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The London Low Emission Zone Baseline Study

Frank Kelly, Ben Armstrong, Richard Atkinson, H. Ross Anderson, Ben Barratt, Sean Beevers, Derek Cook, Dave Green, Dick Derwent, Ian Mudway, and Paul Wilkinson

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with a Critique by the HEI Health Review Committee

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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's research and analyses to public and private decision makers.

HEI typically 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 research programs. 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.

ABOUT THIS REPORT

Research Report 163, *The London Low Emission Zone Baseline Study*, presents a research project funded by the Health Effects Institute and conducted by Professor Frank Kelly, Professor of Environmental Health, Environmental Research Group, School of Biomedical & Health Sciences, King's College London, and his colleagues.

This report contains three main sections.

The HEI Statement, prepared by staff at HEI, is a brief, nontechnical summary of the study and its findings; it also briefly describes the Health Review Committee's comments on the study.

The Investigators' Report, prepared by Kelly and colleagues, describes the scientific background, aims, methods, results, and conclusions of the study.

The Critique is prepared by members of the Health Review Committee with the assistance of HEI staff; it places the study in a broader scientific context, points out its strengths and limitations, and discusses remaining uncertainties and implications of the study's findings for public health and future research.

This report has gone through HEI's rigorous review process. When an HEI-funded study is completed, the investigators submit a draft final report presenting the background and results of the study. This draft report is first examined by outside technical reviewers and a biostatistician. The report and the reviewers' comments are then evaluated by members of the Health Review Committee, an independent panel of distinguished scientists who have no involvement in selecting or overseeing HEI studies. During the review process, the investigators have an opportunity to exchange comments with the Review Committee and, as necessary, to revise their report. The Critique reflects the information provided in the final version of the report.

PREFACE

HEI's Outcomes Research Program

The goal of most air quality regulations is to protect the public's health by implementing regulatory actions or providing economic incentives that help reduce the public's exposure to air pollutants. If this goal is met, air pollution should be reduced, and indicators of public health should improve or at least not deteriorate. Evaluating the extent to which air quality regulations succeed in protecting public health is part of a broader effort — variously termed outcomes research, accountability research, or research on regulatory effectiveness — designed to assess the performance of environmental regulatory policies in general. In recent decades, air quality in the United States and Western Europe has improved substantially, and this improvement is attributable to a number of factors, including increasingly stringent air quality regulations. However, the cost of the pollution-control technologies and mechanisms needed to implement and enforce these regulations is often high. It is therefore prudent to ask whether the regulations have in fact yielded demonstrable improvements in public health, which will provide useful feedback to inform future efforts.

Several U.S. government agencies have concluded that direct evidence about the extent to which air quality regulations have improved health (measured as a decrease in premature mortality and excess morbidity) is lacking. This finding is well documented by the National Research Council (NRC) in its report "Estimating the Public Health Benefits of Proposed Air Pollution Regulations" (NRC 2002), as well as by the California Air Resources Board, the U.S. Environmental Protection Agency (EPA), the U.S. Centers for Disease Control and Prevention (CDC), and other agencies.

In 2003, the Health Effects Institute published a monograph on outcomes research, Communication 11, "Assessing Health Impact of Air Quality Regulations: Concepts and Methods for Accountability Research" (HEI 2003). This monograph was written by the members of HEI's multidisciplinary Accountability Working Group after a 2001 workshop on the topic. Communication 11 set out a conceptual framework for outcomes research and identified the types of evidence required and the methods by which the evidence should be obtained. It has also guided the development of the HEI Health Outcomes Research program, which is discussed below.

Between 2002 and 2004, HEI issued four requests for applications (RFAs) for studies to evaluate the effects of actions taken to improve air quality. The study by Professor Frank Kelly and colleagues described in this Research Report (Kelly et al. 2011c) was funded under RFA 04-4, "Measuring the Health Impact of Actions Taken to Improve Air Quality." HEI funded eight additional outcomes studies resulting from other RFAs (see Preface Table).

This preface describes both the framework of outcomes research as it relates to air quality regulations and HEI's Outcomes Research program.

BACKGROUND

The first step in assessing the effectiveness of air quality regulations is to measure emissions of the targeted pollutants to see whether they have in fact decreased as intended. A series of intermediate assessments, described in detail below, are needed in order to accurately measure the adverse health effects associated with air pollution to see whether they, too, decreased in incidence or severity relative to emissions. Some outcomes studies to date have used hypothetical scenarios (comparing estimated outcomes under existing and more stringent regulations) and risk estimates obtained from epidemiologic studies in an attempt to quantify past effects on health and to predict future effects (U.S. EPA 1999). However, more extensive validation of these estimates with data on actual outcomes would be helpful.

The long-term improvements in U.S. air quality have been associated with improved health in retrospective epidemiologic studies (Chay and Greenstone 2003; Laden et al. 2006; Pope et al. 2009). Considerable

HEI's Outcomes Research Program[a]

RFA / Investigator (Institution)	Study or Report Title	Intervention
RFA 02-1		
Douglas Dockery (Harvard School of Public Health, Boston, MA)	"Effects of Air Pollution Control on Mortality and Hospital Admissions in Ireland" (in review)	Coal ban in Irish cities
Annette Peters (GSF–National Research Center for Environment and Health, Neuherberg, Germany[b])	The Influence of Improved Air Quality on Mortality Risks in Erfurt, Germany (published as HEI Research Report 137, 2009)	Switch from brown coal to natural gas for home heating and power plants, changes in motor vehicle fleet after reunification of Germany
RFA 04-1		
Frank Kelly (King's College London, London, UK)	The Impact of the Congestion Charging Scheme on Air Quality in London: Part 1. Emissions Modeling and Analysis of Air Pollution Measurements. Part 2. Analysis of the Oxidative Potential of Particulate Matter (published as HEI Research Report 155, 2011)	Measures to reduce traffic congestion in the center of London
RFA 04-4		
Frank Kelly (King's College London, London, UK)	The London Low Emission Zone Baseline Study (published as HEI Research Report 163, 2011)	Measures to exclude most polluting vehicles from entering Greater London
Richard Morgenstern (Resources for the Future, Washington, DC)	"Accountability Assessment of Title IV of the Clean Air Act Amendments of 1990" (in press)	Measures to reduce sulfur emissions from power plants east of the Mississippi River
Curtis Noonan (University of Montana, Missoula, MT)	Assessing the Impact of a Wood Stove Replacement Program on Air Quality and Children's Health (published as HEI Research Report 162, 2011)	Woodstove change-out program
Jennifer Peel (Colorado State University, Fort Collins, CO)	Impact of Improved Air Quality During the 1996 Summer Olympic Games in Atlanta on Multiple Cardiovascular and Respiratory Outcomes (published as HEI Research Report 148, 2010)	Measures to reduce traffic congestion during the Atlanta Olympics
Chit-Ming Wong (University of Hong Kong, Hong Kong)	"Impact of the 1990 Hong Kong Legislation for Restriction on Sulfur Content in Fuel" (in press)	Measures to reduce sulfur content in fuel for motor vehicles and power plants
RFPA 05-3		
Junfeng (Jim) Zhang (University of Medicine and Dentistry of New Jersey, Piscataway, NJ)	"Molecular and Physiological Responses to Drastic Changes in PM Concentration and Composition" (in review)	Measures to improve air quality during the Beijing Olympics

[a] Abbreviations: RFA, Request for Applications; RFPA, Request for Preliminary Applications.

[b] As of 2008, this institution is called the Helmholtz Zentrum München–German Research Center for Environmental Health.

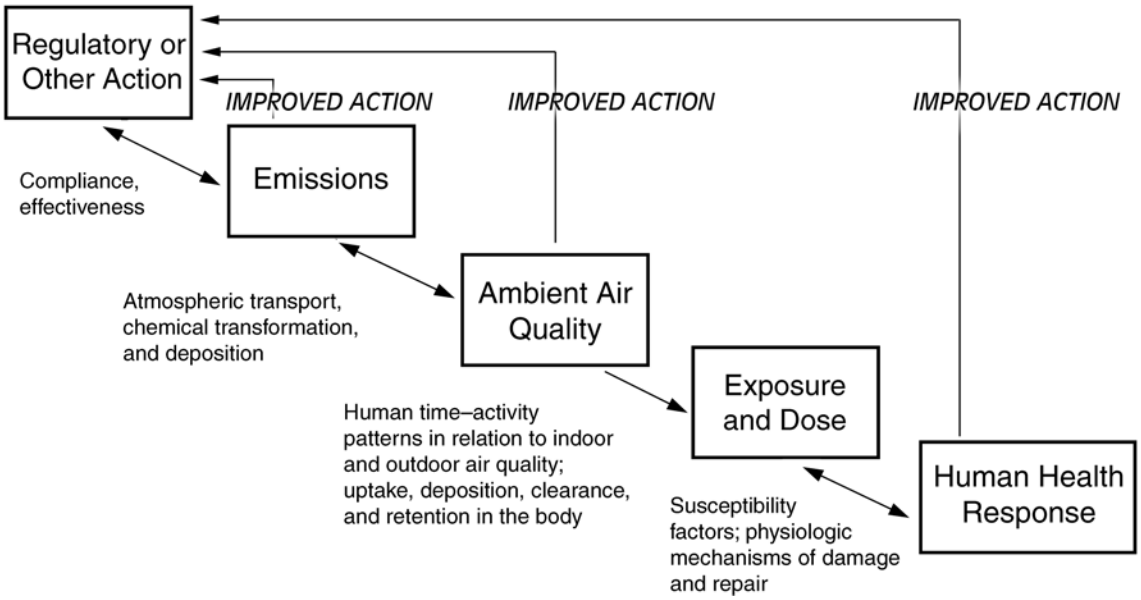
challenges, however, are inherent in the assessment of the health effects of air quality regulations. Different regulations go into effect at different times, for example, and may be implemented at different levels of government (e.g., national, regional, or local). Their effectiveness therefore needs to be assessed in ways that take into account the varying times of implementation and levels of regulation. In addition, other changes at the same time and place might confound an apparent association between pollution reduction and improved health, such as economic trends (e.g., changes in employment), improvements in health care, and behavioral changes (e.g., staying indoors when government warnings indicate pollution concentrations are high). Moreover, adverse health effects that might be caused by exposure to air pollution can also be caused by other environmental risk factors (some of which may have changed over the same time periods as the air pollution concentrations). These challenges become more pronounced when regulations are implemented over long periods and when changes in air quality and health outcomes are not seen immediately, thus increasing the chance for confounding by other factors. For these reasons, scenarios in which regulations are expected to have resulted in rapid changes in air quality tend to be among the first, and most likely, targets for investigation, rather than evaluations of complex regulatory programs implemented over multiple years. Studies in Ireland by Clancy and colleagues (2002) and in Hong Kong by Hedley and colleagues (2002) are examples of such scenarios.

These inherent challenges are well documented in Communication 11 (HEI 2003), which was intended to advance the concept of outcomes research and to foster the development of methods and studies throughout the relevant scientific and policy communities. In addition, recent advances in data collection and analytic techniques provide an unprecedented opportunity to improve our assessments of the effects of air quality interventions.

THE OUTCOMES EVALUATION CYCLE

The NRC's Committee on Research Priorities for Airborne Particulate Matter set out a conceptual framework for linking air pollution sources to adverse health effects (NRC 1998). This framework can be used to identify factors along an Outcomes Evaluation Cycle (see Preface Figure), each stage of which affords its own opportunities for making quantitative measurements of the intended improvements.

