increases in uterine weight.
Hsieh et al. 1988	Brain monoamine neurotransmitters	Mice	Benzene (8 mg/kg) each day in drinking water	Increased levels of catecholamines in the brain.
Jayasekara et al. 1992	Brain biogenic amines and selected metabolites	Male CD-1 mice	Benzo(*a*)pyrene (0, 5, 25, and 100 mg/kg) injected intraperitoneally 2/wk for 3 wk	Increased metabolism of monoamines in the brain.
Li et al. 2006a	Testicular function	Adult male Japanese quail	3-Methyl-4-nitrophenol (78, 103, or 135 mg/kg of body weight) administered by a single intramuscular injection	Exposure caused testicular atrophy associated with reduced sperm formation and lowered plasma LH. A significant reduction of testosterone secretion was seen in a time- and dose-dependent manner.

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Table 5.3 (*Continued*). Summary of Animal Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Animal Model	Exposure Conditions (Concentration, Time)	Findings
Other (*Continued*)				
Lo Pumo et al. 2006	Neurotoxicologic effects	Sprague-Dawley pregnant rats and pups (2-mo-old males for motor activity study)	Benzene (0.1 mg/kg) injected subcutaneously at day 15 of gestation	Long-lasting changes in motor behavior and cognitive processes in the offspring of injected rats.
Lu et al. 2008	Learning and memory capacity (Morris water maze)	Mice	Gaseous formaldehyde (0, 1, or 3 mg/m^3)	Learning and memory were adversely affected at 3 mg/m^3 but not at lower concentrations.
Majumder and Kumar 1995	Male reproductive system health	Male rats	Formaldehyde (10 mg/kg body weight/day) for 30 days	Decreased sperm motility, viability, and count, and lowered DNA content in the testis and prostate.
Martin 1990; Saillenfait et al. 1989; U.S. Department of Health and Human Services 1999; Ulsamer et al. 1984	Teratogenicity	Rats and mice	Various inhalation exposure regimens of formaldehyde	Embryo toxicities including increased mortality and anomalies, decreased concentrations of ascorbic acid, and presence of abnormalities in enzymes of mitochondria, lysosomes, and the endoplasmic reticulum.
Miele et al. 2000	Striatum and brainstem hypoxanthine, xanthine, uric acid and glutamate levels	Rats (3 and 20 mo)	$MnCl_2$ (50–200 mg/kg/day, subchronic oral exposure)	Increases in glutamate and high-energy phosphate levels.
Montes et al. 2001	Striatal dopamine turnover	Bile-duct–obstructed rats	$MnCl_2$ (0.5 and 1 mg/mL of Mn^{2+} in drinking water) for 4 wk	Diminished striatal dopamine content in cirrhotic rats, which increased following $MnCl_2$.
Odeigah 1997	Reproductive system health	Male and female albino rats (12–14 wk)	Formaldehyde (0.125–0.500 mg/kg) five daily intraperitoneal injections	Increased sperm-head abnormalities and a reduction in fertile matings in females mated 1–7 days post treatment of males.

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Table 5.3 (*Continued*). Summary of Animal Studies Discussed in Chapter 5[a]

Reference	Health Endpoint	Animal Model	Exposure Conditions (Concentration, Time)	Findings
Other (*Continued*)				
Pitten et al. 2000	Neurotoxicologic effects	Wistar rats	Formaldehyde or water steam (2.6 ppm or 4.6 ppm) for 90 days (10 min/day, 7 days/wk)	Exposed rats required more time in a maze to find food and made more mistakes than the control group.
Tilson et al. 1980	Neurobehavioral functioning	Male and female Fischer rats	Benzene (550 mg/kg) on days 9, 11, 13 postpartum, injected intraperitoneally	Increased spontaneous motor activity and decreased response to d-amphetamine challenge.
Ungváry and Tátrai 1985 and Hudák and Ungváry 1978	Embryo toxicity	Rats, mice, rabbits	In mice and rabbits, benzene, toluene, xylene, ethylbenzene, Aromatol (500 or 1000 mg/m^3) for 24 hr/day from day 6–15 of pregnancy. In rats, ethylbenzene (600, 1200, or 2400 mg/m^3), xylene (250, 1900, or 3400 mg/m^3), Aromatol (500, 1000, or 2000 mg/m^3) for 24 hr/day from day 7–15 of pregnancy.	Induced skeletal anomalies and retardation of fetal development in rats and mice and spontaneous abortion in rabbits, not teratogenic in any of the species.
Zhou et al. 2006	Testicular structure and function; oxidative damage	Male rats	Formaldehyde (10 mg/m^3) or formaldehyde and vitamin E (orally administered) for 2 wk	Destruction of testicular structure and sperm quantity and quality was partially reversed by vitamin E.

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ABBREVIATIONS AND OTHER TERMS

8-OHdG	8-hydroxy-2′-deoxyguanosine
8-oxo-dG	8-oxo-7,8-dihydro-2′-deoxyguanosine
AL	human–hamster hybrid cell
ADMA	asymmetric dimethylarginine
AP-1	activator protein 1
$ApoE^{-/-}$	apolipoprotein E knockout
BALB/c	laboratory-bred strain of the house mouse
CAPs	concentrated ambient particles
CO	carbon monoxide
CO_2	carbon dioxide
COPD	chronic obstructive pulmonary disease
DE	diesel exhaust
DEP	diesel-exhaust particulate matter (also referred to as DPM)
EC	elemental carbon
ECG	electrocardiogram
FEV_1	forced expiratory volume in 1 second
FMD	flow-mediated dilatation
FSH	follicle-stimulating hormone
FVC	forced vital capacity
GLAST	glutamate–aspartate transporter
GRO-α	growth-regulated oncogene alpha
H_2O_2	hydrogen peroxide
HO-1	heme oxygenase
HPAEC	human pulmonary-artery endothelial cells
HRV	heart-rate variability
ICAM-1	intercellular adhesion molecule-1
IgE	immunoglobulin E
IL	interleukin
JNK	c-jun N-terminal kinase
LDH	lactate dehydrogenase
LH	luteinizing hormone
LPS	lipopolysaccharide
MMT	methylcyclopentadienyl manganese tricarbonyl
Mn	manganese
$MnCl_2$	manganese chloride
Mn_3O_4	manganese tetroxide
mRNA	messenger RNA
MTBE	methyl tertiary butyl ether

NADPH	nicotinamide adenosine dinucleotide phosphate
NF	nuclear factor
NIR	near-infrared
NO	nitric oxide
NO_2	nitrogen dioxide
NO_x	nitrogen oxides
O_2	oxygen
O_3	ozone
PAHs	polycyclic aromatic hydrocarbons
PM	particulate matter
$PM_{2.5}$	PM with an aerodynamic diameter ≤ 2.5 µm
PM_{10}	PM with an aerodynamic diameter ≤ 10 µm
ROS	reactive oxygen species
SH	spontaneously hypertensive
SO_x	sulfur oxides
TNF-α	tumor necrosis factor alpha
U.S. EPA	U.S. Environmental Protection Agency
UFP	ultrafine particles
VOCs	volatile organic compounds

Chapter 6

A Synthesis of Evidence from Epidemiology and Toxicology

CONTENTS

Chapter 6

A Synthesis of Evidence from Epidemiology and Toxicology

6.I INTRODUCTION

As noted in the introduction to Chapter 5, epidemiology and toxicology studies each bring different strengths and limitations to the characterization of the health effects associated with primary traffic-generated pollution. The purpose of this chapter is not to highlight these strengths and limitations but rather to identify the areas where the results from the two disciplines provide complementary evidence for the causality of specific associations observed in human-population studies. In this context, controlled-human-exposure studies — where they exist — potentially carry considerable weight in the synthesis. We have intentionally refrained from further detailed discussion of the relevance of specific types of in vitro or in vivo toxicology studies for understanding the associations between human exposure and disease; these were discussed in Chapter 5, in the section on study-design issues. Instead, we will discuss the extent to which the results from toxicologic studies do or do not provide general mechanistic support for the observations and inferences derived from epidemiology studies. Of necessity, this involves some consideration of the relevance of toxicology-study designs, and where appropriate, we take note of these. With such a limited focus, we realize that we are ignoring important issues related to species-specific dosimetry, target-tissue exposure, and exposure–response differences; the fact that exposure–response relations derived from animal studies might not have direct relevance to humans for a variety of reasons (including anatomy, toxicokinetics, and toxicodynamics); and the constraints on the exposure regimens used in these studies compared with the exposures that humans experience in actual ambient environments.

SIDEBAR 6.1 Classification of Epidemiologic Evidence for Causal Associations Between Traffic Exposure and Mortality and Cardiovascular Outcomes

All-Cause Mortality (section 4.II)

- "Suggestive but not sufficient" to infer a causal association (section 4.II.3)

Cardiovascular Morbidity (section 4.III)

Physiology (section 4.III.1)

- "Suggestive but not sufficient" to infer a causal association
  - Noise and stress not addressed

Acute myocardial infarction and atherosclerosis (section 4.III.2)

- "Suggestive but not sufficient" to infer a causal association
  - Too few well-performed studies

6.II CARDIOVASCULAR-HEALTH EFFECTS

Sidebar 6.1 summarizes the conclusions about the extent to which the epidemiologic data reviewed in this report are sufficient, or not, to infer a causal association between traffic pollution and cardiovascular outcomes. In keeping with some of the conclusions in the epidemiology section, the summary of the toxicologic data (Chapter 5, 5.III.7) also noted the lack of an adequate number of studies examining the cardiovascular effects of traffic emissions specifically. Nonetheless, based largely on the studies that used diesel-exhaust particles in humans, animals, and in vitro, the section concluded that "the recent toxicology literature provides suggestive evidence that exposure to pollutants that are components of traffic emissions, including ambient and laboratory-generated particulate matter (PM*) and diesel- and gasoline-engine exhaust, alters cardiovascular function."

Unfortunately, the number of studies with human volunteers exposed to real-world traffic mixtures is very small, and the evidence from them is not consistent and covers only a limited range of physiologic and cellular outcomes (the human studies discussed in Chapter 5 were summarized in Table 5.2). The evidence from these studies was, therefore, less compelling. Obviously, human-exposure studies by their nature are limited in size in such a way that any one study covers only a limited range of subjects,

* A list of abbreviations and other terms appears at the end of this chapter.

SIDEBAR 6.2 Classification of Epidemiologic Evidence for Causal Associations Between Traffic Exposure and Respiratory Symptoms in Children

Asthma incidence (new onset) (section 4.IV.2.A)

- Between "sufficient" and "suggestive but not sufficient" to infer a causal association (section 4.IV.2.C)

Conclusions dependent on weight given to consistency and precision of results

Asthma prevalence (section 4.IV.2.B)

- Between "sufficient" and "suggestive but not sufficient" to infer a causal association (section 4.IV.2.C)

Exacerbation of respiratory symptoms in children with and without asthma (section 4.IV.2.D)

- "Sufficient" to infer a causal association for exacerbation of asthma, "inadequate and insufficient" for children without asthma (section 4.IV.2.F)

Health-care utilization for respiratory problems (section 4.IV.2.E)

- "Inadequate and insufficient" to infer a causal association (section 4.IV.2.F)

SIDEBAR 6.3 Classification of Epidemiologic Evidence for Causal Associations Between Traffic Exposure and Respiratory Symptoms in Adults

Asthma and respiratory symptoms (sections 4.IV.3.B, 4.IV.3.C, and 4.IV.4)

- "Inadequate and insufficient" to infer a causal association for asthma
- "Suggestive but not sufficient" to infer a causal association for exacerbation of respiratory symptoms
- "Inadequate and insufficient" to infer a causal association for health-care utilization

exposure scenarios, and outcomes. Nonetheless, they do provide consistent evidence for associations between exposure to PM and impaired cardiovascular responses.

Although the evidence from toxicology studies in isolation is not sufficient in terms of a causal association between traffic emissions and the incidence or progression of cardiovascular disease, when viewed together with the epidemiologic evidence, a stronger case could be made for a potential causal role for traffic-related pollutants in cardiovascular-disease morbidity and mortality.

The extent to which these associations apply to individuals who do not already have underlying cardiovascular disease and the specific components of traffic emissions that are responsible for the associations cannot be determined from the (toxicologic and epidemiologic) bodies of evidence available at this time.