At the first stage (regulatory action), one can assess whether controls on source emissions have in fact been put into place. At the second stage (emissions), one can



Outcomes Evaluation Cycle. Each box represents a stage in the process between regulatory action and human health responses to air pollution. Arrows connecting the stages indicate possible directions of influence. The text below the arrows identifies factors affecting the effectiveness of regulatory actions at each stage. At several of the stages, knowledge gained from studies on outcomes can provide valuable feedback for improving regulatory or other actions.

determine whether controls on sources have indeed reduced emissions, whether emitters have changed their practices, and whether there have been unintended consequences. At the third stage (ambient air quality), one can assess whether controls on sources and reductions in emissions have resulted in improved air quality. At the fourth stage (personal or population exposure), one can assess whether the improvement in air quality has reduced people's actual exposure and whether susceptible subpopulations (those most likely to experience adverse health effects) have benefited. At this stage, it is important to take into account changes in time–activity patterns that could either increase or reduce exposure. The actual dose that an individual's organs may be exposed to should also be considered (i.e., whether reductions in exposure have led to reductions in concentrations in body tissues such as the lung). Finally, at the fifth stage (human health response), one can assess whether risks to health have declined, given the evidence about changes in health outcomes such as morbidity and mortality that have resulted from changes in exposure. The challenge at this stage is to investigate the health outcomes that are most directly related to exposure to air pollution.

At each stage in the outcomes evaluation cycle, the opportunity exists to collect evidence that either validates the assumptions that motivated the intervention or points to ways in which the assumptions were incorrect. The collection of such evidence can thus ensure that future interventions are maximally effective.

Ultimately, the framework for outcomes research will need to encompass investigations of the broader consequences of regulations, not just the intended consequences. Unintended consequences should also be investigated, along with the possibility that risks to public health in fact increased, as discussed by Wiener (1998) and others who have advanced the concept of a portfolio of effects of a regulation.

HEI'S OUTCOMES RESEARCH PROGRAM

HEI's Outcomes Research program currently includes nine studies. The study by Professor Frank Kelly and colleagues presented in this report is the fifth of the nine to be published; two additional studies are in press and are expected to be published in 2011. The remaining two studies are in review and are expected to be published in 2012.

These studies involve the measurement of indicators along the entire outcomes evaluation cycle, from regulatory or other interventions to human health outcomes. Some of the studies focused on interventions that were implemented over relatively short periods of time, such as a ban on the sale of coal, the replacement of old wood stoves with more efficient, cleaner ones, reductions in the sulfur content of fuels, and measures to reduce traffic. Other groups focused on longer-term, wider-ranging interventions or events; for instance, one study assessed complex changes associated with the reunification of the former East and West Germany, including a switch from brown coal to natural gas for fueling power plants and home-heating systems and an increase in the numbers of modern diesel-powered vehicles in eastern Germany. HEI is also supporting research, including the development of methods, in an especially challenging area — assessment of the effects of regulations implemented incrementally over extended periods of time, such as those resulting from Title IV of the 1990 Clean Air Act Amendments (U.S. EPA 1990), which aimed at reducing sulfur dioxide emissions from power plants by requiring compliance with prescribed emission limitations. Studies on health outcomes funded by HEI to date are summarized in the Preface Table and described in more detail in an interim evaluation of the HEI Outcomes Research program (van Erp and Cohen 2009).

FUTURE DIRECTIONS

As a part of its new Strategic Plan for 2010 through 2015 (HEI 2010a), HEI has looked closely at opportunities for unique new contributions to health outcomes research. Key recommendations for future research were made at a December 2009 planning workshop (HEI 2010b), which led to HEI issuing a new Request for Applications in January 2011 for a second wave of outcomes research. RFA 11-1, "Health Outcomes Research — Assessing the Health Outcomes of Air Quality Actions," solicits applications for studies designed to assess the health effects of actions to improve air quality and to develop methods required for, and specifically suited to, conducting such research. Preference will be given to (1) studies that evaluate regulatory and other actions at the national or regional level implemented over multiple years; (2) studies that evaluate complex sets of actions targeted at improving air quality in large urban areas and major ports with well-documented air quality problems and programs to address them; and (3) studies that develop methods to support such health outcomes research (see *www.healtheffects.org/ funding.htm*). HEI

hopes to fund 3 or 4 studies, expected to start in 2012, to evaluate the effectiveness of longer-term regulatory actions.

In addition, HEI has funded the development of two Web sites intended to enhance transparency and provide other researchers with access to extensive data and software from HEI-funded studies:

1. Data and software from the National Morbidity, Mortality, and Air Pollution Study (NMMAPS), as described by Zeger and colleagues (2006) (data available at the Johns Hopkins Bloomberg School of Public Health Web site *www.ihapss.jhsph.edu*); and
2. Data from the National Particle Components Toxicity Initiative (NPACT) on concentrations of components of particulate matter with an aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$) collected at or near the 54 sites in the EPA's $PM_{2.5}$ Chemical Speciation Trends Network (STN) (data available at the Atmospheric and Environmental Research Web site *https://hei.aer.com*).

The data on pollution and health from a large number of U.S. cities, as documented by the NMMAPS team and made available on the Internet-Based Health and Air Pollution Surveillance System (iHAPSS) Web site, constitute a valuable resource that allows other researchers to undertake additional analyses, possibly including further outcomes studies. The STN Web site provides scientists an opportunity to investigate specific questions about concentrations of $PM_{2.5}$ components and their association with adverse health effects in regions covered by the STN network and to address questions related to outcomes research when interventions in these regions are being planned.

In January 2008, HEI co-organized and cosponsored, with the CDC's National Environmental Public Health Tracking Program and the EPA, a workshop titled "Methodologic Issues in Environmental Public Health Tracking of Air Pollution Effects." The workshop was part of an effort to implement the initiative outlined in HEI's Strategic Plan for 2005 through 2010 (HEI 2005) to "build networks with the U.S. Centers for Disease Control and Prevention and state public health tracking programs to facilitate accountability research."

The workshop built on the work of the CDC's National Environmental Public Health Tracking Program (see the CDC Web site *www.cdc.gov/nceh/tracking/*) in the development of standardized measures of air pollution–related effects on health at the state and local levels in the United States. It brought together representatives of state and federal agencies and academic researchers to discuss methodologic issues in developing standardized measures and made recommendations for their further development and application in assessing the health impacts of air pollution, including the impacts of actions taken to improve air quality. The recommendations were provided in a September 2008 report to the CDC, and the proceedings were published in the journal *Air Quality, Atmosphere & Health* in December 2009 (Matte et al. 2009). The CDC has subsequently funded a pilot project under the National Environmental Public Health Tracking Program to implement the recommendations of the workshop in selected states and metropolitan areas.

HEI will continue to seek opportunities to work with the CDC and the EPA to apply methods newly developed for tracking public health and assessing the effectiveness of environmental regulations.

Investigators who have identified a distinctive opportunity to evaluate the effects of environmental regulations on air pollution and human health are encouraged to contact HEI.

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HEI STATEMENT

Synopsis of Research Report 163

The London Low Emission Zone Baseline Study

BACKGROUND

The London Low Emission Zone (LEZ) baseline study, conducted by Professor Frank Kelly and colleagues, was funded under an HEI research program aimed at evaluating whether regulatory and other actions taken to improve air quality have resulted in the intended improvements in air quality, exposure, and health outcomes.

The London LEZ was designed to improve air quality in Greater London by restricting entry of the oldest and most polluting vehicles in phases. Beginning in February 2008, heavy-duty diesel-engine vehicles and then other classes of vehicles would have to meet Euro III emissions standards and, by 2012, the more stringent Euro IV standards. Low emission zones, also known as environmental zones, have been implemented in countries all over the world. With coverage of about 2644 km^2, the London LEZ is one of the largest and therefore provides an intriguing opportunity for research.

In planning their evaluation of the LEZ, Kelly and colleagues built upon their earlier investigation of the air quality impacts of London's Congestion Charging Scheme (CCS); they set out to study the potential impacts of the LEZ first on air quality and then on health using existing databases of electronic medical records from primary-care practices serving a majority of London residents. The HEI Research Committee funded the team to evaluate the feasibility of such a study by collecting baseline data before the LEZ went into effect and to develop methodologic approaches.

APPROACH

The investigators first conducted detailed emissions and air pollution modeling. Using an LEZ scenario in which heavy-duty diesel-engine trucks and buses were required to meet Euro IV emissions standards for particulate matter (PM) and nitrogen oxides (NO_x), they projected effects of the LEZ on the mix of vehicles entering the zone, their emissions, and air pollutant concentrations and compared them with those of a "base case" scenario, which assumed the LEZ had not been implemented. Specifically, they predicted total emissions and ambient concentrations of NO_x, nitrogen dioxide (NO_2), PM with an aerodynamic diameter $\leq$ 10 μm (PM_{10}) from exhaust, and PM_{10} from tire and brake wear throughout Greater London.

Using these projections, they evaluated the existing air monitoring network; as a result of this assessment, Transport for London, which is responsible for London's transport system, agreed to add or upgrade air pollution and traffic monitoring at seven key roadside locations. The final monitoring network available for study included 41 sites (28 roadside and 9 urban background sites within London and 2 roadside and 2 urban background sites outside London).

Using methods based on their earlier study of the London CCS, the investigators studied characteristics of PM that they hypothesized might explain its toxicity. They examined the oxidative potential and the metal content in extracts from archived filter samples of PM_{10} and $PM_{2.5}$ (PM with an aerodynamic diameter $\leq$ 2.5 μm) from the monitoring sites. Oxidative potential, an indicator of a compound's ability to cause damage via chemical reactions, was estimated using a cell-free in vitro assay (i.e., the synthetic respiratory tract lining fluid assay) developed by the team. The assay measured the ability of filter extracts to deplete the levels of three common antioxidant compounds (ascorbate, reduced glutathione, and urate) found in the lungs. They also analyzed each filter extract for a panel of metals previously associated with exhaust or with tire and brake wear and assessed their possible contribution to oxidative potential.

Kelly and colleagues assessed the feasibility of obtaining and using electronic medical records from London's primary-care practices to study possible health impacts of the LEZ. The records came from two sources: the Doctors' Independent Network and the Lambeth database, which together covered a total of 42 practices and about 300,000

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Professor Frank Kelly of King's College London, United Kingdom, and colleagues. Research Report 163 contains both the detailed Investigators' Report and a Critique of the study prepared by the Institute's Health Review Committee.

patients. The investigators explored ways to classify practices according to predicted LEZ-related changes in pollutant concentrations while maintaining the confidentiality of patient data. Using NO_x as an index pollutant, they conducted exploratory cross-sectional analyses of the relationships between exposure and indicators of respiratory and cardiovascular diseases and looked at potential confounding factors, such as socioeconomic status, ethnic background, and smoking. They then estimated the statistical power of future epidemiologic studies to detect changes in health outcomes associated with expected LEZ-related improvements in air quality.

RESULTS

The modeling studies predicted modest reductions in total emissions of PM_{10}, NO_x, and NO_2 associated with the LEZ: PM_{10} emissions would decline by 2.6% in 2008 and by 6.6% by 2012, and NO_x would decline by 3.8% in 2008 and by 7.3% by 2012. The largest LEZ-related differences in NO_2 and PM_{10} concentrations were likely to occur along roadways; this finding was instrumental in guiding the design of the LEZ monitoring network.

The investigators reported that oxidative potential appeared to be greater in PM from roadside locations than in that from urban background locations. Oxidative potential was also greater in PM_{10} extracts than in $PM_{2.5}$ extracts, which the investigators suggested might indicate an important contribution from the coarse fraction of PM ($PM_{10-2.5}$). In PM_{10}, but not $PM_{2.5}$, the oxidative potential appeared to be associated with elevated concentrations of metals linked to mechanical wear on tires and brakes (e.g., barium, copper, molybdenum, and iron). In general, the experiments suggested that oxidative potential of PM_{10} was attributable more to the presence of metals than of organic compounds.