6.III RESPIRATORY-HEALTH EFFECTS

6.III.1 RESPIRATORY-HEALTH SYMPTOMS IN CHILDREN AND ADULTS

Sections 4.IV.2 and 4.IV.3 of Chapter 4 discussed the epidemiologic data on asthma and respiratory symptoms in children and adults, respectively. Sidebars 6.2 and 6.3 summarize our conclusions from these sections. The evidence for adults was very sparse; that for children was much more abundant and hence more amenable to evaluation. As noted in Chapter 5, studies have shown that "[e]xposure to components of traffic pollution resulted in mild acute inflammatory responses in healthy individuals and enhanced allergic responses in asthmatic allergic subjects and in animal models." The animal studies, however, did not employ actual traffic exposures, a fact that limited their overall impact on the assessment of the evidence; the section concluded that future research "should include more direct analysis of actual traffic-mixture exposures in vivo and in vitro" to clarify the quality of the evidence. Nonetheless, it is worth noting that the few published * human-exposure studies (section 5.IV.1.A in Chapter 5) in which humans have been exposed to realistic traffic pollution are supportive of the possibility that people with asthma might be more susceptible to adverse health effects related to such exposures. Unfortunately, in the studies that have involved human exposures to concentrated ambient particles (CAPs) in non-urban environments, the relative contribution of traffic components to the CAPs exposures was not specifically measured (section 5.IV.2.A in Chapter 5). Moreover, CAPs exposures are in general difficult to extrapolate to traffic exposures, because CAPs include both traffic- and non-traffic-related pollutants. Finally, results of controlled human exposure to whole diesel exhaust are difficult to interpret; some of the results are at first glance counterintuitive (section 5.IV.3.A in Chapter 5).

* The degree to which publication bias is present for human-exposure studies in which humans have been exposed to realistic traffic pollution cannot be ascertained.

SIDEBAR 6.4 Classification of Epidemiologic Evidence for Causal Associations Between Traffic Exposure and Lung Function and COPD

Lung Function (sections 4.V.2 and 4.V.3)

- "Suggestive but not sufficient" to infer a causal association for either acute or long-term exposure (section 4.V.3)

COPD (section 4.V.4)

- "Inadequate and insufficient" to infer a causal association

When the epidemiologic and toxicologic data are viewed together, a case can be made that there are likely to be causal associations between exposure to traffic-related air pollution and asthma exacerbation and certain respiratory symptoms. The rationale for this judgment is addressed more fully in Chapter 7. However, the lack of a large body of toxicologic data (at the physiologic, cellular, and molecular levels) based on human and animal exposures to real-world traffic pollution and the substantial uncertainties that remain about the exposures in epidemiology studies make it hazardous to conclude that causality has been established at this time for all respiratory symptoms at all ages.

6.III.2 LUNG FUNCTION AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

As indicated in Sidebar 6.4, there have been too few studies of exposure to traffic-related ambient pollution and chronic obstructive pulmonary disease (COPD) to make any statement about the evidence; we focus, therefore, only on the lung-function results of the toxicologic and epidemiologic studies. In terms of toxicology, the very limited amount of data on controlled human exposures indicates reductions in FEV_1 (forced expiratory volume in 1 second) and increases in inflammation that are not necessarily related to each other. Virtually no data are available from animal models. Although, as noted in Chapter 5, exposure to diesel-exhaust PM is associated with inflammation and airway hyperresponsiveness, effects on lung function have seldom been evaluated. Airway inflammation can certainly lead to altered lung function (e.g., after direct exposure to cigarette smoke) in acute- and chronic-exposure settings, and this inflammation has been observed in controlled-human-exposure studies using ozone, PM, and diesel-exhaust PM. Nonetheless, until more studies are conducted with traffic-relevant exposures in humans and animal models, inferences cannot be made about the role, if any, of traffic exposure in altering lung function.

In summary, the aggregate toxicologic and epidemiologic evidence is simply too sparse to permit any inference with respect to causal associations between chronic exposure to traffic-related air pollution and altered lung function in older adults or the occurrence of COPD. CAPs studies to date have uniformly shown no acute-exposure effects on lung function. Although the epidemiology studies do provide suggestive evidence for chronic-exposure effects on lung function in adolescents and young adults, there are too few toxicologic data to indicate what mechanisms underlie these observations.

SIDEBAR 6.5 Classification of Epidemiologic Evidence for a Causal Association Between Traffic Exposure and Nonasthmatic Respiratory Allergy

Allergy (section 4.VI)

- "Inadequate and insufficient" to infer a causal association

6.III.3 NONASTHMATIC RESPIRATORY ALLERGY

As noted above, the toxicologic data provide strong mechanistic evidence for associations between the diesel-PM component of traffic pollution and immunoglobulin E (IgE)-mediated allergic reactions and some evidence for an association between nitrogen dioxide and late-phase response to allergen. However, the epidemiologic data (see Sidebar 6.5) are inconsistent, and it is difficult to determine the relevance of the human-exposure data from toxicology studies (often with nasal instillation with diesel-exhaust PM) to the actual manifestations of nonasthmatic allergic phenotypes (such as allergic rhinitis or conjunctivitis, eczema, serum-specific IgE, and evidence of sensitization to aeroallergens).

6.IV CANCER AND MUTAGENICITY

As noted in section 4.VIII of Chapter 4, we did not review the evidence on the association between occupational exposures and cancer of the lung (the primary target organ for exposure to air pollution) and the blood in adults. Rather, we focused on studies in open populations with general exposure to traffic pollution. Our conclusions are summarized in Sidebar 6.6. Section 5.V.5 of Chapter 5 reached the following conclusion with respect to the toxicologic data: "Although studies in cells demonstrating the

SIDEBAR 6.6 Classification of Epidemiologic Evidence for Causal Associations Between Traffic Exposure and Cancer (section 4.VIII)

Childhood cancers

- Leukemia and brain and other cancers
- "Inadequate and insufficient" to infer causal associations

Adult cancers

- Lung and other cancers from studies in general populations
- "Inadequate and insufficient" to infer causal associations

capacity of DEP [diesel-engine particulate] to induce DNA-strand breaks, base oxidation, and mutagenicity provided a possible mechanism for the induction of carcinogenicity by traffic-related pollution, the applicability of in vitro mutagenicity studies to human-risk assessment has been questioned. Animal studies have demonstrated the ability of high concentrations of exhaust components from both diesel- and gasoline-fueled engines to cause cancer in animals." Although some of these data are compelling, it is almost impossible to relate them directly to data from epidemiology studies in the non-occupational settings reviewed in Chapter 4. Any statement, therefore, that tries to synthesize the two sources of data appears to be premature at this time.

6.V REPRODUCTIVE-HEALTH AND BIRTH OUTCOMES

There is almost no overlap between the toxicologic and epidemiologic data for reproductive-health and birth outcomes. The toxicologic data contain virtually no studies that relate to the types of birth outcomes evaluated in the epidemiology studies, such as pre-term birth and low-weight birth (see section 4.VII in Chapter 4, in which the evidence was judged "inadequate and insufficient"). Conversely, no epidemiology studies were found that investigated effects on fertility, although a substantial number of animal studies were found that investigated effects on reproductive organs and sperm functionality. The conclusions derived from these two chapters therefore do not lend themselves to any overall synthesis.

6.VI NEUROTOXICITY

Both the toxicologic and epidemiologic data on neurotoxicity are inadequate at this time to discuss any further.

6.VII SUMMARY

This chapter has summarized the areas of overlap between findings from epidemiology and toxicology studies. Our analysis has pointed out varying degrees of congruency between the two disciplines. The highest degree was observed for cardiovascular outcomes and for asthma symptoms. What is clear is that epidemiology and toxicology each have their own inherent limitations with respect to the establishment of a causal association between exposure to traffic-related pollution and adverse human-health outcomes. These limitations are such that it is not realistic to expect clear congruency between the findings from the two disciplines. This lack of congruency is not necessarily prima facie evidence against the existence of causal associations — it simply points to the need for a more subtle synthesis of the evidence. Such a synthesis is provided in Chapter 7.

ABBREVIATIONS AND OTHER TERMS

CAPs	concentrated ambient particles
COPD	chronic obstructive lung disease
DEP	diesel exhaust particulate
FEV_1	forced expiratory volume in 1 second
IgE	immunoglobulin E
PM	particulate matter

Chapter 7

Conclusions

CONTENTS

Chapter 7

Conclusions

7.I. INTRODUCTION

The goals of Chapter 7 are to summarize and synthesize the information provided in this special report. The Chapter Summaries section brings together the main conclusions from each chapter — from emissions from motor vehicles (Chapter 2) to exposures to traffic-related air pollution (Chapter 3) to health effects in epidemiologic studies (Chapter 4) and toxicologic studies (Chapter 5) This section also brings together materials from each chapter that can provide guidance for improving future research on the associations between exposure to traffic-related air pollution and health outcomes.

The Synthesis and Conclusions section considers the materials presented on emissions and exposure that provide links between the sources of the pollutants, the measures of exposure, and the health effects observed. The conclusions drawn in Chapter 4 are refined in this section by considering the implications of the data from the other chapters in order that final, overall conclusions can be drawn about causal associations between exposure to traffic-related pollution and human health.

7.II. CHAPTER SUMMARIES

7.II.1 CHAPTER 2: EMISSIONS FROM MOTOR VEHICLES

Emissions from motor vehicles are a major contributor to urban air pollution for all regulated air pollutants except sulfur dioxide (SO_2*) (at least in developed countries, where sulfur is now present only in very low concentrations in gasoline, diesel, and other fuels). They are also increasingly important contributors to global anthropogenic emissions of greenhouse gases. Regulatory actions and considerable technologic advances have helped reduce motor-vehicle emissions of carbon monoxide (CO), hydrocarbons, nitrogen oxides (NO_x), and particulate matter (PM). Additional reductions are anticipated with the introduction of new, cleaner fuels and tailpipe-control technologies for motor vehicles with diesel engines. As discussed in Chapter 2, data from the U.S. EPA showed that significant progress has been made in the United States in reducing the amount of pollutants from motor vehicles despite substantial growth in vehicle numbers and vehicle miles traveled.

Forecasts indicate a continued increase in the worldwide motor-vehicle fleet commensurate with population growth and economic improvements. This trend, together with the rapid expansion of metropolitan areas in developing countries and the increased dependence on motor vehicles (due to the intense development of suburban areas), has resulted in population increases near traffic sources, indicating that emissions from motor vehicles must be considered in the context of their spatial placement in populated areas. Exposure to traffic-related air pollutants will therefore remain a concern with respect to human health in much of the world for some time to come.

Characterization of the release, transformation, and dispersion of traffic emissions is the first step toward understanding the potential (qualitative and quantitative) exposures faced by human populations. Given the high cost of collecting the necessary data (e.g., on the distribution of vehicles in space and time, traffic counts, the types of vehicles and their operational characteristics, the fuels in use, and the emissions controls in place), the Panel concluded in Chapter 2 that, at present, vehicle miles traveled — as estimated on the basis of traffic-demand models — represented the best starting point for estimating regional emissions. Although improvements in computer models that use vehicle emissions to estimate emissions rates for a variety of compounds, including greenhouse gases, regulated pollutants, and selected air toxics (section VI of Chapter 2), have been made, substantial uncertainties about these estimates remain because the models fail to account for the effects of roadway grades, operating modes, and high-emitting vehicles. The recent recognition of the importance of the contribution of noncombustion emissions, such as brake and tire wear and resuspended road dust, to traffic emissions adds even more uncertainties to current emissions estimates, because the emissions rates and composition of these sources have not yet been fully characterized. Uncertainties about noncombustion emissions undermine the reliability of estimates made by source-apportionment models of motor vehicles' contributions to air pollution, because neither emissions inventories nor receptor models adequately characterize the contribution of these dusts. With the introduction of new controls on PM emissions, contributions from noncombustion sources are likely to play a greater role in roadside exposures.

* A list of abbreviations and other terms appears at the end of this chapter.

In Chapter 2, the Panel identified a number of other factors that pose challenges for current estimates of emissions and need to be considered if direct and model-based estimates are to be improved in the future. The Panel also identified new field-measurement approaches, technologies, sampling strategies, and receptor-modeling methods that offer promise in remedying some of these challenges. The most important of the challenges are as follows:

1. The cross-checking of PM-emissions estimates against actual field data has been limited. This represents a major shortcoming in the evaluation of models of emissions simulation and exposure.
2. The limited number of roadside monitors and measurements has made it difficult to track trends in motor-vehicle emissions of CO, volatile organic compounds (VOCs), NO_x, and PM.
3. The same limited number of roadside monitors and the limited availability of instrumentation have made it difficult to track the chemical and physical transformations of pollutants from traffic. The transformations that occur in the early stages of exhaust dilution and in plume entrainment can produce toxic gases as well as semivolatile and particle-phase constituents that might have relevance for human health, but these have not typically been measured.
4. The quality of the emissions profiles used to apportion the chemical composition of species-specific sources is not always adequate or current. Many emissions profiles have not been updated for a decade or more and might not reflect technologic changes that have occurred. Needless to say, this contributes to the uncertainties in species-specific emissions estimates.

In summary, in Chapter 2 the Panel pointed to the need for more extensive monitoring of on-road emissions and for a greater focus on measurements encompassing a wider range of pollutants derived from combustion and noncombustion sources and from the physical and chemical transformations that primary emissions undergo. There is also a need to improve the range and quality of emissions inventories and models by expanding the range of factors associated with roadway traffic and the operation of vehicles. These conclusions are relevant to the interpretation of data from current epidemiologic and toxicologic studies. Estimates of exposure to traffic-related pollutants in large-scale epidemiologic studies, particularly longitudinal studies of the effects of long-term exposure, depend to some extent on our ability to apportion the contributions of these pollutants accurately to ambient air pollution (i.e., by identifying surrogates for exposure to traffic-related pollutants) and on estimates of traffic's contributions from receptor modeling over time. Improvements in the range and quality of surrogates and source estimates (with respect to the "true" exposures) will therefore depend on improved characterization of emissions and their transformations and dispersion over space and time on their own and in relation to other sources. Toxicologic studies, too, depend on similar knowledge, particularly studies of traffic-source mixtures in human, animal, and in vitro exposure models. Understanding the health effects of sources and mixtures will be an important new consideration for future human controlled-exposure and epidemiologic studies (Nadadur et al. 2007).

7.II.2 CHAPTER 3: EXPOSURE TO TRAFFIC-RELATED AIR POLLUTION

The emphasis in Chapter 3 (as well as in Chapters 4 and 5) is on primary traffic-generated pollution,* not on the more broadly dispersed secondary pollutants, such as ozone, that are derived from primary traffic-generated pollution and that appear to have important, independent health effects.

Accurate assessment of exposure to traffic-related pollution and identification of its associated health effects are a sine qua non for evaluating the causal character of the epidemiologic associations. Given the complexity of emissions from motor vehicles and the chemical transformations they undergo in the atmosphere, surrogates† of primary traffic-generated pollution (such as concentrations of specific pollutants present in motor-vehicle emissions or measures of traffic density and distance from major roads) have played, and will continue to play, a central role in estimating exposure in epidemiology studies of traffic-related pollution and its health effects. Modeling approaches have also played an important role. Thanks to methodologic advances in computing distances from emissions sources and in the incorporation of measures of land use and pollutant dispersion, the role of modeling in estimating exposure is likely to expand.

In section 3.II.3 of Chapter 3, the theoretic characteristics of an ideal surrogate were listed: (1) traffic is the surrogate's only or major source, (2) concentrations of the surrogate vary over time with those of other constituents of traffic emissions, (3) the surrogate can be measured accurately and reasonably cheaply, and (4) the surrogate does not have independent adverse health effects associated with it at the concentrations observed in various environments. (The fourth criterion applies almost exclusively to

* *Primary traffic-generated pollution* refers to pollution emitted directly from the tailpipes of motor vehicles and to its rapidly formed near-source physical and chemical transformation products.

† Here, *surrogate* refers to a measure used to represent exposure to a traffic source.

single-pollutant surrogates such as CO or NO_2 [nitrogen dioxide]; it is not applicable to traffic exposure estimates derived from exposure models.) While recognizing that this ideal cannot be achieved, the criteria are a useful touchstone by which to judge the quality of assessments of exposure to traffic-related pollutants in human health studies. The Panel considered the surrogates that have been most commonly used in epidemiology studies to assess the health effects of traffic-related air pollution, including CO, NO_2, PM mass and number, elemental carbon (EC; also referred to as black carbon, or BC), and benzene as well as direct measures of traffic.

The utility of a surrogate for primary traffic-generated pollution, even apart from its quality, depends on identifying the extent of the area over which the primary traffic-generated pollution is likely to influence human health. Based on a synthesis of the best available evidence, the Panel identified an exposure zone within a range of up to 300 to 500 m from a major road as the area most highly affected by traffic emissions (the range reflects the variable influence of background pollution concentrations, meteorology, and season). It is estimated that 30% to 45% of people in large North American cities are likely to be inside one or more such zones.

In terms of their relevance to epidemiology studies of human health, several additional points emerged from the chapter and are summarized separately below.

7.II.2.A Modeling Approaches (Section 3.IV in Chapter 3)

A useful hierarchical framework for the evaluation of approaches to exposure modeling is presented in this section of Chapter 3 in order to assess the quality of assignments of exposure. This hierarchy of modeling approaches is based on the degree of closeness with which the various models approximate actual exposures. Because of the importance of the exposure-modeling framework to the criteria for causal inference (see summary in section 7.II.3 of this chapter), part of the framework is summarized here (see Table 7.1). In Table 7.1, as we move down the rows (i.e., up the hierarchy), the requirements for both better emissions data and more proximate measurement data increase.

Although simple proximity models (such as distance to major road) are the easiest to implement, they are error prone because they ignore the parameters that affect the dispersion

Table 7.1. Exposure-Assessment Models[a]

Model	Theory–Concept Match	Data Requirements	Utility to Health Studies
Proximity	Low	Distance to roads, traffic volume, questionnaire data	Low (crude, error prone)
Geostatistical	Medium	Topography, socioeconomic data, location of monitors, monitoring data	Depends on the density of the monitoring network; most standard government networks do not support interpolation of traffic pollutants
Land-Use Regression	Medium	Traffic volumes, land cover, meteorologic data, monitoring data	Depends on the density of monitoring and quality of land-use data
Dispersion	Medium	Meteorologic data, traffic volumes, emissions data from point and line sources, topographic data, background concentrations	Often lacks adequate data to support; depends on quality of data input
Hybrid[b]	High[c]	Personal monitoring data, questionnaire data (socioeconomic data, activities), monitoring data, other depending on the combination	Very good but expensive

[a] For more details, see Table 3.3 in Chapter 3.

[b] Requires personal monitoring plus one or more of the previous methods.

[c] Recent advances in Bayesian modeling enable integration of personal monitoring data with data from central-site monitors and intra-urban models. See Appendix C of Chapter 3 (available on the HEI Web site).

and physicochemical activity of air pollutants. Moreover, estimates based on proximity models can be confounded by factors such as socioeconomic status, with its many implications for human health and exposure to pollutants, and exposure to noise (although there are at this time few data to support noise as a confounder). Geostatistical models are best implemented in conjunction with dense, well-distributed monitoring networks; their chief limitations are the size of the network and the number of measurements needed over time to estimate pollution surrogates accurately. Land-use regression is appealing in that it can account for the diversity of sources that contribute to a surrogate; however, unless the true contribution (in terms of associated variance) of traffic to the regression is known, it is difficult to interpret the estimated exposure as related to air pollution from traffic. Dispersion models explicitly incorporate meteorologic data but must be calibrated correctly to realize their advantages. These models are very data- and computation-intensive and depend on the validity of the model assumptions. Hybrid models that combine measurements of personal exposure to traffic surrogates with other exposure data come closest to a logistically feasible "best" estimate of human exposure. However, although personal-exposure sampling is extremely useful in estimating exposure-measurement errors in the other data sources, it is necessarily limited in practice by cost and subject-compliance issues.

7.II.2.B Measurement of Surrogates for Urban Exposure (Section 3.II.3 in Chapter 3)

Several points relevant to the evaluation of the health effects of exposure to traffic-related pollution were raised by the Panel in Chapter 3:

1. Emissions from both light- and heavy-duty vehicles have varied greatly over time, as have emissions of surrogates. The implication of this fact for studies of human health is that estimates of health associations based on past estimates of exposure (by whatever method of exposure assignment; see Table 7.1), although reflective of past exposures, might not be useful for estimating health associations in the future. Emissions have changed, and will continue to change, both quantitatively and qualitatively. Because the traffic emissions used in the past do not provide data on specific emissions components that are actually responsible for the observed health effects, we can only approximate what the effects will be as emissions continue to change in the coming years. Even if, for example, concentrations of traffic-related pollution decrease overall, it is possible that (independent of possible measurement errors or modeling uncertainties) changes in the relative concentrations of its components could cause associated health effects to increase, decrease more than expected, or remain unchanged.
2. None of the surrogates considered in the chapter met all the criteria for an ideal surrogate. Data are not available on the ratios of the surrogates to the complex pollutant mixtures emitted by traffic and how these ratios have varied over time. CO, benzene, and NO_x (in this case NO_2), found in on-road vehicle emissions, are components of emissions from all sources. All also have significant ambient and microenvironmental sources, making it difficult to disentangle the contributions from motor vehicles. Primary on-road emissions of PM represent a small contribution to emissions from all sources. Our understanding of the quality of the surrogates (i.e., their degree of association with "true" traffic exposure) therefore depends very much on our understanding of the contributions from other sources (this is the principal reason why Chapter 4 was limited to studies in which the surrogates used [e.g., NO_2 or BC] were documented to have been derived primarily from traffic).
3. The use of ultrafine particles (UFP) is limited because, while they are very high in vehicle-exhaust plumes, they decrease rapidly with distance from the road. These distance-decay gradients present significant challenges for exposure assessment, because they are difficult to characterize over space and time in a way that supports epidemiologic research. Although UFP might have toxic effects on humans (see Chapter 5), we do not yet have adequate data on actual exposure to traffic-related or other UFP. The Panel addressed this point in terms of the current limitations of our monitoring networks in Chapter 2 (see below as well).
4. In recent years, EC has been used as a surrogate, primarily for diesel exhaust (DE). However, there is a need to better understand the contributions of gasoline-fueled vehicles and other anthropogenic sources to the amount of EC measured. Nondestructive methods of sampling EC need to be standardized and calibrated. The U.S. Interagency Monitoring of Protected Visual Environments network and the U.S. Environmental Protection Agency's Speciation Trends Network measure 24-hour average EC concentrations (typically for 1-in-6-day sampling periods for regional monitoring sites and 1-in-3-day sampling periods for urban sites, respectively). However, very few of these sites are near traffic. The quality and usefulness of EC

as a traffic-source surrogate in complex urban environments will therefore need to be evaluated more fully when more frequent monitoring is carried out on the small spatial scales needed to pinpoint exclusive traffic contributions. (Issues related to actual measurements were discussed in Chapter 2.)

5. Measurements made at central monitoring sites are by themselves not sufficient for use in exposure assessments and epidemiologic studies, because they do not capture spatial variability of traffic-related pollutants at the local scale, the scale at which their concentrations are highest and most variable. Unfortunately, traffic-specific monitors have generally been lacking, especially in the United States. There is a need, therefore, for ambient monitoring either alone or in combination with various modeling techniques that can capture the variability in traffic-related exposures at the local scale. This is not to suggest that in some locations central monitors cannot detect a "traffic signal." However, the signal-to-noise ratio, as it were, of such monitors depends on the extent to which traffic-related pollution is a dominant contributor to the ambient atmosphere. Even in cases where traffic-related pollution is in fact the dominant contributor, the density of central monitors is typically too low to capture the spatial variability in exposures resulting from factors such as street canyons, the proportion of diesel- and gasoline-fueled vehicles, idling time on streets, average speeds, and other vehicle operating characteristics. Recent studies that have demonstrated the substantial influence of exposure variability on the magnitude of estimated associations between pollutants and health highlight the need to address this issue (Jerrett et al. 2005).
6. Because measurements of personal exposure are not feasible for large numbers of subjects, especially over time, the deployment of large numbers of monitors in a given geographic region is likely to be useful, even necessary, in areas where exposure to traffic-related pollutants is expected to be highly variable and population density is high. Recently, optimization schemes have been developed that begin to address these issues; they were discussed briefly in section 3.III.2 of Chapter 3.
7. Although source-apportionment models are useful for developing surrogates for exposure to specific sources, including traffic-related pollution (section 3.IV.8 in Chapter 3), they have several important limitations, including failure to identify specific sources; misidentification of sources among commingled sources; inconsistency among, or implausibility of, results for the same location when using two or more models; and failure to distinguish statistically based factors from actual sources. Apart from improvements in statistical methods that might be needed, the successful application of source apportionment will continue to depend on the collection of data of sufficient quantity and quality (by improving the characterization of emissions from sources, increasing the density of monitors in appropriate places, measuring with sufficient frequency to capture variability over time, and identifying traffic-specific surrogates).