The investigators were successful in demonstrating that data from medical practices could be electronically linked to air pollution data at the postal code level. However, in some cases patterns of NO_x, NO_2, and PM_{10} concentrations were distinctive enough to permit identification of individual practices. Given potential concerns about patient confidentiality, they limited their analyses to NO_x.

The investigators' exploratory cross-sectional analyses largely found no statistically significant associations between baseline NO_x concentrations and selected indicators for respiratory and cardiovascular outcomes. The exception was a negative association in school-age children and young adults between NO_x and ever having had a diagnosis of asthma or obtained prescriptions for asthma drugs. This result could not be explained by smoking habits or socioeconomic status; chance or uncontrolled confounding remained possible explanations. Nonetheless, using their results, the authors estimated that a full-scale longitudinal study of the LEZ could have the power to detect a 5% decline in measures such as number of prescriptions for asthma drugs or consultations for respiratory infections in the part of the population experiencing the largest decreases in air pollution.

INTERPRETATION AND CONCLUSIONS

In its independent evaluation of the study, the Health Review Committee thought the investigators had taken a careful approach by building on methods first used in their study of the London CCS. A strength of the study was that the investigators identified and addressed gaps in the monitoring network before undertaking full-scale health studies. They showed that it was feasible to link potential LEZ-related changes in air quality to electronic health records from primary-care databases. However, some major providers of medical records were not convinced that patient confidentiality could be maintained and thus access to data for a large number of patients was not available; if unaddressed, the statistical power of future health studies could be limited.

The Committee thought the analyses of patterns in modeled air pollution concentrations and in the metal content and oxidative potential of archived PM filter samples were interesting and potentially useful for further research. However, it was concerned that, despite the large area affected by the LEZ, the predicted changes in PM_{10} and NO_2 concentrations were generally small and, as in the earlier CSS study, would be difficult to detect in actual monitoring data. The Committee thought the in vitro assay of oxidative potential was intriguing, but largely exploratory. Its usefulness for this study was limited because it primarily measured the oxidative potential of metals associated with tire and brake wear, not the tailpipe emissions targeted by the LEZ.

In summary, the LEZ baseline study was a creative effort to lay the groundwork for studying spatial and temporal changes in air pollutant concentrations and health outcomes in advance of a major regulatory intervention. It provides important lessons for future research into the health outcomes of actions to improve air quality.

INVESTIGATORS' REPORT

The London Low Emission Zone Baseline Study

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ABSTRACT

On February 4, 2008, the world's largest low emission zone (LEZ*) was established. At 2644 km^2, the zone encompasses most of Greater London. It restricts the entry of the oldest and most polluting diesel vehicles, including heavy-goods vehicles (haulage trucks), buses and coaches, larger vans, and minibuses. It does not apply to cars or motorcycles. The LEZ scheme will introduce increasingly stringent Euro emissions standards over time.

The creation of this zone presented a unique opportunity to estimate the effects of a stepwise reduction in vehicle emissions on air quality and health. Before undertaking such an investigation, robust baseline data were gathered on air quality and the oxidative activity and metal content of particulate matter (PM) from air pollution monitors located in Greater London. In addition, methods were developed for using databases of electronic primary-care records in order to evaluate the zone's health effects.

Our study began in 2007, using information about the planned restrictions in an agreed-upon LEZ scenario and year-on-year changes in the vehicle fleet in models to predict air pollution concentrations in London for the years 2005, 2008, and 2010. Based on this detailed emissions and air pollution modeling, the areas in London were then identified that were expected to show the greatest changes in air pollution concentrations and population exposures after the implementation of the LEZ. Using these predictions, the best placement of a pollution monitoring network was determined and the feasibility of evaluating the health effects using electronic primary-care records was assessed.

To measure baseline pollutant concentrations before the implementation of the LEZ, a comprehensive monitoring network was established close to major roadways and intersections. Output-difference plots from statistical modeling for 2010 indicated seven key areas likely to experience the greatest change in concentrations of nitrogen dioxide (NO_2) (at least 3 µg/m^3) and of PM with an aerodynamic diameter ≤ 10 µm (PM_{10}) (at least 0.75 µg/m^3) as a result of the LEZ; these suggested that the clearest signals of change were most likely to be measured near roadsides. The seven key areas were also likely to be of importance in carrying out a study to assess the health outcomes of an air quality intervention like the LEZ. Of the seven key areas, two already had monitoring sites with a full complement of equipment, four had monitoring sites that required upgrades of existing equipment, and one required a completely new installation. With the upgrades and new installations in place, fully ratified (verified) pollutant data (for PM_{10}, PM with an aerodynamic diameter ≤ 2.5 µm [$PM_{2.5}$], nitrogen oxides [NO_x], and ozone [O_3] at all sites as well as for particle number, black smoke [BS], carbon monoxide [CO], and sulfur dioxide [SO_2] at selected sites) were then collected for analysis. In addition, the seven key monitoring sites were supported by other sites in the London Air Quality Network (LAQN). From these, a robust set of baseline air quality data was produced. Data from automatic and manual traffic counters as well as automatic license-plate recognition cameras were used to compile detailed vehicle profiles.

This Investigators' Report is one part of Health Effects Institute Research Report 163, which also includes a Critique by the Health Review Committee and an HEI Statement about the research project. Correspondence concerning the Investigators' Report may be addressed to Professor Frank Kelly, Professor of Environmental Health, Environmental Research Group, School of Biomedical & Health Sciences, King's College London, 150 Stamford Street, London SE1 9NH, U.K., Telephone ++44 20 7848 4004; Fax ++44 20 7848 3891, e-mail *frank.kelly@kcl.ac.uk*

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* A list of abbreviations and other terms appears at the end of the Investigators' Report.

This enabled us to establish more precise associations between ambient pollutant concentrations and vehicle emissions.

An additional goal of the study was to collect baseline PM data in order to test the hypothesis that changes in traffic densities and vehicle mixes caused by the LEZ would affect the oxidative potential and metal content of ambient PM_{10} and $PM_{2.5}$. The resulting baseline PM data set was the first to describe, in detail, the oxidative potential and metal content of the PM_{10} and $PM_{2.5}$ of a major city's airshed. PM in London has considerable oxidative potential; clear differences in this measure were found from site to site, with evidence that the oxidative potential of both PM_{10} and $PM_{2.5}$ at roadside monitoring sites was higher than at urban background locations. In the PM_{10} samples this increased oxidative activity appeared to be associated with increased concentrations of copper (Cu), barium (Ba), and bathophenanthroline disulfonate–mobilized iron (BPS Fe) in the roadside samples. In the $PM_{2.5}$ samples, no simple association could be seen, suggesting that other unmeasured components were driving the increased oxidative potential in this fraction of the roadside samples. These data suggest that two components were contributing to the oxidative potential of roadside PM, namely Cu and BPS Fe in the coarse fraction of PM (PM with an aerodynamic diameter of 2.5 µm to 10 µm; $PM_{2.5–10}$) and an unidentified redox catalyst in $PM_{2.5}$.

The data derived for this baseline study confirmed key observations from a more limited spatial mapping exercise published in our earlier HEI report on the introduction of the London's Congestion Charging Scheme (CCS) in 2003 (Kelly et al. 2011a,b). In addition, the data set in the current report provided robust baseline information on the oxidative potential and metal content of PM found in the London airshed in the period before implementation of the LEZ; the finding that a proportion of the oxidative potential appears in the PM coarse mode and is apparently related to brake wear raises important issues regarding the nature of traffic management schemes.

The final goal of this baseline study was to establish the feasibility, in ethical and operational terms, of using the U.K.'s electronic primary-care records to evaluate the effects of the LEZ on human health outcomes. Data on consultations and prescriptions were compiled from a pilot group of general practices (13 distributed across London, with 100,000 patients; 29 situated in the inner London Borough of Lambeth, with 200,000 patients). Ethics approvals were obtained to link individual primary-care records to modeled NO_x concentrations by means of postcodes. (To preserve anonymity, the postcodes were removed before delivery to the research team.) A wide range of NO_x exposures was found across London as well as within and between the practices examined. Although we observed little association between NO_x exposure and smoking status, a positive relationship was found between exposure and increased socioeconomic deprivation. The health outcomes we chose to study were asthma, chronic obstructive pulmonary disease, wheeze, hay fever, upper and lower respiratory tract infections, ischemic heart disease, heart failure, and atrial fibrillation. These outcomes were measured as prevalence or incidence. Their distributions by age, sex, socioeconomic deprivation, ethnicity, and smoking were found to accord with those reported in the epidemiology literature. No cross-sectional positive associations were found between exposure to NO_x and any of the studied health outcomes; some associations were significantly negative.

After the pilot study, a suitable primary-care database of London patients was identified, the General Practice Research Database responsible for giving us access to these data agreed to collaborate in the evaluation of the LEZ, and an acceptable method of ensuring privacy of the records was agreed upon. The database included about 350,000 patients who had remained at the same address over the four-year period of the study. Power calculations for a controlled longitudinal analysis were then performed, indicating that for outcomes such as consultations for respiratory illnesses or prescriptions for asthma there was sufficient power to identify a 5% to 10% reduction in consultations for patients most exposed to the intervention compared with patients presumed to not be exposed to it.

In conclusion, the work undertaken in this study provides a good foundation for future LEZ evaluations. Our extensive monitoring network, measuring a comprehensive set of pollutants (and a range of particle metrics), will continue to provide a valuable tool both for assessing the impact of LEZ regulations on air quality in London and for furthering understanding of the link between PM's composition and toxicity. Finally, we believe that in combination with our modeling of the predicted population-based changes in pollution exposure in London, the use of primary-care databases forms a sound basis and has sufficient statistical power for the evaluation of the potential impact of the LEZ on human health.

INTRODUCTION

AIR QUALITY IN LONDON

The quality of air in London is much improved compared with that of the first half of the twentieth century.

Like many other large cities around the world, however, London continues to experience high concentrations of air pollution — the worst in the U.K. and among the worst in Europe. Significant declines have occurred in concentrations of lead (Pb) (> 90%) after the phase-out of lead in gasoline; CO (10% to 18%), and of volatile organic carbons (10% to 20%), owing to the mandatory implementation of three-way catalysts and evaporative canisters in gasoline-powered motor vehicles. In contrast with these declines, the annual percentage declines in NO_x concentrations (again achieved through the implementation of three-way catalysts in gasoline-powered vehicles) have been minimal (3% to 5%). For the most part, these minimal declines are the result of substantial and growing contributions to NO_x emissions from diesel-powered motor vehicles, which until recently have not been the subject of emission controls. The increasing use of diesel-powered vehicles also means that PM is still a major concern despite enormous reduction in BS concentrations due to the introduction of the Clean Air Act. As a consequence, there are areas of London, generally near busy roads, where NO_x and PM regularly exceed recommended guidelines or standards for the protection of human health.

LONDON'S AIR QUALITY STRATEGY

In view of widespread public concern over the problem of poor air quality for those who live in, work in, or visit the city, the Mayor of London launched an air quality strategy in 2002, *The Mayor's Air Quality Strategy: Cleaning London's Air* (Greater London Authority 2002), which put forward a range of policies and proposals designed to move London toward the point where air pollution no longer poses a significant risk to human health. The primary focus of the strategy was the reduction of pollution from emissions related to road traffic, because these emissions make a large contribution to London's air quality problems and are considered to be the most harmful to human health. In 2005, emissions from road transport contributed approximately 38% of all NO_x emissions (Figure 1) and 66% of all PM_{10} emissions (Figure 2) in the inner London area (Greater London Authority 2006). The reduction in London's road traffic emissions would be achieved in two ways: through a decrease in the number of vehicles on the road and through the reduction of emissions from individual vehicles (i.e., modernization of the fleet vehicle). To help achieve the first aim, the Mayor introduced the London CCS on February 17, 2003. Although the CCS applied to just 1.4% of the Greater London area, it reduced traffic entering central London by 18%, increased vehicle speed by 21%, and relieved congestion by 30% within the charging zone (Transport for London 2007). To help achieve the second aim, the Mayor of London introduced the London LEZ (the subject of this report), a larger area that could only be entered freely by vehicles meeting certain emissions standards.