In summary, considerable advances have been and are being made in assessing human exposure to traffic-related air pollution. However, the quality of today's assessments is still far from optimal when measured against the characteristics of an ideal assessment. Data of sufficient density in terms of space, time, and species complexity must be collected to improve exposure assessment and, thereby, the robustness of the health associations found in epidemiologic studies. Such improvements are tightly linked to needed improvements in the quality of emissions data, summarized earlier. Without such collective improvements, it will be difficult to further raise the quality of health studies and the level of confidence in our ability to distinguish causal from noncausal associations between exposure to traffic-related pollutants and human health effects in epidemiologic studies. Such improvements would also help formulate relevant exposure scenarios for controlled human-exposure studies.

7.II.3 CHAPTER 4: HEALTH EFFECTS: EPIDEMIOLOGY OF TRAFFIC-RELATED AIR POLLUTION

In Chapter 4, the Panel laid out the criteria for the selection of studies to be reviewed in this report and the evaluation of causal inferences and the approach for summarizing results across studies. The Panel did not derive meta-analytic summary estimates of the associations between exposure to traffic-related air pollution and the outcomes evaluated by pooling results from various studies because of the heterogeneity across studies in traffic-exposure measures and in the populations examined. The criteria for assessing whether the reported associations are causal or not are listed in Table 7.2 (adapted from Tables 4.2a and 4.2b). The criteria lay out issues of study bias, precision, and consistency (coherence) in broad epidemiologic terms, with the added specificity of exposure to pollution that is traffic-related. They provide a framework (1) for the materials presented in Chapter 4 on epidemiology and Chapter 5 on toxicology and (2) for the synthesis of evidence from epidemiology and toxicology that is presented in Chapter 6. More discussion of the criteria is provided in

Table 7.2. Criteria for Assessing the Presence or Absence of Causal Associations in Studies of the Health Effects of Traffic-Related Air Pollution[a,b]

A. *Sufficient Evidence to Infer the Presence of a Causal Association*

The evidence was deemed sufficient to conclude that an association observed between a metric of traffic exposure and a disease (or biomarker of disease) risk was causal in studies where chance, bias, and confounding could be ruled out with reasonable confidence, and the effect estimates were consistent in direction with reasonable precision.

Traffic-specific criterion. Classification A was applied:

When all studies were of the appropriate quality, at least one study measured traffic density or modeled traffic exposure[c], measures of socioeconomic status were taken into account in distance-only studies, and the studies' results were consistent.

B. *Suggestive but Not Sufficient Evidence to Infer the Presence of a Causal Association*

The evidence was deemed suggestive but not sufficient to conclude that an association between a metric of traffic exposure and a specific disease (or biomarker of disease) risk was causal in studies where chance, bias, and confounding could not be ruled out with reasonable confidence.

Traffic-specific criterion. Classification B was applied:

When all the criteria for Classification A were met except that only studies that used distance-based metrics were available

OR

When all the criteria for Classification A were met except that not all the studies that used distance-only metrics took into account measures of socioeconomic status or the studies took into account measures of socioeconomic status but the results were not consistent.

C. *Inadequate and Insufficient Evidence to Infer the Presence or Absence of a Causal Association*

The evidence was deemed inadequate and insufficient when the available studies were of insufficient quality, consistency, or statistical power to conclude whether a causal association was present or absent.

Traffic-specific criterion. Classification C was applied:

When the results from studies that used distance-only metrics were not consistent

OR

When the results of all studies using distance-only metrics were consistent but all those studies failed to include measures of socioeconomic status

OR

When the results from at least one study based on traffic density or modeled traffic exposure were inconsistent with those from distance-only studies

OR

When the number of distance-only studies was too small.

D. *Evidence Suggestive of No Causal Association*

The evidence was deemed suggestive of no causal association when there were several adequate studies, covering the full range of human exposure levels, that were consistent in not showing a positive association, at any level of exposure, between exposure to a metric of traffic exposure and a disease outcome. (Of course, a conclusion of "no association" is inevitably limited to the conditions, level of exposure, and length of observation covered by the available studies. In addition, the possibility of a very small elevation in risk at the levels of exposure studied cannot be excluded.)

Traffic-specific criterion. Classification D was applied:

When studies were of adequate quality (using distance-only metrics or at least some measures of traffic density or modeled traffic exposure) and were consistent in failing to find an association.

[a] The Panel did not use exposure–response gradations as a criterion because, in virtually all epidemiologic studies, it is difficult to infer meaningful exposure–response gradations from the types of exposure metrics used or the forms of data presented.

[b] This table was adapted from Tables 4.2a and 4.2.b in Chapter 4.

[c] In some cases, this criterion was met when modeling or source-apportionment data were cited to show that a pollution surrogate in the study was reasonably accurate in representing the traffic sources in the study area.

Chapter 4. In addition to the brief summaries of results relevant to Chapter 4 that are provided in Chapter 6, more detailed summaries by disease category are provided here along with elaboration of a number of important issues pertaining to the studies reviewed.

7.II.3.A All-Cause and Cardiovascular Mortality (Section 4.II in Chapter 4)

Mortality associated with ambient air pollution in general has been the subject of a large number of studies and is often the primary outcome considered in estimating the health effects of air pollution (see, for example, U.S. Environmental Protection Agency 2004). However, as noted in Chapter 4, very few studies of all-cause mortality (Figure 4.1) or cardiovascular mortality (Figure 4.3) and long-term exposure met the criteria for inclusion in this report, although there were additional studies that purported to show such associations related to traffic exposure but did not meet the criteria. Mostly because of the small number of studies, the evidence for an association between all-cause mortality and long-term exposures was classified as "suggestive but not sufficient" to infer a causal association. Additional factors that led to this classification were the substantial differences among populations, time periods, and confounders from study to study. Only four time-series studies of all-cause mortality associated with short-term exposure met our criteria; these, too, were classified as "suggestive but not sufficient," largely on the strength of one well-done study (Maynard et al. 2007). Two time-series studies using source-apportionment models were found to have a number of limitations that prevented a stronger statement about inferred causality.

Many of the issues that applied to the studies of all-cause mortality applied as well to the studies of cardiovascular mortality associated with long-term exposure; these issues led, similarly, to a classification of the studies as "suggestive but not sufficient" to infer a causal association. The strongest study supporting this classification was that of Hoek and colleagues (2002), which was based on a 5000-person sample of a large cohort (of approximately 120,000 persons) in the Netherlands. However, subsequent follow-up of the full cohort did not fully support the findings of the study (Beelen et al. 2008). Too few studies were available to evaluate specific categories, such as cardiac or cerebrovascular mortality. Only two time-series studies of cardiovascular mortality met our criteria, and although they both showed positive associations, the Panel concluded that the overall paucity of studies made it difficult to come to any conclusions about causality associated with short-term exposures.

Several factors were identified that raised additional uncertainties about whether associations with mortality could be considered more than "suggestive" of a causal association:

1. The heterogeneity of the populations studied, making it difficult to evaluate the consistency of the results.
2. The heterogeneity of the time periods studied and of the contributions of other pollution sources to the exposure mixtures. This was of concern even where a highly specific surrogate for exposure to traffic-related pollution was being used as the exposure measure. The issue was highlighted in a study by Laden and colleagues (2000) in which lead, the surrogate for traffic-related pollution, had highly variable associations with the "traffic source" (Figure 4.2).
3. Uncertainty about the accuracy of estimated traffic-related contributions to source-apportioned pollution data, as illustrated by the data in the study by Ito and colleagues (2006).
4. Nearly complete reliance on BC as the sole marker for traffic-related pollution in studies in which source-apportionment had not been carried out.

7.II.3.B Cardiovascular Morbidity (Section 4.III in Chapter 4)

Studies that documented changes in cardiac physiology (e.g., heart-rate variability) after short-term exposure to traffic-related pollution (using surrogates, source apportionment, or pseudo-personal monitoring) pointed consistently to the existance of a causal association with the exposure. However, the failure of some studies to consider stress and noise as potential confounders led the Panel, again, to classify them as "suggestive but not sufficient" to infer a causal association. This potential limitation was most evident in a study by Adar and colleagues (2007) in which cardiac function measurements made on elderly subjects exposed to traffic-related pollution during standardized bus trips were compared with measurements made on the subjects at other times. It is possible that noise and stress during the bus trips could have been uncontrolled confounders in this otherwise very well executed study.

Among the studies that evaluated cardiovascular morbidity, two well-executed studies on hospitalization for acute myocardial infarction were identified (Rosenlund et al. 2006; Tonne et al. 2007) (Figure 4.4). In addition, a prospective study in a German cohort reported an association between living near a major road and coronary-artery calcification as well as higher prevalence of coronary heart disease (Hoffmann et al. 2006; 2007). Collectively, these studies made a strong case for an association between

exposure to traffic-related pollutants and atherosclerosis. However, because of the small number of studies, the Panel classified them as "suggestive but not sufficient" to infer a causal association.

7.II.3.C Asthma and Respiratory Symptoms (Section 4.IV in Chapter 4)

Definition of Disease (Section 4.IV.1 in Chapter 4)

Asthma is a complex inflammatory disease of the lung airways characterized by episodic obstruction of the airways that can lead to chronic obstructive pulmonary disease (COPD). Even apart from the inherent biologic diversity of the phenotypes of asthma, the evaluation of this disease is complicated by the methods and criteria used to define it in epidemiologic studies.

The criteria used by clinicians tend in general to be more objective and standardized and to be based on more widely accepted classification protocols (National Heart Lung and Blood Institute 2007). However, in epidemiologic studies, asthma is most frequently identified by means of responses to questionnaires that do not make use of a single, universally accepted set of questions, alone or in combination with other criteria that have been accepted as the "standard" for identifying asthma. The challenges of identifying asthma are further complicated by the challenges of distinguishing factors that affect its onset from those (often the same factors) that lead to its episodic worsening. Finally, the use of medications to control asthma has been shown to decrease responses to air pollutants (Delfino et al. 1998), which adds considerable complexity to the concept of "current" asthma and susceptibility to noxious compounds.

The same challenges arise in connection with atopy (i.e., IgE [immunoglobulin E]-mediated diseases that include asthma, allergic rhinitis and conjunctivitis, and eczema), which has been identified in epidemiologic studies by a variety of methods used singly or in combination (as reviewed in Chapter 4). The immune mechanisms involved in allergic asthma are briefly summarized in Sidebar 7.1.

The dominant paradigm for asthma — still a subject of debate — holds that children are born without asthma and that some will develop it as a result of endogenous (e.g., genetic) factors and exogenous exposures (e.g., inhaled antigens and dietary factors). Although this paradigm has generally held sway in epidemiologic studies of air pollution, it comes with some important caveats:

1. A history of asthma symptoms is often used in epidemiologic studies as part of the definition both of asthma's onset (incidence) and of its prevalence and exacerbation. Symptoms, which typically vary over time and reflect the expression of the acute nature of the disease, are triggered by air pollutants and other endogenous and exogenous factors. Because many epidemiologic studies assess symptoms "over the last 12 months" regardless of the study design, it is not unambiguously clear whether they are characterizing the contribution of air pollution to the acute, intermittent nature of asthma or to the onset of the disease among previously nonasthmatic persons.
2. Traffic-exposure studies of asthma incidence (i.e., cohort studies) and of asthma prevalence (i.e., cross-sectional studies) should yield similar results and conclusions.
3. Although wheezing is an important symptom in the expression and diagnosis of asthma, the presence of wheezing by itself is not necessarily synonymous with the presence of asthma as a disease.
4. Because childhood- and adult-onset asthma might be two distinct phenotypes with distinct etiologic patterns, it is worth distinguishing between traffic studies conducted in children and those conducted in adults.

SIDEBAR 7.1 Immune Mechanisms Involved in Asthma and Allergy

Asthma is a chronic obstructive and inflammatory disease of the lung airways. The most prevalent form of asthma in children and young adults is allergic asthma, which develops as an immune response to an inhaled allergen. Key features of the allergic response are elevated levels of IgE (immunoglobulin E) and the involvement of a subset of T cells known as Th2. People with asthma and other allergic conditions who have an increased tendency to develop immediate and localized reactions that are generally mediated by IgE are referred to as "atopic."