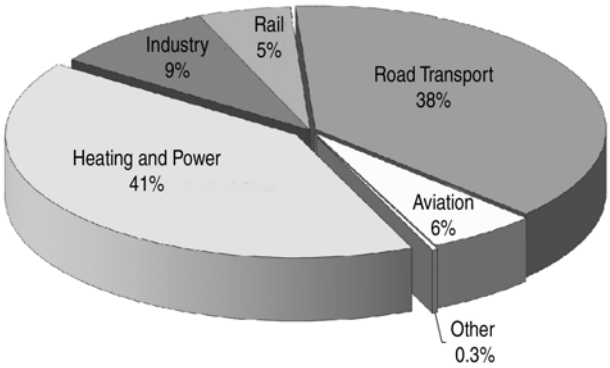

Figure 1. Estimated contributions of road traffic to NO_x emissions in London. Information from Greater London Authority (2006).

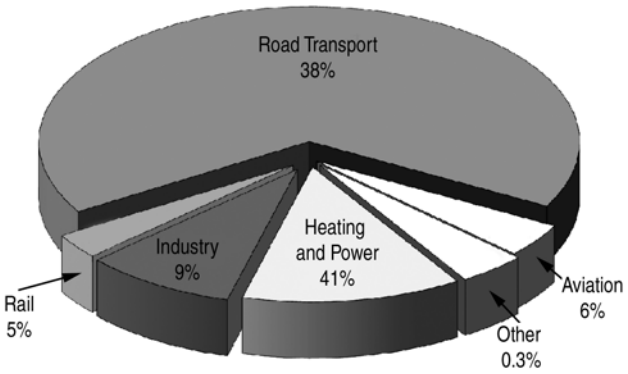

Figure 2. Estimated contributions of road traffic to PM_{10} emissions in London. Information from Greater London Authority (2006).

THE LONDON LOW EMISSION ZONE

The main impetus for the introduction of the LEZ was to improve the health and quality of life of people in London by improving the quality of the air. In addition, the scheme was designed to move London closer to achieving national and E.U. air quality objectives for 2010. The LEZ, covering an area of 2644 km^2, aimed to tackle these objectives by restricting the entry of the oldest and most polluting vehicles into Greater London (Figure 3) (London Mayor 2007). The scheme's regulations are in effect 24 hours a day, 365 days a year. Cameras are used to record vehicle registration numbers, and a Driver and Vehicle Licensing Agency database is used to identify noncompliant vehicles. The LEZ

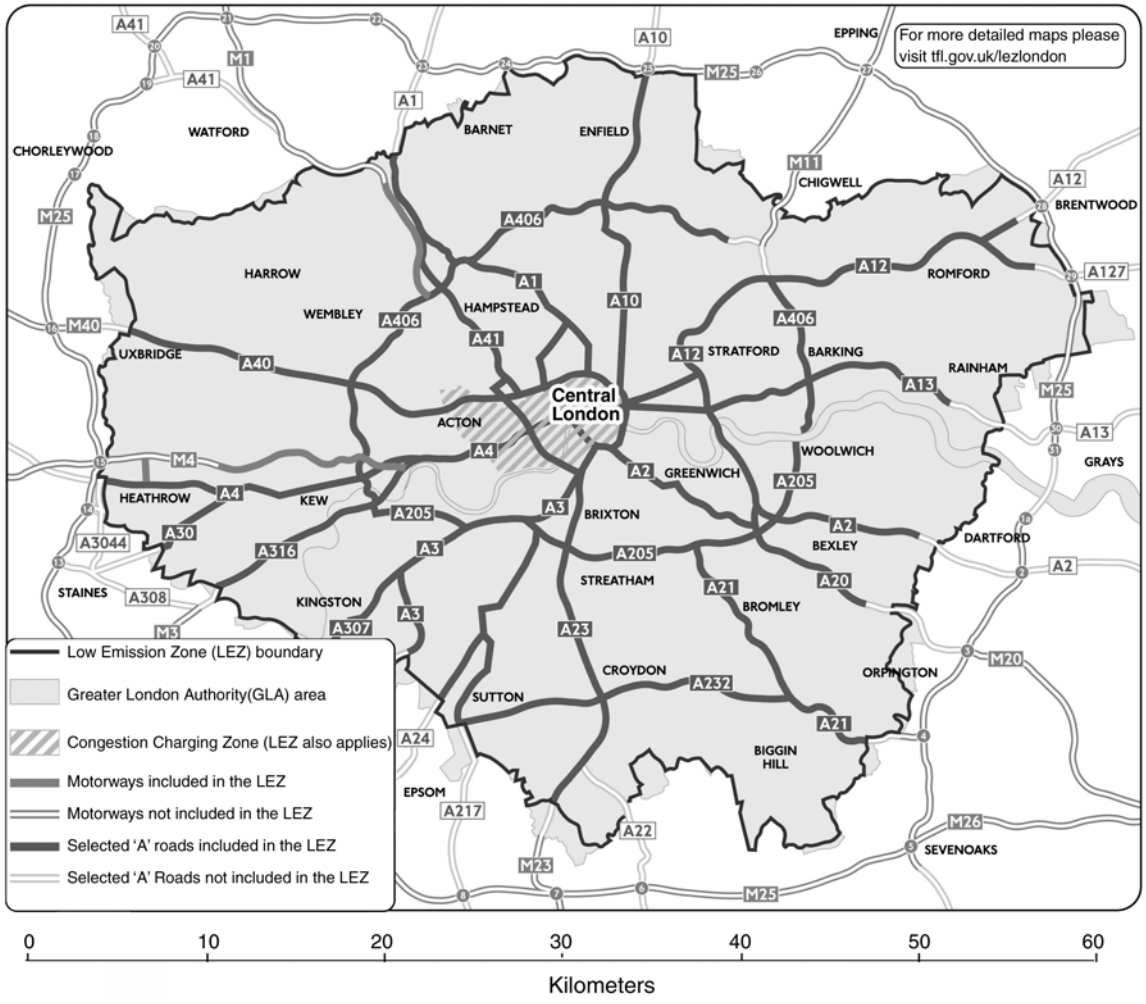

Figure 3. Greater London area showing the extent of the LEZ.

scheme applies to diesel-powered heavy-goods vehicles, buses and coaches, larger vans, and minibuses (Table 1). As shown in the table, the vehicles first affected by the implementation of the LEZ (as of February 4, 2008) were those with disproportionately high emissions (i.e., trucks weighing more than 12 tons). These vehicles were required to meet modern Euro emission standards, which set limit values for exhaust emissions for new vehicles sold in Europe and with which these vehicles must comply when manufactured (Table 1). As of July 7, 2008, lighter heavy-goods vehicles, buses, and coaches were included, and as of October 3, 2010, large vans and minibuses were also scheduled to be included. Specifically, the LEZ scheme requires heavy-duty vehicles to meet the Euro III emission standard for PM_{10} and then, in 2012, the Euro IV standard. Should the European Commission set a new standard for ultrafine particles ($PM_{2.5}$), the Mayor of London would consider including it in the LEZ scheme. A standard for NO_x has not been included in the scheme, because there are currently too many unresolved issues around the certification and testing of NO_x abatement equipment. Although it was decided at the time that the LEZ scheme should concentrate on the most individually polluting vehicles, the Mayor also asked Transport for London, the authority managing the LEZ, to investigate the implications of including cars at a later date.

In order to deter the use of high-polluting vehicles in the LEZ and to encourage operators to upgrade their vehicles,

Table 1. Vehicles and Minimum Emissions Standards Included in the LEZ Scheme

Vehicle Type and Definition	Emissions Standards
Heavy-goods vehicles[a] Heavy diesel-engine vehicles exceeding 12 tonnes gross vehicle weight, including goods vehicles, motor caravans, motorized horseboxes, and other specialist vehicles	**All Euro III vehicles meet the LEZ standard** • Vehicles first registered as new on or after October 1, 2001, are assumed to be Euro III, so will meet the LEZ emissions standards • Vehicles not meeting the Euro III emissions standards could be made to do so by modifying the vehicles to meet the standard for PM • Vehicles not meeting the emissions standards would need to pay a daily charge if used in the LEZ **From January 2012 the required emissions standards are raised to Euro IV; all Euro IV vehicles will meet the LEZ standard** • Vehicles registered as new on or after October 1, 2006, are assumed to be Euro IV, so will meet the LEZ emission standards • Vehicles not meeting the Euro IV emissions standards could be made to do so by modifying the vehicles to meet the standard for PM • Vehicles not meeting the emissions standards would need to pay a daily charge if used in the LEZ
Light-goods vehicles[b] Heavy diesel-engine vehicles between 3.5 and 12 tonnes gross vehicle weight, including goods vehicles, motor caravans, motorized horseboxes, and other specialist vehicles	
Buses and coaches[b] Diesel-engine passenger vehicles with > 8 seats plus the driver's seat exceeding 5 tonnes gross vehicle weight	
Large vans[c] Diesel-engine vehicles between 1.205 tonnes unladen and 3.5 tonnes gross vehicle weight and motor caravans and ambulances between 2.5 tonnes and 3.5 tonnes gross vehicle weight	**All Euro III vehicles meet the LEZ standard** • Vehicles registered as new on or after January 1, 2002, are assumed to be Euro III, so will meet the LEZ emission standards • Vehicles not meeting the Euro III emissions standards could be made to do so by modifying the vehicles to meet the standard for PM • Vehicles not meeting the emissions standards would need to pay a daily charge if used in the LEZ
Minibuses[c] Diesel-engine passenger vehicles with > 8 seats plus the drivers' seat < 5 tonnes gross vehicle weight	

[a] Euro III emissions standards went into effect February 2008 and Euro IV standards will be put into effect January 2012.

[b] Euro III emissions standards went into effect July 2008 and Euro IV standards will be put into effect January 2012.

[c] Euro III emissions standards will be put into effect Ocober 2010.

operators of vehicles that fail to meet LEZ standards are required to pay a fee of £200 (about U.S. $400 at the time of this writing) for trucks, coaches, and buses and £100 for vans and minibuses for each day the vehicles are driven into the zone. Should an operator of a noncompliant vehicle not pay the daily fee, penalty fees of £1,000 for trucks, coaches, and buses and £500 for vans and minibuses apply (reduced by 50% if paid within 14 days or increased by 50% if not paid within 28 days). U.K. and foreign military vehicles, historic vehicles (i.e., manufactured before 1973), off-road vehicles (e.g., tractors and excavators), and circus vehicles are exempt from the fee. It should be noted that the majority of vehicles affected by the LEZ already meet the minimum emissions standards and pay no fee.

LEZs for freight vehicles have already been successfully implemented in Sweden. The cities of Stockholm, Gothenburg, and Malmö in 1996 and Lund in 2002 introduced "Environmental Zones" in their city centers to improve air quality and reduce noise (Watkiss et al. 2003). Tokyo has had an LEZ since October 2003 and has been successful in reducing emissions of heavy-goods vehicles. More recently, Berlin, Cologne, Hanover, and Stuttgart have implemented LEZs in their central city areas. Similar schemes have also been implemented or are being considered by other cities in Europe (for a complete list, see *www.lowemissionzones.eu/emission-standards-table/by-start-date-othermenu-46*). The London LEZ is the largest such zone in the world and the first to use a charging mechanism rather than an outright ban.

POTENTIAL HEALTH AND ENVIRONMENTAL IMPACTS OF THE LONDON LEZ

The LEZ scheme has the potential to help improve the health of large numbers of people, given that it affects the whole of Greater London, an area in which more than 8 million people live and work. Indeed, a wide-ranging modeling program undertaken by Transport for London in cooperation with Environmental Research Group at King's College London (*www.tfl.gov.uk/roadusers/lez*) to understand the likely impacts of various LEZ scenarios showed that the LEZ could provide improvements in London's air quality. For example, the modeling predicted a reduction in PM_{10} emissions of 64 tons (2.6%) for 2008, leading to a decrease in the areas of Greater London that exceeded E.U. air quality limit values for PM_{10}. For 2012, modeling predicted a reduction in PM_{10} emissions of 6.6% and a decrease of 16.2% in the area exceeding the annual PM_{10} limit value. For annual mean NO_2, modeling predicted progress toward the U.K. objective and E.U. limit value of 40 $\mu g/m^3$.

Modeling also predicted that for 2008 the LEZ would decrease NO_x emissions by 1288 tons (3.8%) and decrease the area exceeding the U.K. annual mean NO_2 2010 objective by 3.7%. For 2012, modeling predicted that the LEZ would reduce NO_x emissions by 2475 tons and thus reduce the area exceeding the annual mean NO_2 objective by 15.6%. Given this overall decline in air pollution, the LEZ would effectively accelerate the attainment of air quality standards by as much as 3 to 4 years (Transport for London 2006).

Studies support the supposition that a decline in air pollution on this scale might lead to improved health, including studies indicating that living in the vicinity of roads carrying heavy-duty vehicle traffic is associated with an increased prevalence of chronic respiratory symptoms (Brunekreef et al. 1997; Venn et al. 2001; Nicolai et al. 2003). Moreover, convincing evidence from the Netherlands suggests that children attending schools close to motorways with high truck traffic counts experienced more respiratory symptoms than children attending schools near motorways with low truck traffic counts (Janssen et al. 2003). Also of relevance are studies of the relationship between proximity to road pollution and the prevalence of lower-respiratory-tract symptoms (Studnicka et al. 1997; Ciccone et al. 1988; Hirsch et al. 1999; Venn et al. 2001; Brauer et al. 2002b; Shima et al. 2003) as well as associations between traffic-related pollution and upper-respiratory-tract symptoms (Brauer et al. 2006). A number of cohort studies have observed intra-urban variations in mortality associated with air pollution (Hoek et al. 2002; Finkelstein et al. 2004; Nafstad et al. 2004; Jerrett et al. 2005; Gehring et al. 2006); three of these pertained specifically to proximity to traffic (Hoek et al. 2002; Finkelstein et al. 2004; Gehring et al. 2006). In Duisburg, Germany, an association between exposure to traffic and coronary atherosclerosis was reported (Hoffmann et al. 2007). If real, this association would provide a link with cardiovascular mortality and might be reflected in greater morbidity from coronary heart disease.

It should be noted that, despite the studies mentioned above, the causality of associations between traffic-related air pollution and respiratory and cardiovascular health effects is still open to debate. To strengthen the argument for causality, more evidence is needed for the hypothesis that reductions in pollution, specifically in traffic-related pollutants, deliver quantifiable improvements in respiratory health. A recent Swiss study in support of this hypothesis observed significant reductions in respiratory symptoms in children concurrent with a moderate decline in pollution seen in Switzerland since the 1990s brought about by pollution-abatement measures (Bayer-Oglesby et al. 2005). Notably, the largest reduction in respiratory symptoms was observed in children from areas with the most pronounced decreases in PM_{10}. However, this study did not specifically address traffic-related pollutants.

LEZ BASELINE STUDY

The London LEZ is the first of its kind in the U.K. and the largest LEZ in the world. As such, it offers important opportunities for estimating the impact of vehicle emissions on air quality and human health. London's air quality is already assessed by a comprehensive monitoring network throughout the city and surrounding districts, and British primary-care clinics maintain electronic patient records, presenting researchers with a novel and potentially powerful approach for evaluating the health effects of the LEZ. The current study has served as a baseline exercise in accumulating robust data on air quality and PM oxidative activity in Greater London and in developing a method for using primary-care databases to evaluate the health outcomes of the LEZ.

The first step in our study was to undertake detailed emissions modeling, recognizing that the magnitude of changes in air pollution brought about by the LEZ would vary depending on the relative contributions made by traffic at various locations and by various vehicle types. A variety of specific base case scenarios were modeled to predict air pollution for the years 2005, 2008, and 2010; the models included the year-on-year vehicle fleet changes that would occur as newly purchased vehicles replaced older ones. In order to estimate the range of possible LEZ impact scenarios, modeled air pollution data were combined with population exposure estimates for Greater London.

We then developed a comprehensive monitoring network to collect robust data for assessing pollutant concentrations before the implementation of the LEZ. The detailed emissions modeling outlined above was used to identify gaps in London's existing monitoring network. Recommendations for the location and nature of additional monitoring stations were then made to Transport for London, which provided funding for additional equipment in key locations.

The introduction of the LEZ was expected to result in changes in traffic densities and vehicle mixes (and hence fuel use) throughout Greater London. These changes, in addition to possibly altering ambient PM concentrations, could also affect particle composition (i.e., bioavailable surface metal and organic components), which has been reported to influence oxidative activity (Doelman and Bast 1990; Squadrito et al. 2001; Aust et al. 2002; Kelly 2003; Mudway et al. 2004). Evidence that ambient PM creates oxidative stress in the lung as well as systemically might suggest a unifying hypothesis to explain the health effects associated with air pollution (Gilliland et al. 1999; Kelly 2003). In order to obtain baseline data pertinent to this hypothesis, the oxidative properties and soluble metal content of London PM_{10} and $PM_{2.5}$ were investigated. This included consideration of metals known to catalyze the formation of reactive oxygen species in vivo. Metal-dependent and -independent oxidative activities were measured in small quantities of PM recovered from tapered element oscillating microbalance (TEOM) filters collected at sites in and outside of Greater London. This work has enabled us to perform the first detailed citywide assessment of PM oxidative activity; we examined differences between roadside and urban background locations and developed a preliminary estimate of the difference in PM's oxidative potential between London and the surrounding areas.

As part of the baseline study, a novel method for evaluating health effects was developed, using electronic primary care databases of consultations and medical prescriptions. The work, undertaken in conjunction with the Division of Community Health Sciences at St. George's, University of London, took advantage of the fact that in the U.K. a substantial proportion of general medical practices have computer systems for recording linked patient data on reasons for consultations and actions taken, such as the prescription of drugs. In addition, nearly the entire population is registered with a general practice and access is free of charge. Our approach established the ethical and operational feasibility of linking modeled air pollution estimates to electronic primary-care records using postcodes (geographically small areas, each comprising an average of 15 households). The linkage was carried out using two primary-care databases on 300,000 patients in 43 practices. A variety of issues were explored, including outcome definition, statistical approach and power, and the potential for confounding by smoking, socioeconomic deprivation, and ethnicity. In addition, a network of practices with sufficient patients for later, broader evaluations was identified. In this way, the feasibility of using electronic primary-care records for evaluating the health effects of the LEZ was established.

SPECIFIC AIMS

The objective of the study was to collect baseline data on air quality and human health in Greater London prior to the implementation on February 4, 2008, of one of the world's largest environmental regulatory interventions, London's LEZ. The results of the study could then be used to conduct health outcomes research, that is, assessing the impact of the LEZ (and related vehicle emissions) on air quality and health. To achieve this objective, the following specific aims were agreed upon and pursued:

1. To produce model predictions of the effects of the LEZ on vehicle emissions and to identify the areas in London that might experience the greatest changes in air pollution concentrations and population exposures;
2. To identify sites for monitoring stations in Greater London that would provide robust air quality data sufficient to assess impact of the LEZ and to establish or re-equip these stations as needed;
3. To obtain data on the oxidative potential of PM in Greater London and to map it in the London airshed; and
4. To develop a methodology for the use of electronic primary-care records to evaluate the health effects of the LEZ.

ESTABLISHMENT OF A MONITORING NETWORK

INTRODUCTION

The first step toward developing the baseline data necessary to assess the impact of the LEZ was to undertake, detailed modeling of emissions and air pollution, comparing a 2010 base case (i.e., a model run without an LEZ scenario) with Transport for London's planned scenario (i.e., a model including the effects of an LEZ with Euro IV standards for PM and NO_x emissions from heavy-goods vehicles and coaches). Results from these modeling runs for PM_{10} and NO_2 were then used to identify gaps in the

existing monitoring network that could have compromised the ability to detect LEZ-associated changes in pollution concentrations and PM oxidative potential. This assessment identified existing monitoring sites likely to be of importance in carrying out our study (as well as future health outcome studies) and sites where the placement of additional equipment or monitoring stations would be the most valuable. Recommendations for the locations and nature of additional monitoring equipment or stations were then made to Transport for London, informed by experience gained during the CCS project, which aimed to detect changes in air quality due to congestion charging in Central London (Kelly et al. 2011a,b). These recommendations were accepted by Transport for London, which provided capital and revenue funding for the additional monitoring equipment to complete the LEZ key indicator site network.

METHODS

Production of Modeled Outputs

The King's College London Emissions Toolkit, a linked set of databases and emission models, was used to provide detailed traffic emission scenarios for 6344 road links and for each major vehicle type. Emissions included in the models were NO_x, NO_2, PM_{10} from vehicle exhaust, and PM_{10} from tire and brake wear. The model simulates exhaust emissions based on hourly traffic flows and speeds along each of the road links using vehicle stock data from the National Atmospheric Emissions Inventory (NAEI). Exhaust emissions were based on speed-related emissions curves, as described by Barlow and colleagues (2001), and tire and brake wear emissions (Ntziachristos and Boulter 2003). A number of assumptions were made to simulate the fitting of after-treatment exhaust devices (a detailed description is available in Appendix B, which is available on the HEI Web site).

Recent evidence has pointed to the importance of the contribution of primary NO_2 emissions to ambient NO_2 levels in urban areas, and particularly the influence of changes in primary NO_2 emissions associated with new vehicles and vehicles using after-treatment devices such as particle traps (Carslaw and Beevers 2004, 2005; Carslaw et al. 2007). Inclusion of primary NO_2 in the air pollution model was therefore important in the accurate prediction of annual mean NO_2 concentrations.

The King's College London Air Pollution Toolkit (whose databases, algorithms, and dispersion models use a combined modeling–measurement approach to predict London's air pollution) was used at an output grid resolution of 20×20 m. Emission sources, other than road transport, were taken from both the 2002 and 2003 London Atmospheric Emissions Inventory (LAEI). The model assumed two principal source types: the road network close to the monitor location and the combined emissions from all sources, including road traffic, from more distant locations. All model runs were based on the year 2002 and used hourly average meteorologic data from the U.K. Meteorological Office's Heathrow Airport site.

The Air Pollution toolkit uses specially derived relationships for the conversion of annual average NO_x to NO_2 (Carslaw et al. 2001), including a component for primary NO_2 emissions (Carslaw and Beevers 2005), and for future trends in regional O_3 (Jenkin 2004). The predictions of annual mean PM_{10} concentrations used a combination of emissions from the detailed road network as well as other PM_{10} sources, represented as volume sources of varying dimensions. PM_{10} arising from outside London was taken from the analysis of measurements and was split into primary, secondary, and natural particles. Primary particles are made by anthropogenic processes and are ejected directly into the atmosphere. Secondary particles are created in the atmosphere after chemical or physical transformations of precursor gases. Natural particles, such as soils and sands, are also ejected directly into the atmosphere (Fuller et al. 2002; Fuller and Green 2006).