Th2 cytokines activate IgE synthesis by B cells and activate eosinophils and other cell types. IgE in turn activates mast cells to synthesize or release pharmacologically active molecules that together trigger the symptoms typical of allergic asthma, such as airway hyperresponsiveness, inflammation, and airway obstruction. Th1 cells are another subset of T cells, distinct from Th2 cells, and are primarily involved in the response to viruses and bacteria. Th1 and Th2 cells secrete different sets of cytokines and activate different sets of effector cells. Interleukin-4 is one of the "signature" cytokines synthesized by Th2 cells, and interferon-gamma is the signature cytokine synthesized by Th1 cells. Some evidence suggests that certain air pollutants preferentially enhance the production of Th2 cytokines and IgE and reduce the development and function of Th1 cells.

These four caveats form the basis of the organization of the studies reviewed in Chapter 4 and summarized below.

Respiratory-Health Problems in Children (Section 4.IV.2 in Chapter 4)

Asthma Incidence and Prevalence Seven studies conducted in four separate cohorts and one case-control study qualified as studies of asthma incidence in children (Table 4.8). Eleven studies qualified as studies of asthma prevalence in children (Table 4.9). From these studies, the Panel came to the conclusion that living close to busy roads appears to be an independent risk factor for the onset of childhood asthma. The Panel considered the evidence for a causal relation to be in a gray zone between "sufficient" and "suggestive but not sufficient." An argument can be made for either category (section 4.IV.2.C in Chapter 4), but the decision depends on how one evaluates the role of chance in the numerous findings that were positive without being necessarily statistically significant (i.e., had somewhat imprecise point estimates of associations). The results found across the studies followed a pattern that would be expected under the plausible assumption that the pollutants really are causally associated with asthma development, if only among a subset of children with some accompanying pattern of endogenous or exogenous susceptibility factors. Despite the fact that several studies clearly supported the notion of heterogeneity of effects, with significant results in various subgroups, the assessment of the factors had not been carried out to the extent necessary to determine the characteristics of persons with increased susceptibility. Moreover, the statistical power needed to detect a "significant interaction" was usually limited. Given the diversity of potential causes of uncertainty and of approaches to investigating susceptibility, the conditions that underlie an increased risk for asthma development among children exposed to traffic-related pollutants are not known with certainty, and the results across studies that addressed these conditions were in some cases not consistent and in other cases not comparable.

Exacerbation of Symptoms in Children with and without Asthma and Health-Care Utilization for Respiratory Problems Among the more than 20 cohort and cross-sectional studies reviewed in section 4.IV.2.D of Chapter 4 that examined the association between exposure to traffic-related pollution and wheezing in children, there was a high degree of consistency in finding positive associations, many of which reached statistical significance (i.e., had reasonably precise point estimates of associations). This was true particularly for the large majority of studies that used models to assign estimates of local concentrations of pollutants, such as NO_2 or soot, to the places of residence of the study participants. Studies based on proximity or traffic density also indicated an association between exposure and wheezing (and asthma exacerbation). In addition, exacerbations of cough or dry cough were consistently associated with exposure across a variety of exposure metrics. Although most studies were not restricted to children with asthma, all these symptoms were more prevalent among children with asthma, and it is very likely that the observed associations were driven by exacerbations of asthma in mixed groups of participants. The Panel therefore concluded that the evidence is "sufficient" to infer a causal association between exposure to traffic-related pollution and exacerbation of asthma but that it is "inadequate and insufficient" to infer a causal association between exposure and symptoms in children without asthma.

Nine studies assessed the association between exposure to traffic-related pollution and the use of health-care services to treat respiratory problems in children (section 4.IV.2.E and Table 4.12 in Chapter 4). Most of the studies reported positive associations between traffic exposure and hospital-admission rates, but the majority had methodologic problems that hampered their interpretation. One study, for example, used the filling of prescriptions for asthma medications as a surrogate for respiratory problems (Livingstone et al. 1996). The Panel considered this to be a poor surrogate, because filling prescriptions to maintain control of asthma is indistinguishable from filling them for exacerbations or failures of other treatments. All but one of the studies were ecologic (i.e., studies in which the unit of analysis is a population). The Panel concluded that there was "inadequate and insufficient" evidence to infer a causal association.

Respiratory-Health Problems in Adults (Section 4.IV.3 in Chapter 4)

Adult-Onset Asthma In epidemiologic studies with adults, determining the time of asthma onset can be even more problematic than with children, because it can be difficult to be certain the onset was not just a recurrence of childhood asthma that had not been reported. As a result, the Panel identified only one study that could be interpreted as having found an association between exposure to traffic-related pollution and adult-onset asthma. In general, no conclusions about causal associations could be drawn from the studies reviewed.

Respiratory Symptoms in Adults The main results of the 14 studies reviewed were summarized in section 4.IV.3.B of Chapter 4. All but one of these (Sunyer et al. 2006) relied on proximity to roads or traffic-density measures instead of on specific traffic-pollutant measurements or models. The analyses by Sunyer and colleagues, which were based

on modeled NO_2 exposure, showed significant associations with cough and phlegm, but not with wheezing, in women; all of the proximity-based studies reported positive and mostly statistically significant associations with cough, phlegm, and wheezing. The Panel concluded that the evidence for a causal association was "suggestive but not sufficient." Insufficient data were available to try to discern the existence of susceptible subgroups.

7.II.3.D Lung Function and Chronic Obstructive Pulmonary Disease (Section 4.V in Chapter 4)

Spirometric measures of lung function, such as forced vital capacity (FVC), peak expiratory flow (PEF), and especially forced expiratory volume in one second (FEV_1), are reliable markers of health that reflect the effects of endogenous and cumulative exposure to exogenous factors that might have adverse health consequences. Reduced lung function is strongly associated with future morbidity from a variety of causes and is well known as a strong predictor of life expectancy (Hole et al. 1996). Lung function and COPD are considered together here, because the chief criterion for the diagnosis of COPD is based on lung-function measures (such as FEV_1 and the ratio FEV_1/FVC). Spirometry can also provide measures of airflow at various points during a forced exhalation such as PEF. The measures of mean expiratory flows, especially flows at low lung volumes (e.g., forced expiratory flow at 75% of exhaled volume [FEF_{75}]), are correlated and have been shown to reflect the status of small airways, which are the principal sites of chronic obstruction in asthma and COPD. Change in small-airway function is considered an early preclinical marker of pathologies associated with exogenous risk factors, such as smoking, and is thus of particular importance. These changes are being reported more frequently in studies of health effects associated with air pollution. PEF, a measure of large-airway obstruction, shows substantial within-subject variation over time; for this reason, it is widely used in the short-term monitoring of asthma to assess variations in obstruction. In this sense, PEF is a proxy for the state of asthma and, as such, is an outcome comparable to the occurrence of asthma symptoms or the use of medication among people with asthma. PEF was therefore not discussed in this section of Chapter 4, and in fact only two of the studies reviewed provided PEF results.

The relation of study design to the interpretation of associations between measures of lung function and exposure is important to understand. Cross-sectional studies primarily reflect lung function as a result of long-term exposure to relevant factors superimposed on short-term variations in function caused by recent exposures (such as respiratory infection and indoor or outdoor air pollution) or physiologic factors (such as diurnal variation). If air pollution also affects the growth or decline of lung function over time, cross-sectional studies can be used to assess associations between an achieved level of lung function and both long-term and more recent exposures, conditional on the availability of long- and short-term exposure data. By contrast, cohort studies primarily reflect changes in lung function over an extended period of time and can also assess how changes in exposure affect changes in function. Both types of studies are limited by the healthy-survivor effect (the tendency for healthy people to remain in a workforce or other population, while unhealthy people leave) and the fact that the ability to perform high-quality lung-function tests itself depends on health status. Both of these factors tend to result in underestimates of association with exposure.

Lung Function in Children and Adults (Section 4.V.2 in Chapter 4) The Panel noted that the use of heterogeneous study designs, approaches to exposure assignment, and lung-function measures limited the comparability of the studies. A review by Götschi and colleagues (2008) reached similar conclusions. Given this, the Panel concluded that the evidence is "suggestive but not sufficient" to infer a causal association between exposure to traffic-related pollution and decrements in lung function. Although the studies of lung function are suggestive of an adverse association with air pollution in general in both the short and long term, an assessment of the relevance to public health of the small, short-term deficits observed cannot be made at this time. Short-term changes in lung function are a marker of altered physiology, but the correlations between acute changes in lung function and acute symptoms are weak. In the case of long-term exposure to traffic-related pollution, there is some coherence in the data, suggesting (1) that long-term exposure is associated with changes in lung function in adolescents and young adults, (2) that lung-function measures are lower in people who live in more polluted areas, and (3), in one study, that changing residence to less-polluted areas is associated with improvements in lung function (Burr et al. 2004). The first and second points are consistent with longer-lasting effects on lung structure or function. Moreover, as noted previously, decrements in lung function (in particular as a function of FEV_1 measures) have been shown repeatedly to be a strong predictor of life expectancy. The lung-function findings were thus consistent with what one would expect if both lung-function development and life expectancy were associated with cumulative exposure to air pollutants. The third point can also be interpreted to indicate that some component of the apparent effects on lung function is reversible or is more the result of short-term exposure.

A particular problem for the studies of lung function was the difficulty in disentangling the effects of traffic-related pollution from those of general urban air pollution. The surrogates of exposure used in even the studies with the strongest design and evidence of a causal role of pollution in affecting the growth and aging of lung function, namely, the Children's Health Study (Gauderman et al. 2007) and the Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) (Downs et al. 2007), cannot easily be characterized as pertaining specifically to pollution from traffic. The studies based on proximity or traffic density were mostly cross-sectional, and although these were suggestive of an adverse effect on lung function, there was a lack of consistency in their results, most likely related to the heterogeneous exposure measures.

Chronic Obstructive Pulmonary Disease (Section 4.V.4 in Chapter 4) Given the substantial overlap in the compounds found in cigarette smoke (a known risk factor for COPD) and air pollution (discussed in more detail in Appendix A at the end of this chapter), it is reasonable to consider the possibility that traffic-related air pollution might be a risk factor for COPD. However, an assessment of the role of air pollution, especially traffic-related pollution, in the development of COPD is very difficult, for a number of reasons:

1. The disease is poorly defined. Despite the existence of an internationally recognized classification protocol (Global Initiative for Chronic Obstructive Lung Disease, 2007), the definitions of COPD used in the various studies often differed and ranged from questionnaire-based assertions of doctors' diagnoses (such as chronic bronchitis, emphysema, or COPD) or chronic symptoms (such as cough or phlegm) to measures of lung function. Post-bronchodilator measures of FEV_1 and FEV_1/FVC are considered the gold standard for classification, but these were often not available in the studies, which made distinguishing between asthma and COPD difficult, particularly in adults.
2. Because the definition of COPD often dichotomizes the lung function measure (FEV_1/FVC), defining the "diseased" as having a ratio of < 0.7, it was not clear how to interpret studies that used FEV_1/FVC as a continuous measure.
3. The link between lung development in early life and future COPD is poorly understood. Studies of air pollution and lung development in children could not be used in assessing the evidence for COPD in adults despite strong evidence of an association between FEV_1 and ambient air pollution.
4. It is not clear whether obstructive airway disease among adults who were never-smokers results in the same clinical phenotype as COPD among smokers.

Because only two of the COPD studies fulfilled the criteria for review and their results were not consistent, the Panel concluded that there is "insufficient" evidence to form a conclusion about causal associations.

7.II.3.E Allergy (Section 4.VI in Chapter 4)

There is a substantial literature on human and animal controlled-exposure studies that provides mechanistic support for a role for components of traffic-related pollutants (i.e., diesel exhaust) in affecting pathways that lead to enhanced IgE-mediated responses to aeroallergens (see Chapter 5 for details). The epidemiologic studies reviewed in this category not only had to meet the criteria for the quality of their exposure data, but also had to report at least one of the following: (1) skin-prick testing for reactivity to common aeroallergens, (2) serum IgE specific to common aeroallergens, (3) a physician's diagnosis of eczema or allergic rhinitis, or (4) questionnaires that used the terms hay fever, seasonal runny nose or rhinitis, conjunctivitis, or itchy eyes.

The Panel concluded that there is "inadequate and insufficient" evidence to infer a causal association, or even a noncausal association, between exposure to traffic-related pollution and IgE-mediated allergies. With a few inconsistent exceptions, results based on skin-prick test reactivity or allergen-specific IgE failed to show associations with any of the traffic-exposure surrogates. In light of various human-exposure studies with diesel-exhaust particles (DEP) (see Chapter 5 for details), one would have expected more consistent positive associations. Many of the controlled-human-exposure studies used nasal instillation, which might not have been an appropriate model for typical inhalation exposures, and at pollution concentrations far greater than those encountered in most ambient environments. None of the studies considered the potential for exposure to the allergens in road dust. The inconsistency across epidemiologic studies might also have reflected a failure to identify susceptible subgroups. A study published in late 2008, not formally included here, would appear to point in this direction (Melén et al. 2008). In this study, traffic-related pollution estimated by means of local-NO_2 models was associated with sensitization at age 4 only among a genetically defined subgroup of the study's birth cohort.