The impact of the LEZ was assessed by comparing two model runs for 2010 with and without the impacts of LEZ implementation. The impacts of the LEZ implementation on vehicle-stock changes are given in Appendix Tables B.1, B.2, and B.3. Detailed descriptions of the scenario case models, the King's College London Emissions Toolkit and Air Pollution Toolkit, and the methods used in this study are also given in Appendix B. Because the model forecasts assume that the meteorologic data are the same as in 2002 for both model runs (i.e., with and without LEZ scenarios), any changes in pollutant concentrations are associated only with the LEZ.

No formal uncertainty estimate has been undertaken for the King's College London air pollution model. However, from previous evaluation studies (Kelly et al. 2011a,b) a comparison of the model predictions based on London measurements from 2002 (from more than 50 sites for NO_x and more than 40 sites for PM_{10}) was undertaken, and details of the results for 2002 are included in Appendix B. In the absence of a formal uncertainty analysis, the root mean square and bias results provide a reasonably robust estimate of model uncertainty.

It is also worth noting that, because the model is used to provide a comparison of air pollution concentrations with and without the LEZ, the uncertainties are more closely associated with the assumed differences. These differences

were based on an assumed, rather than the actual, effect of the LEZ scheme, which had only just begun. The model uncertainty was therefore associated with the accuracy of Transport for London's forecast of changes in the heavy-goods-vehicle fleet operators' behavior in response to the LEZ scheme and with the relative improvements in emissions brought about by those changes. For example, fleet operators could have chosen to purchase new vehicles, replace the engines of existing vehicles, fit particle traps to vehicle exhausts, or (for larger fleets) to divert older vehicles so that they no longer operated in London. The diversion of older vehicles would have had an effect throughout the U.K. but would have been countered somewhat by the benefits of new vehicles bought to operate in London as well as throughout the U.K. and Europe.

At the time of this study, no estimate of the predictive performance of the Transport for London assumptions could be made. However, since implementation of the LEZ, a specific LEZ emissions inventory is being developed using automatic plate-recognition cameras to assess on-road vehicle changes. This inventory will be used for future estimates of the LEZ's impact.

Identification of Predicted Hot Spots

Our analysis used modeling outputs from the runs with and without the LEZ scenario to highlight those areas predicted to experience the greatest change in NO_2 and PM_{10} concentrations for 2010 (Appendix B). From the model outputs, differences in predicted annual mean concentrations with and without the LEZ were calculated for each of the 20×20–m grids across London and a spatial difference plot of concentration differences was created. A subjective assessment was made to select a concentration-difference contour that would highlight such hot spots. Concentration difference contours of 3 $\mu g/m^3$ NO_2 or greater and 0.75 $\mu g/m^3$ PM_{10} or greater were selected to highlight "hot spots" because they identified a sufficient range of locations with effects extending beyond the curb of the road. The maps highlighted areas within the hot spot contours, i.e., areas predicted to experience at least a 3 $\mu g/m^3$ (NO_2) or 0.75 $\mu g/m^3$ (PM_{10}) change in concentration as a result of the implementation of the LEZ. All other areas were predicted to experience less change. The locations of fixed long-term monitoring sites in operation on June 1, 2005, were overlaid on the maps, with symbols indicating the type of monitoring site (roadside, curbside, intermediate, or background). The road network was also overlaid on the map.

RESULTS

The annual mean NO_2 (Figure 4) and PM_{10} (Figure 5) concentration-difference plots both indicated that the clearest signal of change caused by the LEZ is likely to be recorded by roadside and curbside continuous monitoring sites. (See Appendix E, which is available on the HEI Web site, for site codes and names.) Figure 4 shows the 3-$\mu g/m^3$ concentration-difference plot for annual mean NO_2 in Greater London. At this level, change caused by the LEZ would be limited to those areas immediately adjacent to certain sections of major trunk routes throughout Greater London and a number of major roads within Central London. Figure 5 shows the 0.75-$\mu g/m^3$ concentration-difference plot for annual mean PM_{10}. The distribution of hot spots is very similar to that for NO_2 hot spots. Relatively few hot spots were identified south of the Thames, but the North Circular ring road and certain northern sections of the M25 motorway were clearly defined.

After dividing Greater London into five sectors (central, north west, north east, south east, and south west), an assessment was made as to the extent of continuous pollutant monitoring in June 2005, in areas highlighted by the modeling as likely to experience the greatest changes.

Central Sector

The concentration-difference plot for annual mean NO_2 and PM_{10} for the central sector is shown in Figures 4 and 5, respectively. It should be noted that although each site shown in the figure is equipped to monitor NO_2 not all sites monitor PM_{10}. The plot suggested that the sites best placed to monitor the impacts of the LEZ scheme were Westminster—Marylebone Road (MY1), Hackney—Old Street (HK6), Lambeth—Vauxhall Cross (LB5), and City of London—Thames Street (CT6). However, City of London—Thames Street was excluded because it monitored NO_2 using a type of analyzer not approved for use on the Automatic Urban and Rural Network. Lambeth—Vauxhall Cross was excluded because of its proximity to a London Underground vent.

North West Sector

The concentration-difference plot for NO_2 and PM_{10} for the north west sector is shown in Figures 4 and 5. The main hot spot areas in the north west were along the North Circular and the A40 roads (see Figure 3). NO_2 and PM_{10} were monitored on the Brent section of the North Circular at IKEA (Brent—Ikea, BT4). The Ealing—Hanger Lane (EA6) site was well placed to monitor concentrations of NO_2 on the North Circular and A40 intersection but was not equipped to monitor PM_{10}, and adding equipment was not possible because cabinet space was limited.

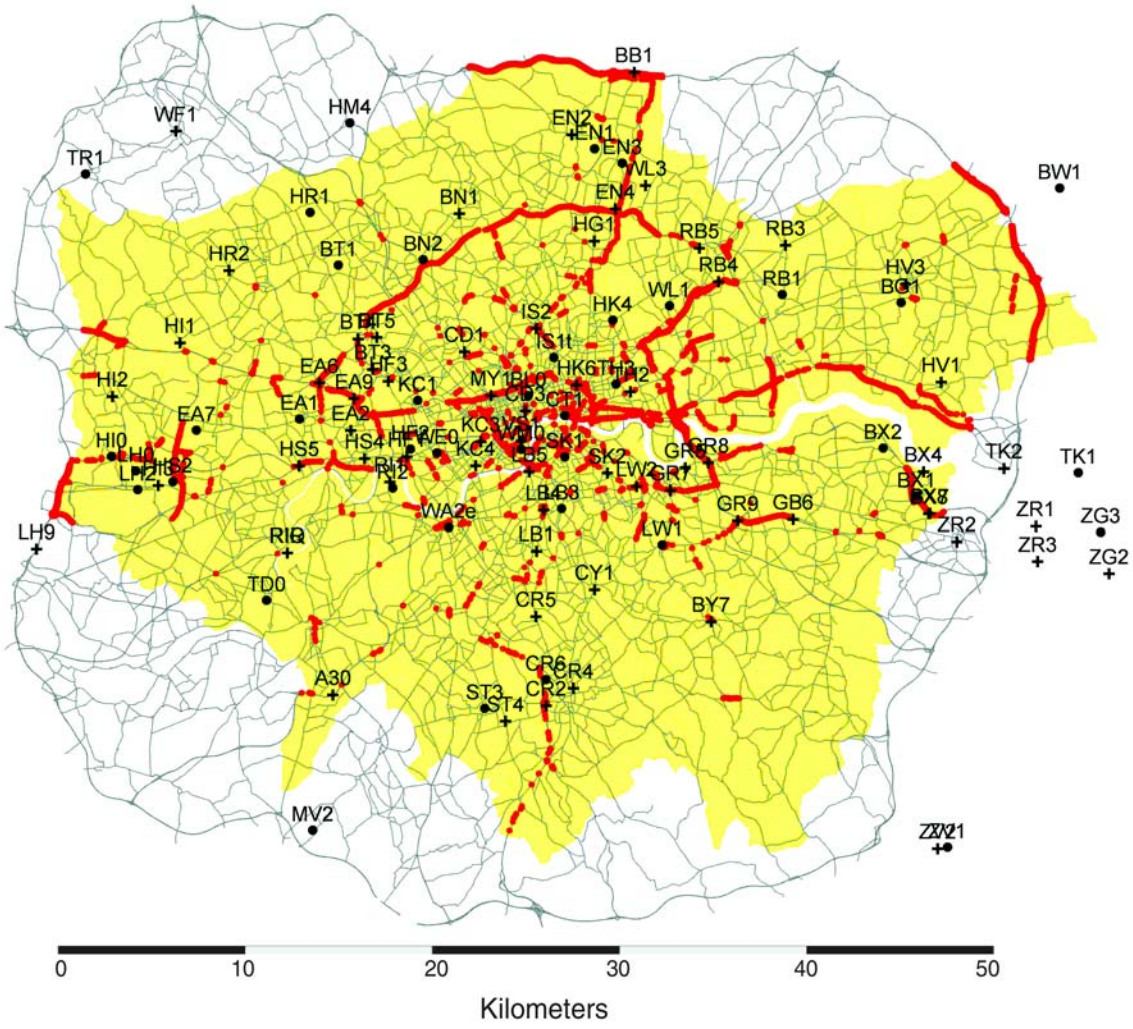

Figure 4. Annual mean NO_2 3-μg/m³ concentration-difference plot (red) for the 2010 base case versus LEZ Scenario 6 in Greater London. The LEZ is shown in yellow, major road links in gray. The locations of continuous monitoring sites are shown as crosses for curbside and roadside sites, and as dots for urban background and suburban sites. See Appendix E for site codes and names.

North East Sector

The concentration-difference plot for NO_2 and PM_{10} for the north east sector is shown in Figures 4 and 5. The principal hot spots were the major radial routes and certain sections of the M25 motorway (see Figure 3). The greatest predicted impact was along the A12, the A13 in East London (as shown in Figure 3), and the Blackwall Tunnel Northern Approach. The Blackwall Tunnel Northern Approach, identified as an important hot spot, did not have a monitoring site, and a monitoring site was therefore installed, and the site was referred to as Tower Hamlets—Blackwall Tunnel (TH4).

South East Sector

The concentration-difference plot for NO_2 and PM_{10} for the south east sector is shown in Figures 4 and 5. The principal areas of effect in this sector were along the Blackwall Tunnel Southern Approach, the A2 through Greenwich, and the A206 in Bexley (see Figure 3). Monitoring sites were well represented in each location. The Greenwich—Woolwich Flyover site (GR8) on the Woolwich Flyover monitored NO_2 and PM_{10}. The Greenwich—Westhorne Avenue site (GR9) monitored roadside NO_2, PM_{10}, and $PM_{2.5}$ (by Filter Dynamics Measurement System [FDMS]) on the interchange of the South Circular and the A2. There

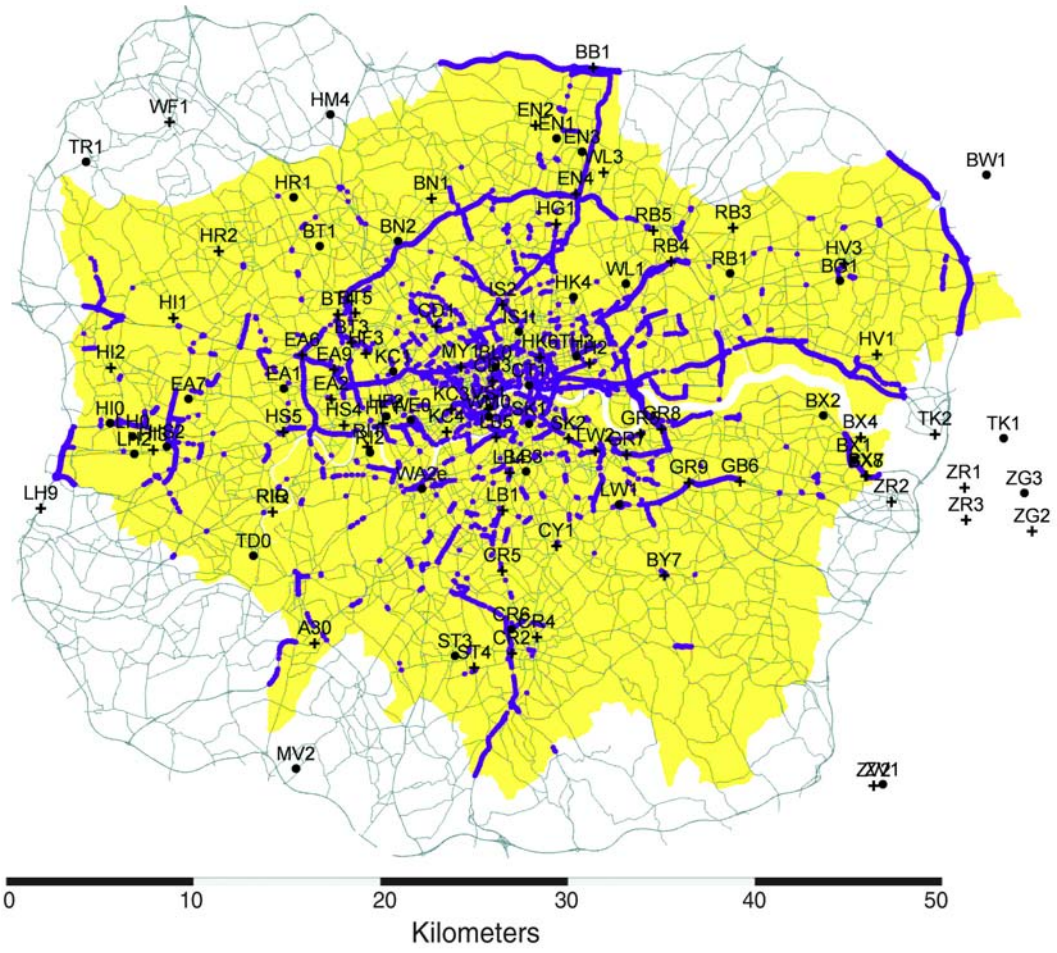

Figure 5. Annual mean PM_{10} 0.75-μg/m³ concentration-difference plot (blue) for the 2010 base case versus LEZ Scenario 6 in Greater London. The LEZ is shown in yellow, major road links in gray. The locations of continuous monitoring sites are shown as crosses for curbside and roadside sites, and as dots for urban background and suburban sites. See Appendix E for site codes and names.

was also a monitoring site for NO_2, PM_{10}, and $PM_{2.5}$ on each side of the A206 at Cray, albeit about 20 m from the curb (Bexley—Thames Road North [BX7] and Bexley—Thames Road South [BX8]).

South West Sector

The concentration-difference plot for NO_2 and PM_{10} for the south west sector is shown in Figures 4 and 5. There were only two major hot spots in this sector, namely the Wandsworth Gyratory (a circular traffic intersection) and the M25 north of Junction 14 at Heathrow (see Figure 3, Wandsworth—Wandsworth Town Hall [WA2]). The Wandsworth Gyratory has monitoring of roadside NO_2 and PM_{10}.

Monitoring of Other Relevant Pollutants

The most widespread monitoring of PM in the LAQN was of PM_{10} mass concentration by TEOMs or beta attenuation monitors. Although modeling indicated that the LEZ scheme would have little impact on PM_{10} mass concentrations in most areas (less than 1-μg/m³ change in concentration), it was likely that changes in emissions would have a more significant impact on smaller size fractions and specific PM components, i.e., related to diesel emissions.

BS monitoring is now scarce in Greater London: there is a perceived lack of relevance to air pollution in the London Boroughs, and there is no longer any national government funding for monitoring BS. One major factor in

the demise of BS monitoring was the high cost of manually appraising exposed filters. Only one BS monitor, located curbside at Westminster—Marylebone Road, was scheduled to remain in operation to the end of 2005. The development of the aethalometer, a continuous BS analyzer installed in the bypass flow line of the TEOM analyzer, presents an opportunity for the re-establishment of BS monitoring.

Conversely, $PM_{2.5}$ monitoring has expanded rapidly in recent years. In June 2005 there were 12 continuous $PM_{2.5}$ monitors within the LAQN, six of which were at roadside or curbside locations. Four of these locations (Westminster—Marylebone Road, Greenwich—Westhorne Avenue, Bexley—Thames Road North, and Bexley—Thames Road South) were identified in the above analysis as being particularly relevant to monitoring the effects of LEZ scheme implementation.

In response to the criticism that the TEOM method heats the sampled air and therefore does not measure the volatile fraction of PM, TEOM manufacturers recently introduced the FDMS TEOM. This new monitor uses a dual-cycle method to produce separate concentrations of volatile and non-volatile PM. The equipment can operate with PM_{10} or $PM_{2.5}$ sampling heads, allowing assessment of changes in specific components of the particulate fraction. In June 2005, FDMS analyzers were in operation at the Westminster—Marylebone Road (measuring PM_{10}) and Greenwich—Westhorne Avenue (measuring PM_{10} and $PM_{2.5}$) sites, both of which were identified as being particularly relevant to the LEZ impacts study.

Recent analysis shows a clear correlation between particle number and NO_x at roadside locations, more so than between PM_{10} or $PM_{2.5}$ and NO_x (Harrison and Jones 2005). A variable but significant proportion of PM_{10} recorded at the roadside is from background sources independent of exhaust emissions (Kelly et al. 2011b). Of this proportion, relatively small numbers of larger particles might have a large influence on PM_{10} mass compared with far greater numbers of smaller particles. Therefore, monitoring particle number would be more likely to identify LEZ impacts than monitoring particle mass. Although condensation particle counters (CPCs) are currently installed at Marylebone Road and at the North Kensington background site as part of the national U.K. Particles Monitoring Network, additional CPCs to monitor roadside particle numbers would be advantageous to the LEZ impacts study.

Another relevant pollutant of concern in future roadside monitoring in London is that of direct emissions of primary NO_2. Changes in direct emissions of NO_2 are not currently fully understood, and additional studies are required. An effective way of assessing the contribution of directly emitted NO_2 to ambient concentrations at the roadside is by co-locating NO_2 and O_3 analyzers, which is required to measure total oxidant load (Clapp and Jenkin 2001 and Carslaw and Beevers 2004). Because of the phenomenon known as NO_x scavenging of O_3, O_3 concentrations at the roadside are typically well below those considered harmful to health, and consequently very little roadside O_3 monitoring is carried out.

Establishment of the Monitoring Network

Seven key sites identified using the above approach formed the basis of our LEZ pollution impacts monitoring network (Table 2). Two of these sites already had all the necessary monitors in operation. Funding was sought from

Table 2. Locations and Capabilities of Seven Key LEZ Monitoring Sites[a]

Site Name and Location	Parameters Monitored
Westminster—Marylebone Road (MY1), Central London	FDMS PM_{10}, $PM_{2.5}$, P_{NUM}, BS, NO_x, O_3, CO, SO_2, Hydrocarbons, traffic count, ANPR camera, meteorology
Hackney—Old Street (HK6), Central London	PM_{10}, NO_x, O_3, $PM_{2.5}$, traffic count, ANPR camera
Bexley—Thames Road South (BX8), East London	FDMS PM_{10}, FDMS $PM_{2.5}$, NO_x, O_3, traffic count, ANPR camera, meteorology
Greenwich—Westhorne Avenue (GR9), South East London	FDMS PM_{10}, FDMS $PM_{2.5}$, NO_x, O_3, traffic count, ANPR camera, meteorology
Greenwich—Woolwich Flyover (GR8), South East London	PM_{10}, $PM_{2.5}$, NO_x, O_3, traffic count, ANPR camera
Brent—Ikea (BT4), North West London	PM_{10}, $PM_{2.5}$, NO_x, O_3, SO_2, P_{NUM}, BS, traffic count, ANPR camera, meteorology
Tower Hamlets—Blackwall Tunnel (TH4), East London	FDMS PM_{10}, FDMS $PM_{2.5}$, P_{NUM}, BS, NO_x, O_3, traffic count, ANPR camera, meteorology

[a] Sites were fully operational as of October 2006. ANPR indicates automatic plate-number-recognition camera and P_{NUM} indicates particle number.

Transport for London to augment four of the sites, where some existing monitoring was in place, and to establish a monitoring site at the seventh site, on the Blackwall Tunnel Northern Approach road. Capital and revenue funding was provided in early 2006, and equipment was installed between May and September 2006. Installation of monitoring equipment at the Blackwall Tunnel Northern Approach site took place during July 2006 (Figure 6), the electricity supply was connected in August, and the site was commissioned in September. Transport for London installed automatic traffic counters, which record vehicle numbers classified by speed and length, and automatic number-plate-recognition cameras adjacent to each of the monitoring sites during May 2006 and December 2006, respectively. Transport for London will also carry out bi-annual manual traffic count campaigns at each site.

Establishment of the LEZ Analysis Database

Measurements from each site were collated into the LAQN database and underwent ratification to defined quality assurance and quality control standards. Pollutant data were at 15-minute or hourly resolution. The automatic traffic count data comprised aggregate 15-minute vehicle counts classified by speed and length. Data from the automatic plate-recognition cameras included individual date- and time-stamped vehicle details, such as year of manufacture, fuel type, chassis configuration, EURO emissions class, and engine capacity.

Figure 6. Installation of the Tower Hamlets—Blackwall Tunnel monitoring site.

As mentioned above, the seven key sites were only part of the LEZ impacts monitoring network. The wider network comprised all long-term continuous monitoring sites in the LAQN database, which included a high-density network of continuous monitoring sites, all operated to meet defined and comparable quality assurance and quality control standards. Figure 7 shows the distribution of LAQN monitoring sites that measured the four major pollutants (NO_x, PM_{10}, $PM_{2.5}$, and O_3) as of September 2006.

DISCUSSION

The emissions controls enforced by the LEZ scheme in London were expected to have the greatest effect close to major roads with high volumes of heavy-goods-vehicle traffic. The great majority of long-term continuous air quality monitoring carried out in Greater London has been established to measure pollution concentrations where there is the most public exposure. There is therefore very little monitoring close to trunk routes or large motorway intersections in outer London. Owing to the lack of public exposure, monitoring in these locations would be largely of academic interest and was therefore not recommended. Population density increases toward inner London, and public exposure is more widespread as the proximity of residents and pedestrians to major routes increases. The analysis undertaken to improve the LEZ impact monitoring network revealed a good distribution of monitoring sites close to trunk routes and major intersections. Six key existing sites were identified as being of primary importance, of which four have been upgraded to monitor a wider range of pollutants. A seventh site was installed where the analysis identified a hot spot with no existing monitoring.

The work described in this section opened up a number of opportunities for analyzing the impact of the LEZ in London:

- The ability to plan an extensive impacts monitoring program before the implementation of the LEZ, including the placement and scope of monitoring, provided an invaluable foundation for assessing the effects of the LEZ on air quality and human health. Indeed, the results of this analysis helped to inform the choice of primary-care general practice surgeries (as detailed below in the section on Development of Methodology to Evaluate the Impact of the LEZ on Morbidity).