7.II.3.F Birth Outcomes (Section 4.VII in Chapter 4)

A considerable body of data from around the world has identified consistent associations between exposure to

ambient air pollution in general and various birth-outcome measures (such as low birth weight, small for gestational age, and pre-natal and post-natal mortality). The Panel found only four studies of exposure to traffic-related pollution, however, that met the criteria for review for these outcomes (Figure 4.13). The small number of studies and their limited geographic coverage, and uncertainty about the traffic exposure metric in one study led to a classification of the evidence as "inadequate and insufficient" to infer a causal association. One very recent study, however, requiring corroboration, has shown some very consistent associations between proximity to roads and certain birth outcomes (Brauer et al. 2008).

7.II.3.G Cancer (Section 4.VIII in Chapter 4)

Chapter 4 made particular note of the fact that the Panel's review focused only on associations between cancers and exposure to traffic-related pollution in populations not exposed in occupational settings (e.g., those exposed occupationally to traffic emission constituents such as benzene and diesel exhaust). Five studies of childhood cancers (mainly leukemias, lymphomas, and cancers of the central nervous system), two studies of adult lung cancer, a study of female breast cancer, and a study of several adult cancers were summarized in Chapter 4. Data on childhood cancers were inconclusive in terms of overall consistency and of specific cancers. Too few data were available on adult exposure to traffic-related pollution and cancer to make any meaningful causal inference about adult cancers, including lung cancers. Therefore, the Panel concluded that the evidence is "inadequate and insufficient" to make such inferences.

7.II.3.H Non-Cancer Health Outcomes and Exposure to Traffic-Related Pollutants in Occupational Settings (Section 4.IX in Chapter 4)

Sixteen studies were reviewed and briefly summarized in Chapter 4. In theory, occupational settings are potentially useful environments in which to study health effects associated with exposure to traffic-related pollutants. Unfortunately, the studies reviewed were plagued with so many methodologic problems that no meaningful inferences could be drawn from their data. Briefly, these problems consisted of the following:

1. Exposure estimates were based solely on job status, not on direct exposure measurements.
2. Sample sizes were small and unlikely to have been representative of specific groups.
3. Control groups were used that might not have been valid.
4. The consideration given to confounding factors was limited.

7.II.4 CHAPTER 5: HEALTH EFFECTS: TOXICOLOGY OF TRAFFIC-RELATED AIR POLLUTION

The goal of Chapter 5 was to review the known toxicology and mechanisms of the health effects associated with exposure to traffic-related air pollution. The chapter covered controlled exposure studies in humans and animals and in vitro studies in the context of the plausibility criteria used to make causal inferences in research studies (Hill 1953). The Panel noted that toxicologic studies of air-pollution exposure have often been undertaken to test hypotheses generated through epidemiologic studies. It also acknowledged the fact that toxicologic studies are limited (as are epidemiologic studies, to a large extent) in their ability to capture the full complexity of human exposure and, in animal studies, to produce data that are relevant to humans.

Because traffic-related pollution is a complex mixture that changes over time and space, it presents substantial challenges to the design of toxicologic studies that try to tease effects from traffic-related pollutants out of the broader mix of air pollutants. Indeed, it is difficult even to envision, let alone implement, experimental exposures for human or animal studies that capture effects exclusively from traffic pollution.

Toxicologic studies of dose–response are usually limited by their experimental design and the compounds (either alone or in various combinations, such as concentrated ambient particles) chosen for the exposure. Controlled human-exposure studies are usually limited by their short durations, small sample sizes (resulting from cost considerations), relatively simple environments, and the types of susceptible subjects that can be studied given safety concerns.

Animal studies offer considerable opportunity to explore more complex, defined exposures for longer time periods and to create genetically susceptible animals for more refined investigations of specific pathophysiologic mechanisms. However, these studies too have limitations, most importantly when it comes to extrapolating their findings to human health effects and physiologic responses. In addition, there are important differences in responses to a given pollutant among various animal strains and species, and dosimetry is affected by body size, airway structures, and metabolic pathways in the animals chosen. Diet, diurnal cycles, stress responses, and disease susceptibility individually and in combination can also affect outcomes related to exposure and complicate relevance to humans. For both types of studies, the exposure mixtures that can

be generated experimentally might not be representative of the pollution mix as whole. For example, although particle concentrators can produce particles in fractions ranging from the coarse to the ultrafine (down to about 40 nm), they cannot concentrate gases and might alter the composition or surface characteristics of the particles in ways that alter their health effects.

In vitro studies can provide useful data as well. The major limitation of these studies is the difficulty of extrapolating their results to humans and animals.

7.II.4.A The Oxidative-Stress Hypothesis (Section 5.II in Chapter 5)

The Panel summarized the evidence for the oxidative-stress hypothesis, explaining the mechanism by which acute and chronic exposures to ambient air pollution in general (including primary traffic-generated pollution) can lead to adverse health effects in humans. Oxidative stress is caused by an imbalance between pro-oxidant exposures (exposures that cause damaging oxidation reactions, or oxidative stress) and a biologic system's antioxidant defense mechanisms; it can occur at any level in the system, from cells to tissues to the whole organism. An increased oxidant burden (from the production of free radicals) may also play a role in transcriptional activation of pro-inflammatory genes, contributing to tissue injury.

Although the evidence in the studies reviewed supported the notion that oxidative stress is an important determinant of health effects associated with PM from ambient air pollution in general, only a limited number of studies quantified the capacity of primary traffic-generated PM to generate free radicals. Some data suggested that near-road $PM_{2.5}$ (PM $\leq$ 2.5 μm in aerodynamic diameter) has a greater capacity to generate reactive oxygen species than background $PM_{2.5}$ does. However, other studies have not always shown similar results. As noted previously, near-road monitoring sites are not plentiful at this time. Consequently, the extent to which primary traffic-generated pollutants contribute to the burden of reactive oxygen species experienced by humans near roadways remains undefined.

7.II.4.B Studies of Health Effects

Cardiovascular System (Section 5.III in Chapter 5)

There have been few studies that investigated cardiovascular health effects specific to exposure to primary traffic-generated pollutants. PM is the component of traffic pollution that has been studied most carefully in relation to its effects on cardiovascular outcomes, and a variety of pathways have been identified through which such effects could occur. These pathways were summarized in Figure 5.3 in Chapter 5. After review of the relevant human, animal, and in vitro toxicologic studies, the Panel concluded that the studies that investigated air pollution mixtures without regard to sources have provided an increasingly coherent body of evidence suggesting that exposure to pollutants that are components of traffic emissions (i.e., concentrated PM from ambient air, generated in the laboratory, or from DE and DEP) does affect cardiovascular function. Specifically, adverse effects on vascular homeostasis and atherosclerotic processes appeared to be enhanced by PM, although the data were not entirely consistent and the exposure concentrations used were frequently higher than those found in actual environments. The mechanisms and the PM components (including the specific contributions from traffic) that cause these effects remain undefined, although there is some evidence to support the involvement of oxidative stress. The role of emitted gases is also undefined, as are the roles of polycyclic aromatic hydrocarbons (PAHs), other volatile and semivolatile organic compounds, and air toxics that are associated with traffic-related PM.

Respiratory System (Section 5.IV in Chapter 5) A relatively small number of studies were found that directly investigated the effects of traffic-related pollution on the respiratory system in humans or in animal models. These studies did provide evidence of mild acute inflammatory responses and some decrements in lung function in normal individuals. Evidence of enhanced allergic responses in previously sensitized individuals was found as well. Based on these observations, several conclusions were offered in this section of Chapter 5:

1. Direct, intentional (real-world) exposure of humans to traffic emissions (in tunnels or at roadsides, for example) causes decrements in lung function and enhanced response to allergens in people with mild to moderate asthma.
   - These changes were most notable in subjects with moderate asthma and were associated with inflammation.
   - The paucity of such studies to date makes it impossible, so far, to identify the specific components of traffic emissions causing, or the pathogenic pathways leading to, the observed effects.
2. Controlled exposure in human volunteers and animal models and in vitro studies of components of traffic-related pollution (PM and DEP) all provided strong clues about the occurrence of various respiratory-tract outcomes (such as IgE-mediated inflammation and enhanced responses to allergens). However, because

PM and DEP are not perfect surrogates for traffic-pollutant mixtures, specific studies based on actual traffic exposures in vivo and in vitro are needed.

3. Direct traffic-exposure studies and controlled-human-exposure studies in otherwise healthy individuals have not yielded consistent results on changes in lung function or inflammatory response.

Cancer and Mutagenicity (Section 5.V in Chapter 5) Research examining the effects of traffic-related air pollutants on mutagenicity and cancer is an extensive and complicated area to evaluate. The mechanisms by which exposure to traffic-related pollution may be associated with an increased risk of cancer involve damage to DNA (including the formation of bulky DNA adducts, base oxidations and deletions, and chromosomal aberrations), which in turn may lead to a broad spectrum of mutations. Among DNA base oxidations (a consequence of oxidative stress), 8-oxo-7,8-dihydro-2′-deoxyguanosine (8-oxo-dG; also reported as 8-hydroxy-2′-deoxyguanosine, or 8-OHdG) is probably the most studied product because of its relative ease of measurement and premutagenic potential (Kasai 1997). Indeed, accumulation of 8-oxo-dG is considered an important factor in enhancing the mutation rate leading to lung cancer.

In vitro studies into the relationship between PM sampled from areas with varying volumes of traffic and mutagenicity have generated a mix of positive and negative results. Although studies in cells demonstrating the capacity of DEP to induce DNA-strand breaks, base oxidation, and mutagenicity provide a possible mechanism for the induction of carcinogenicity by traffic-related pollution, the applicability of in vitro mutagenicity studies to human risk assessment has been questioned. Animal studies have demonstrated the ability of high concentrations of exhaust components of both gasoline and diesel engines to cause cancer in animals. However, caution must be exercised in extrapolating these data to ambient concentrations and, as such, to risk to humans. Finally, as with all health effects, continued research is needed to assess the risk of mutagenesis and carcinogenesis of exhaust from new-technology diesel and the biodiesel alternatives.

Reproductive Health (Section 5.VI in Chapter 5) The toxicologic outcomes reviewed in Chapter 5 included effects on reproductive endocrine function; sperm production, motility, and viability; fertility; and birth outcomes. Selected occupational-exposure studies were included. Among the challenges in assessing from the toxicologic viewpoint the risk of traffic-related pollution adversely affecting human reproductive health were the limited data and the almost universal use of very high exposure concentrations, with questionable relevance to ambient concentrations. Therefore, the findings currently available must be interpreted with caution. Further research is needed using other components of traffic pollution, including gasoline exhaust, at more relevant concentrations.

Neurotoxicity (Section 5.VII in Chapter 5) It was difficult for the Panel to draw meaningful conclusions from the available data on the neurotoxicity of traffic-related pollutants. Of the few published studies available to review, a diverse collection of protocols (with respect to both agents and routes of exposure), animal models (in vivo and in vitro), and end points have been investigated. The study most relevant to human ambient exposure identified neuropathologic markers, physical damage to the blood–brain barrier, and neurodegenerative pathology in 32 dogs exposed to high concentrations of PM in Mexico City compared with 8 dogs from a less-polluted control city (Calderón-Garcidueñas et al. 2002). In contrast, toxicologic studies must be interpreted with caution, owing to the use of often irrelevant routes of exposure or of elevated pollutant concentrations. The studies of exposure to concentrated ambient PM (which reported increased markers of inflammation in the brains of mice) are of interest, but data are not yet available to determine whether such a biologic response translates into an adverse health outcome.

7.III. SYNTHESIS AND CONCLUSIONS

Underpinning our evaluation of the findings from epidemiologic studies of traffic pollution and its health effects has been our evaluation of data on emissions characterization and their relation to the methods of exposure assessment that have been used to date and that are likely to be used in the future. For the discussion in this section of the chapter, the Panel used the hybrid exposure model in Table 7.1 as the current optimal model* for assigning exposures to primary traffic-generated pollution, and the Panel evaluated the adequacy of other exposure-assessment methods by comparison with it. The hybrid model depends on additional data from one or more of the other models described in the table.† Each of these models depends, in turn, to a greater or lesser extent, on data on the quantitative

* The Panel does not assume that it will always be feasible, in terms of cost and practicality, to use the hybrid model in every study in the future. It is considered here in part as a heuristic device to help formulate the Panel's synthesis.

† For this discussion, the Panel did not consider the proximity model or data deriving from it because, in the absence of data from additional models in the hierarchy, proximity measures tend to be crude and error prone and can potentially be confounded by other factors (such as socioeconomic status) that are not related to exposure.

and qualitative characterization of traffic emissions and their near-road transformations, for the following reasons:

1. Surrogates for traffic-related exposure have played, and are likely to continue to play, a preeminent role in exposure assessments in epidemiologic studies. The optimal selection of relevant surrogates (especially surrogates that are single chemicals) depends on accurate knowledge of the degree to which they represent the chemical and physical properties of the actual traffic-pollution mixtures to which humans are exposed, which depends in the first place on accurate knowledge of the chemical and physical properties of the emission components and their near-source transformations.
2. The ability of source-apportionment models to characterize pollution sources accurately depends (apart from the statistical issues considered earlier) on the availability of a rich emissions-profile database extending over time and over appropriately small-scale spatial areas. The same can be said for dispersion models, insofar as their outputs are surrogates for emissions mixtures. The quality of emissions data over time is particularly important when investigating the health effects of long-term exposures. With the upcoming changes in engines and fuels that were discussed in Chapter 2, the quality of data over time will become critical to determining the extent to which quantitative and qualitative changes in traffic emissions are affecting human health over the near and long term. Failure to see health improvements in the elderly related to improved emissions, for example, could easily be explained by cohort effects related to the character of past emissions. This might make it appear that the emissions improvements were having little near-term (up to a generation's worth) effect on the cardiovascular and other major chronic diseases that are causally associated with exposure, because of the cohort's previous exposure to more highly concentrated or toxic emissions. Such a possibility was clearly implied in a study of atherosclerosis by Künzli and colleagues (2005).
3. Knowledge of emissions and their transformation products will also help toxicologists design studies that more accurately identify the chemical and physical characteristics of traffic-related pollution that are potentially toxic and might play a role in the pathophysiology of the health effects observed in epidemiologic studies. Improved understanding of the toxicology of emissions might also lead to hypotheses that can then be tested in epidemiologic studies through the identification of possible new and more specific biomarkers of exposure to emissions components. This would constitute a reversal of the current situation, in which most toxicologic studies try to uncover evidence in support of findings from epidemiologic studies. Current biomarkers, such as those related to the oxidative-stress hypothesis and chemical damage to DNA, are not specific to exposure to primary traffic pollutants and thus have only limited utility in identifying the health effects of these exposures.

Without improvements in the quality and quantity of emissions data and of the models used for quantifying emissions from motor vehicles, investigators making exposure assessments for epidemiologic studies in the years ahead will be hard pressed (1) to improve the accuracy of health-effect estimates for effects about which substantial uncertainties still remain, (2) to strengthen exposure assessments for the health effects for which causal inferences appear to be warranted but for which population exposure–response relations are not well understood, and (3) to test new hypotheses about exposures and health effects as motor-vehicle fleets and fuels change over time. Controlled human- and animal-exposure studies will be similarly constrained.

With regard to the evaluation of the exposure models, the question remains as to the extent to which the proximity model (i.e., the use of simple measures of proximity to traffic [Table 7.1]) should be employed in future epidemiologic studies. The other exposure-assessment models outlined in Table 7.1 have limitations of their own, relating to data quality or modeling assumptions. The Panel concluded, however, that the most compelling reason to discourage the use of the proximity model in future studies is that it is particularly prone to yielding "impure" surrogates — in other words, measures potentially containing extraneous information that can lead to the confounding of associations between health effects and exposure. Confounding could be due to associations between health effects and other factors (such as socioeconomic status) and also to seemingly causal associations for health effects that in fact arose independently of the exposure. The other models probably suffer from inaccuracy caused by measurement errors and could suffer as well from bias related to the errors. However, any potential confounding of exposure–outcome associations in these models (unlike the proximity model) is related to physical factors, particularly meteorologic factors, chemical transformations, and the presence of other pollutant sources with similar emissions characteristics; accurate measurements of these physical factors can in principle be made, thereby reducing the data problems to random measurement errors and errors in

model specification. The major known confounders (such as socioeconomic status) and potential confounders (such as noise and stress) for traffic-related pollutants are not easily measured. Socioeconomic status is particularly difficult to measure, because it reflects a complex construct for which none of the elements (such as education, income, diet, emotional stress, poor housing, or indoor environments) nor any of the indices derived from them is necessarily a good surrogate for the overall construct. As a result, despite the inclusion of socioeconomic status in various statistical models, the probability of residual confounding remains, making this a problem that is not simply one of random measurement errors or errors in model specification.

Table 7.3 summarizes our findings on determinations of causality based on the current evidence from the epidemiologic data. The Panel found that there was "sufficient" evidence to infer causality for the exacerbation of asthma. For other important health outcomes (i.e., all-cause and cardiovascular mortality, cardiovascular morbidity, asthma incidence, non-asthma respiratory symptoms, and lung function), the Panel concluded that the combined evidence from epidemiologic data was "suggestive but not sufficient" to infer causal associations with traffic-related pollution. For cardiovascular mortality and morbidity, the Panel concluded that the combined evidence from toxicologic data appeared to be coherent but was of insufficient quantity to add support (to the epidemiologic evidence) for inferences of causality at this time. The same was true for toxicologic data (especially data based on exposure to actual traffic emissions) about respiratory outcomes. The situation was different for allergic diseases and for cancer, for which there were toxicologic data from human-exposure, animal, and in vitro studies supporting a somewhat stronger inference of causality than was derived from the epidemiologic studies.

For the disease categories that were classified as having "inadequate and insufficient" evidence to infer a causal association, the Panel found evidence of effects, albeit not adequate or sufficient to draw conclusions about causality at this time. This lower classification indicates the need for additional studies, particularly studies that address deficiencies identified in the existing evidence. The Panel did not find any studies that in the aggregate provided clear evidence that was "suggestive of no causal relation" between a studied health outcome and exposure to primary traffic-generated pollution.

The challenge that remains is to determine how, and whether, it will be possible to bring these diverse data together to shine a clearer light on the question of causal associations. Although drawing parallels and arguing from analogy might appear to be weak ways of approaching the question, the large body of data on health effects associated with exposure to constituents of secondhand tobacco smoke (including exhaled smoke and sidestream smoke) might provide some insight. The evidence on secondhand tobacco smoke has been systematically reviewed over many years by a number of expert groups (National Research Council 1986; U.S. Environmental Protection Agency 1992; National Cancer Institute 1999), all of which came to the same conclusions as those of the most recent Surgeon General's Report (U.S. Department of Health and Human Services 2006).

The Panel's brief review of the secondhand-smoke data to identify similarities and differences with the traffic data can be found in Appendix A at the end of this chapter. The table in Appendix E (available on the HEI Web site) of Chapter 2 lists the species identified in motor vehicle emissions. Overall there is a noticeable overlap between the two sets, although the relative proportions of the various constituents may vary. There are also some similarities in the patterns of exposure to each source.

Table A.1 in Appendix A presents summaries of toxicologic and health evidence from the Surgeon General's Report, *The Health Consequences of Involuntary Exposure to Tobacco Smoke* (U.S. Department of Health and Human Services 2006), for the outcomes evaluated in relation to exposure to traffic-related air pollution in this report. Toxicologic studies of secondhand tobacco smoke have identified mechanisms similar to those that have been suggested in this review for traffic-related air pollution and more broadly for general air pollution. An example of a common mechanism is the induction of the same pattern of immune markers of allergic response in the nose of subjects exposed to tobacco smoke or DEP in combination with an allergen (Gilliland et al. 2004) (see Table A.2 in Appendix A). However, it is difficult to find studies of the effects of real-world exposure to secondhand smoke and primary traffic-generated pollutants at similar concentrations and routes of exposure that would allow one to assess the comparability of these two pollutant mixtures.

The potential parallels between secondhand smoke and primary traffic-generated pollutants are of interest and lend some plausibility to the conclusions drawn here from the much more limited literature on exposure to primary traffic-generated pollutants; however, these considerations did not change any of the Panel's conclusions about the effects of exposure to primary traffic-generated pollution.

Future Research The Panel's attempt to compare these two sources, and our broader review of the traffic literature, helped identify a number of important areas for

Table 7.3. Summary of Health Outcomes and Classification of Causal Associations[a]

Health Outcomes	Classification of Causal Associations	Reasons for Classification[b]	
		Unrelated to Exposure Assessment	Related to Exposure Assessment
Mortality and Morbidity			
All-cause and cardiovascular mortality	Suggestive but not sufficient	Too few studies; population and temporal heterogeneity	Limited range of surrogates
Cardiovascular morbidity	Suggestive but not sufficient	Failure to include potentially important confounders	None
Asthma and Respiratory-Symptom Outcomes in Children			
Asthma incidence and prevalence	Sufficient or Suggestive but not sufficient	Concerns about precision of estimates in many studies	None
Exacerbations of symptoms With asthma Without asthma	 Sufficient Inadequate and insufficient[c]	In studies with both types of subjects, associations appeared to be driven by those with asthma; large number of studies of children with asthma with adequate control of confounding and mostly with precise estimates of association	None
Health-care utilization	Inadequate and insufficient[c]	Concern about validity of outcome measures	None
Asthma and Respiratory-Symptom Outcomes in Adults			
Adult-onset asthma	Inadequate and insufficient[c]	Only one study that separated adult-onset from childhood asthma	Not applicable
Respiratory symptoms	Suggestive but not sufficient	Inconsistent results between proximity and model-based estimates of association	Only one study not based on proximity measure
Respiratory-Symptom Outcomes			
Pulmonary function (all ages)	Suggestive but not sufficient	Heterogeneity of function measures and of study designs	None
COPD	Inadequate and insufficient[c]	Only two studies; inconsistent results	Not applicable
Allergy	Inadequate and insufficient[c]	Inconsistent application of methods and inconsistent results; unexplored response heterogeneity	None
Other Health Outcomes			
Birth outcomes	Inadequate and insufficient[c]	Only four studies	Not applicable
Cancer (not related to occupational exposure to diesel exhaust)	Inadequate and insufficient[c]	Too few studies of any one type of cancer in both children and adults	Not applicable

[a] For more information, see Table 7.2 and Chapter 4.

[b] See text for discussion and synthesis of the limitations of exposure assessment.

[c] For health outcomes classified as inadequate and insufficient, the Panel found evidence of effects but determined that it was not sufficient to draw firmer conclusions about causality at this time. The Panel found no clear evidence of "no effect" for any health outcome.

Table 7.4. Key Future Research

Epidemiology

Research in children

- Identify susceptible subgroups of children at risk for the onset or exacerbation of asthma consequent to exposure (an issue not addressed satisfactorily in the studies reviewed here).
- Examine associations between exposure and nonasthmatic, atopic allergy using the same standardized methods used to assess atopy and allergy.
- Develop additional data on associations between exposure and subclinical vascular disease in children and adolescents.
- Define the role of long-term exposure to primary traffic-related pollutants as a causal risk factor for atherosclerotic cardiovascular disease in later adult life.
- Investigate associations between exposure during pregnancy and various birth outcomes.
- Investigate associations between childhood exposure and childhood cancers, particularly lymphomas, leukemia, and brain cancer.

Research in adults

- Investigate associations between nonoccupational exposure to primary traffic-related pollutants and lung cancer.
- Define the risks of subclinical vascular disease associated with exposure in adults less than 65 years of age (the typical lower cut-off point used to define "elderly" groups).
- Develop additional data on susceptible subgroups at risk for cardiovascular morbidity and mortality in populations less than 65 years of age.
- Investigate associations between exposure and the onset or exacerbation of COPD, identifying, in particular, susceptible subgroups at risk for accelerated declines in lung function consequent to exposure.

Toxicology

- Undertake studies based on more realistic exposure scenarios.
- Make realistic exposure studies more informative; place emphasis on the identification of specific markers of biologic exposure to individual chemicals and mixtures.
- Undertake studies that combine realistic human exposures, such as the "natural" exposures in ambient settings investigated by McCreanor et al. (2007), with parallel exposures of animals and in vitro studies in order to define mechanisms.
- Undertake animal and in vitro toxicologic studies of the near-roadway transformation products of traffic emissions.

future research on the health effects of primary traffic-generated pollutants. Even in cases where the evidence is already sufficient, reasons remain to consider conducting additional health and toxicologic studies.* The Panel's suggestions for future research can be found in Table 7.4. They are not meant to be all-encompassing; instead, they reflect a number of obvious future research opportunities† that emerge from the conclusions of this report.

* The Panel assumes that the concerns noted earlier about emissions characterization and exposure assessment will be addressed before or concurrently with any new studies. For this reason, no further remarks about emissions, exposure, or exposure–response relations at the population level will be made in the discussion that follows; nor will the feasibility or design of particular types of studies be discussed.

† The Panel prefers the phrase "research opportunities" over "research priorities," because it is not the intention of this report to specify a comprehensive set of hierarchical research priorities.

7.III.1 OVERALL CONCLUSIONS

Traffic-related pollutants affect ambient air quality on a broad variety of spatial scales, ranging from the roadside to the urban and regional background scales. Based on a synthesis of the best available evidence, the Panel has identified an exposure zone within a range of up to 300 to 500 m from a major road as the area most highly affected by traffic emissions. To help to improve the quality of the evidence, for the purposes both of science and of policy making that depends on it (particularly for the health outcomes for which the evidence has been classified as other than "sufficient"), the Panel has endeavored to do the following:

1. Identify areas in which improving the quantity and quality of emissions-monitoring data should be a priority, recognizing the fundamental importance of this

task in improving the validity of exposure assessments (see Chapter 2);

2. Provide guidance on specific methods to help improve the validity of exposure assessments in epidemiologic studies (see Chapter 3); and
3. Identify the types of approaches that should be considered as priorities for future epidemiologic and toxicologic studies (Table 7.4).

Many aspects of the epidemiologic and toxicologic evidence relating adverse human health effects to exposure to primary traffic-generated air pollution remain incomplete. However, the Panel concluded that the evidence was sufficient to support a causal association between exposure to traffic-related air pollution and exacerbation of asthma. The Panel also found suggestive evidence of a causal association with onset of childhood asthma, nonasthma respiratory symptoms, impaired lung function, total and cardiovascular mortality, and cardiovascular morbidity, although the data were not sufficient to support causality fully. For a number of other health outcomes, there was limited evidence of associations with primary traffic-generated air pollution, although the data were either inadequate or insufficient at this time to draw firmer conclusions. The Panel's conclusions have to be considered in the context of the progress made to reduce emissions from motor vehicles. Since the epidemiologic studies are based on past estimates of exposure to emissions from older vehicles, they might not provide an accurate guide to estimating health associations in the future.

In light of the large number of people residing within 300 to 500 m of major roads, the Panel concludes that the "sufficient" and "suggestive" evidence for inferring causal associations between exposure and these health outcomes indicates that the exposures are likely to be a public health concern and to deserve public attention. Although policy recommendations based on these conclusions are beyond the scope of this report, the Panel has tried to organize, summarize, and discuss the primary evidence in ways that will facilitate its usefulness to policy makers in the years ahead.

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APPENDIX A. Evidence from the Surgeon General's Review of Secondhand Tobacco Smoke

To attempt to draw an analogy between exposure to secondhand tobacco smoke and primary traffic-generated pollutants, the Panel reviewed the most recent efforts by the Surgeon General to assess the evidence for secondhand-smoke exposure and compared them to its own analysis of the literature on traffic exposure.

EXPOSURES

Comparison of the constituents of secondhand smoke with those listed in the table in Appendix E (available on the HEI Web site) of Chapter 2 shows that there is a substantial overlap between the two sets, although the relative contributions of the various constituents may vary.

It is difficult to find studies that allow one to assess the comparability of real-world exposures to secondhand smoke and to traffic-related air pollution. There are similarities in the patterns of exposure to each source, including (1) episodic exposure to high concentrations (e.g., in public places such as restaurants and bars where smoking is or was once permitted and in vehicles with the windows closed) (U.S. Department of Health and Human Services 2006) and (2) daily prolonged exposure in buildings where smoking is or was once permitted and exposure in buildings downwind of highways.

HEALTH EVIDENCE

Table A.1 presents summaries of toxicologic and health evidence from the 2006 Surgeon General's Report, *The Health Consequences of Involuntary Exposure to Tobacco Smoke* (U.S. Department of Health and Human Services 2006), for the health outcomes evaluated in this report in relation to exposure to traffic-related pollution. Toxicologic studies of secondhand smoke have identified potential mechanisms of carcinogenesis that are the same as those that have been suggested for general ambient air pollutants in other studies and that could be inferred for traffic-related pollutants on the basis of the similarities cited above. The Surgeon General's Report stated that the evidence was "sufficient" to conclude that there is a causal association between exposure to secondhand smoke and adult lung cancer. The evidence for childhood cancers was judged to be "inadequate."

The Surgeon General's Report also concluded that the evidence was "sufficient" to infer a causal association between exposure to secondhand smoke and cardiovascular morbidity and mortality and "suggestive but not sufficient" for subclinical vascular disease. The potential mechanisms

identified in studies of primary traffic-generated pollutants are accepted as likely mechanisms through which secondhand smoke exerts its effects on the cardiovascular system.

The Surgeon General's Report also concluded that the evidence was "suggestive but not sufficient" to infer a causal relationship between secondhand-smoke exposure from parental smoking and the onset of childhood asthma but did not specify mechanisms to explain the association. However, several mechanisms that might be relevant to exposure to primary traffic-generated pollutants were mentioned in the report in connection with asthma in children.

There are few direct comparisons of the effects of secondhand smoke and primary traffic-generated pollutants. As described in Chapter 5, Gilliland and colleagues (2004) found evidence of effects on various markers of immune response among 19 ragweed allergen-sensitive subjects

Table A.1. Causal Classifications from the Surgeon General's Report[a] of Toxicologic Findings and Health Outcomes for Involuntary Exposure to Tobacco Smoke that Are Relevant to Exposure to Primary Traffic-Related Pollutants

Outcomes	Toxicologic Findings	Epidemiologic Findings
Cancer	Increased cancer risk (Sufficient), but lung cancer risk less than for smokers	Adult lung cancer (Sufficient) Childhood cancers (Suggestive but not sufficient)
Cardiovascular system	Systemic inflammation (Not classified) Prothrombotic effect (Sufficient) Endothelial dysfunction (Sufficient) Atherogenic in animals (Sufficient) Autonomic dysfunction (e.g., decreased heart rate variability) (Not classified)	Mortality and morbidity (Sufficient) Stroke (Suggestive but not sufficient) Subclinical vascular disease (Suggestive but not sufficient)
Respiratory system	Asthma Immune skewing toward Th4 (increased IgE, IL-4, and IL-13) (Not classified) Multiple mechanisms (Not classified)	Children Ever asthma (Sufficient) Asthma onset (Suggestive but not sufficient) Wheeze onset (Sufficient) Respiratory symptoms (cough, phlegm, wheezing, breathlessness) (Sufficient) Changes in lung function Persistent effects of in utero exposure (Sufficient) Lower level across childhood (Sufficient) Atopy (Inadequate and insufficient) Adults Asthma onset (Suggestive but not sufficient) Asthma exacerbation (Suggestive but not sufficient) Acute respiratory symptoms (Suggestive but not sufficient) Chronic respiratory symptoms (Suggestive but not sufficient) Changes in lung function Acute decline in people with asthma (Suggestive but not sufficient) Acute decline in healthy persons (Inadequate and insufficient) Small decrement after chronic exposure in general population (Suggestive but not sufficient) COPD onset (Suggestive but not sufficient) COPD increased morbidity (Inadequate and insufficient)
Reproductive system		Changes in fertility (Inadequate and insufficient) Pre-term delivery (Suggestive but not sufficient) Low birth weight (Sufficient)

[a] U.S. Department of Health and Human Services 2006.

after intranasal challenges with high concentrations of DEP from an older diesel engine and an allergen. Using a similar protocol, Gilliland and colleagues (2006) separately showed that the same subjects exposed by inhalation to secondhand tobacco smoke plus allergen had responses similar to those for the DEP and allergen. The results of the two studies are compared in Table A.2. Across all subjects, the correlations of various markers of immune response in the two challenge protocols ranged from 0.54 for histamine release in nasal lavage to 0.79 for interleukin-4 (one of the cytokines produced by Th2 cells that stimulates IgE production). All were statistically significant. These data thus support the possibility that pathophysiologic mechanisms related to exposure to secondhand smoke could also be related to exposure to primary traffic-generated pollutants.

The potential parallels between secondhand smoke and primary traffic-generated pollutants are of interest and lend some plausibility to the conclusions the Panel drew from the much more limited literature on exposure to the pollutants; however, these considerations did not change any of the Panel's conclusions about the effects of exposure to primary traffic-generated pollution.

Table A.2. Nasal Responses in 19 Ragweed Allergen-Sensitive Subjects after Exposure to Clean Air plus Allergen, DEP plus Allergen, or Secondhand Tobacco Smoke plus Allergen

	Gilliland et al. 2004[a]			Gilliland et al. 2006[b]		
	Clean Air + Allergen	DEP + Allergen	*P* Value	Clean Air + Allergen	SHS + Allergen	*P* Value
IgE, U/mL	9.8 ± 6.4	121 ± 134.1	0.002	12.2 (1.1 to 27.5)	101.5 (23.5 to 746.5)	< 0.0001
IL-4, U/mL	0.3 ± 0.1	6.0 ± 5.0	< 0.0001	0.2 (0.2 to 0.7)	3.5 (0.2 to 13.3)	< 0.0001
IFN-γ, ng/L	1.2 ± 0.6	0.6 ± 0.5	0.002	0.6 (0.2 to 16)	0.3 (0.1 to 1.4)	< 0.0001
Histamine, nM	3.1 ± 1.3	15.0 ± 7.4	< 0.0001	3.6 (0.9 to 6.8)	12.5 (0.9 to 24.7)	< 0.0001

Definition of abbreviations: DEP = diesel exhaust particles; SHS = secondhand tobacco smoke; IgE = immunoglobulin E; IL-4 = interleukin-4; IFN-γ = interferon gamma.

[a] DEP was delivered to the nose in a single dose of 300 µg. Values are mean ± standard deviation; *P* value from paired *t* tests for means.

[b] SHS was inhaled during a 2-hr exposure period (at a particle concentration of 310 µg/m^3). Values are median (maximum and minimum); *P* value determined by two-sided Wilcoxon matched-pairs signed-rank tests for difference medians.

ABBREVIATIONS AND OTHER TERMS

8-OHdG	8-hydroxy-2′-deoxyguanosine
8-oxo-dG	8-oxo-7,8-dihydro-2′-deoxyguanosine
CO	carbon monoxide
COPD	chronic obstructive pulmonary disease
DE	diesel exhaust
DEP	diesel exhaust particles
FEV_1	forced expiratory volume in one second
FVC	forced vital capacity
IgE	immunoglobulin E
NO_2	nitrogen dioxide
NO_x	nitrogen oxides
PAHs	polycyclic aromatic hydrocarbons
PEF	peak expiratory flow
PM	particulate matter
$PM_{2.5}$	PM ≤ 2.5 µm in aerodynamic diameter
SAPALDIA	Swiss Study on Air Pollution and Lung Diseases in Adults
SO_2	sulfur dioxide
UFP	ultrafine particles
VOCs	volatile organic compounds

APPENDICES ON THE WEB

Chapter 2: Appendix A: Global Trends in Motor Vehicle Types by Region and Pollution Controls

Chapter 2: Appendix B: Fuel Composition Changes Related to Emission Controls

Chapter 2: Appendix C: Summary of Source Apportionment Studies in the Past Decade

Chapter 2: Appendix D: Summary of Tunnel Studies in the Past Decade

Chapter 2: Appendix E: Subset of U.S. EPA Master List of Mobile-Source Air Toxics

Chapter 3: Appendix B: Summary of Some Studies of Measures of Traffic and Traffic-Related Pollutants

Chapter 3: Appendix C: Bayesian Hierarchical Modeling

ACKNOWLEDGMENTS

The Panel wishes to acknowledge the considerable support given to this project by the leadership and staff of HEI. In particular, the work of Maria Costantini, HEI principal scientist, was central to the intellectual and factual coherence of the final text; the Panel owes her a special debt of gratitude for her tireless efforts to enhance its accuracy and clarity. The Panel would like to acknowledge the efforts of Amara Ezeamama, former HEI staff scientist, in the assembly of the database for the epidemiology studies and the preparation of related figures and tables. The Panel is also grateful to the HEI editorial staff who helped to create a clear, coherent final document.

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January 2010