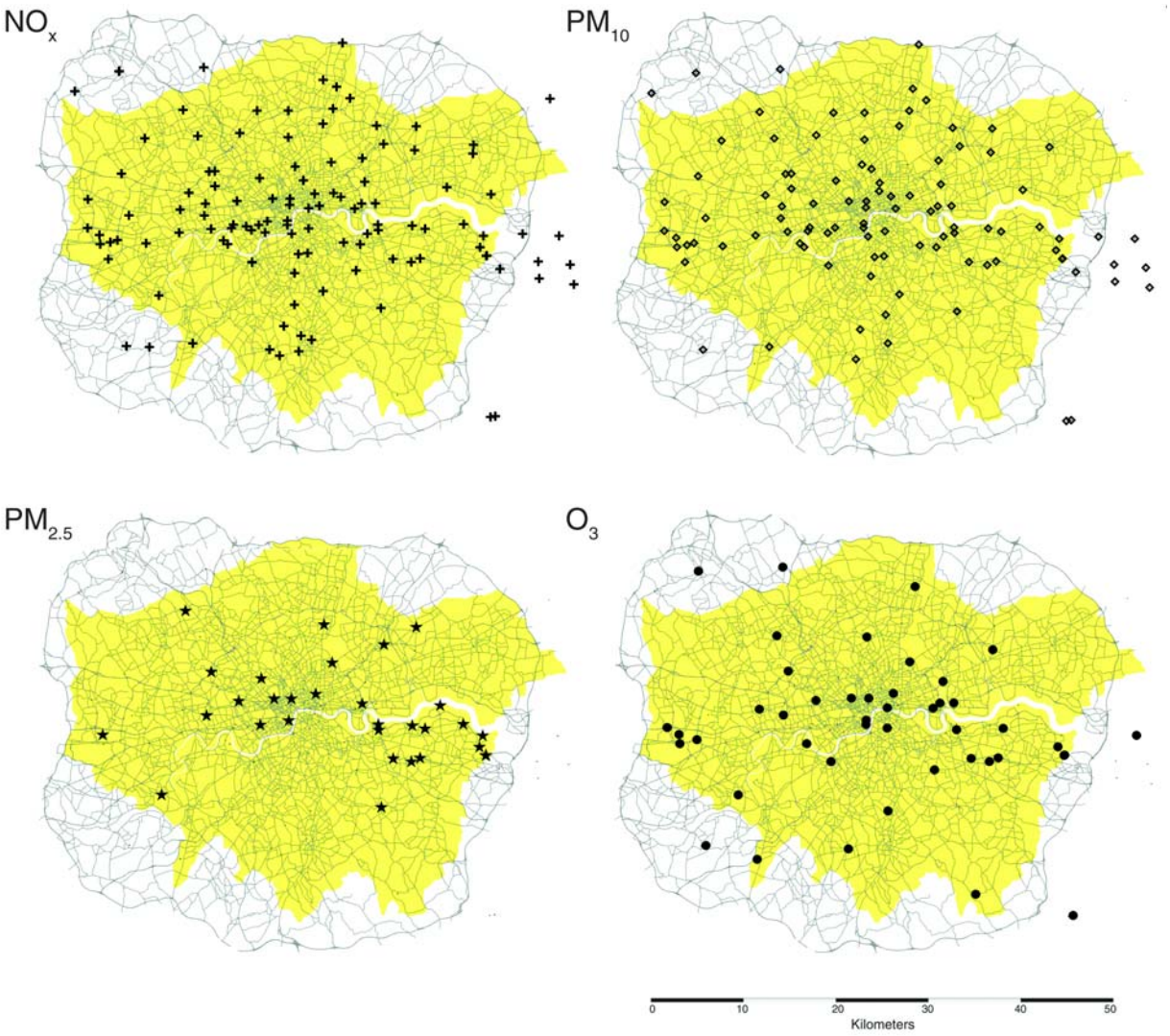

Figure 7. Distribution of all NO_x, PM_{10}, $PM_{2.5}$, and O_3 continuous monitors in the LEZ. Information from the LAQN database as of September 2006. The LEZ is shown in yellow, major road links in gray. Symbols indicate locations of continuous monitors.

- The increased availability of roadside data necessary to improve the scope and repeatability of statistical analysis methods developed in the HEI-funded London CCS project (Kelly et al. 2011a,b), drive the development of further statistical methods, and allow expansion of the toxicity study (described in the following section).
- The vehicle profiling available in unprecedented detail at each of the seven key monitoring sites, through automatic and manual traffic counts and automatic plate-recognition camera data, made possible a more detailed study of the relation between vehicle emissions and ambient pollutant concentrations.
- The range of available particle metrics will help in the identification of the effect of the LEZ on specific components of PM, assist in the interpretation of the toxicity study, and further our understanding of the relative importance of particulate sources, including tire and brake wear.
- The increased availability of data on roadside O_3 concentrations will also further understanding of the behavior of primary NO_2 emissions, an issue that is little understood but of great concern to researchers and policymakers.

ASSESSING THE OXIDATIVE PROPERTIES OF AMBIENT PM_{10} AND $PM_{2.5}$ ACROSS GREATER LONDON

INTRODUCTION

The work outlined in this section focused on characterizing PM_{10} and $PM_{2.5}$ in terms of their potential to initiate oxidative stress in biologic systems (i.e., oxidative potential) and in terms of traffic-related metal content. The determination of PM oxidative potential has evolved over the last five to 10 years out of the attempt to connect the health effects observed in epidemiologic studies and the pathophysiologic processes underpinning these effects. A robust epidemiologic literature exists, with studies that demonstrate significant associations between ambient PM concentrations and premature mortality and negative impacts on cardiorespiratory health (Brunekreef and Holgate 2002). Although these associations appear consistent across studies, considerable heterogeneity in the PM-effect-size estimate exists in the literature (Samet et al. 2000; Katsouyanni et al. 2001; Janssen et al. 2002; Zanobetti et al. 2002; Bell et al. 2004). Evidence has indicated that PM derived from traffic sources is particularly harmful (McCreanor et al. 2007; Janssen et al. 2003). Thus, even though the use of ambient PM concentrations has proved strong evidence of a causal relationship between PM and health effects, it is clearly not an ideal metric, because it ignores the sources, constituents, and biologic activity of the particulates themselves. This is an important consideration, because much of the mass of ambient PM consists of compounds of low or negligible toxicity and only trace concentrations of metals (Aust et al. 2002), polyaromatic hydrocarbons (Bonvallot et al. 2001), quinones (Squadrito et al. 2001), and endotoxin (Monn et al. 2003). These trace concentrations could be predicted to contribute significantly to any observed pathologic response. At one level this argues for the use of a component-driven rather than a mass-driven metric; however, because of the compositional complexity of ambient PM and potential synergies between components, a component-based approach is difficult to achieve. Because of the difficulty, approaches based on describing PM as a mixture of source contributions (Hopke et al. 2006) or on deriving a measure of biologic activity per unit mass (Borm et al. 2007) have been used. The latter approach is attractive because it effectively integrates differences in PM size distribution and composition into a single endpoint while still permitting the critical determinants driving the oxidative consumption of antioxidants to be isolated through the use of selective inhibitors, or the fractionation of the PM sample. In addition, depending on the complexity of the biologic model employed and its pertinence to PM interactions at the air–lung interface in vivo, the chemistry or biologic response observed may provide valuable insights into the mechanism of PM-induced toxicity. It should be stated up front, however, that our oxidative potential metric is not being proposed as an alternative to existing mass or number metrics but rather as a complementary measure with which to examine the heterogeneity of PM health effects estimates that are not explained by mass alone.

The capacity of inhaled particles to induce oxidative stress at the air–lung interface has been proposed as a mechanistic link between their content of redox-active components and the induction of inflammation and tissue injury by way of the upregulation of redox-sensitive transcription factors (Pourazar et al. 2005; Borm et al. 2007). We and others have argued that deriving a metric that describes the potential of inhaled particles to drive damaging oxidation reactions might result in a measure of the "harmfulness" of ambient air (Borm et al. 2007). Because large-scale screening of ambient PM in cell and animal models is impractical, we have developed an acellular model of the respiratory tract-lining fluid (RTLF), which is the aqueous compartment that particles first enter when inhaled into the lungs. The synthetic RTLF used in our model contains physiologic concentrations of three antioxidants (ascorbate [AA], urate, and reduced glutathione [GSH]) to measure particle oxidative potential (Zielinski et al. 1999; Mudway et al. 2004, 2005; Künzli et al. 2006). We proposed that the capacity of a particle, or a component of a particle, to deplete the antioxidants in the RTLF provided a physiologically relevant measure of its oxidative potential.

Metal and organic components derived from motor-vehicle exhaust and non-exhaust sources (e.g., resuspension of road dust and brake and tire wear) influence the redox activity of PM. We previously demonstrated that the oxidative potential of PM collected is higher at roadside sites, reflecting increased concentrations of bioavailable metals, predominantly Fe and Cu (Künzli et al. 2006). As such, we proposed that changes in PM_{10} and $PM_{2.5}$ oxidative potential would occur after the introduction of the LEZ in London as a consequence of changes in traffic densities and vehicle mix (hence fuel use). To test this hypothesis it was necessary, as an initial step, to establish a robust baseline data set describing the oxidative potential and redox-active metal content of PM_{10} and $PM_{2.5}$ measured in London before the introduction of the LEZ scheme.

To establish this baseline data set, PM collected from 37 monitoring sites within the designated LEZ area and 4 monitoring sites outside of the London conurbation was examined for its capacity to deplete antioxidants from synthetic RTLF during a fixed amount of time. Using the

extent to which these antioxidants were depleted over time, per equivalent mass of extracted PM_{10}, or $PM_{2.5}$, we derived two expressions for the oxidative potential of PM collected in London over the period from July 2005 to August 2006, one per unit mass of extracted PM and the other per cubic meter (m^3) of ambient air. This work provided the opportunity to perform the first detailed city-wide assessment of PM oxidative potential — examining the differences in oxidative potential of PM between roadside and urban background locations in London and comparing the oxidative potential of London's PM collected to that of PM collected from surrounding areas. Finally, to assess the redox-active metal content of London PM, a panel of metals with known traffic sources was examined (Table 3). We also used a high-throughput method, based on the capacity of PM to deplete AA from a single antioxidant solution over a fixed period of time, with or without co-incubation with the metal chelator diethylenetriamine pentaacetic acid (DTPA), in an attempt to derive expressions for metal-dependent and metal-independent oxidative activity (described in detail below).

The work described in this section addressed the following two key objectives:

- To examine the oxidative activity and metal content of PM_{10} and $PM_{2.5}$ collected at various sites in Greater London and its environs with contrasting traffic densities and vehicle contribution.
- To combine these data with those obtained for central London in our CCS study (Kelly et al. 2011a,b) in order to produce an overall spatial view of PM oxidative activity across Greater London.

METHODS

Site Selection

TEOM filters (representing PM_{10} collected from all selected sites and $PM_{2.5}$ collected from sites where available) were obtained within the LAQN from July 2005 to September 2007. The selected sites included 27 roadside locations believed most likely to show impacts of the introduction of the LEZ and 9 background sites. These sites are described in Table 4; their geographic locations are represented in Figure 8. More information about the sites, the handling of the PM_{10} filter archive, and the measurement of oxidative potential is provided in Appendix C, and a complete list of site codes is in Appendix E; both are available on the HEI Web site.

Table 3. Source Attribution of Selected Metals Found in PM[a]

Potential PM Component / Source(s)	Reference(s)
Ba	
Lubricating oil	de Miguel et al. 1997
Brake wear	Harrison et al. 2003
Cd	
Diesel fuel	Onianwa 2001
Lubricating oil	Harrison et al. 2003
Brake wear	Weckwerth 2001
Carriage wear[b]	de Miguel et al. 1997
Cu	
Diesel fuel	Manoli et al. 2002
Lubricating oil	de Miguel et al. 1995
Brake wear	Weckwerth 2001, Harrison et al. 2003, Laschober et al. 2004
Fe	
Brake wear	Weckworth 2001
Mo	
Diesel fuel	Harrison et al. 2003
Brake wear	Weckwerth 2001
Ni	
Diesel fuel	Weckwerth 2001
Lubricating oil	de Miguel et al. 1997
Pb	
Brake wear	Laschober et al. 2004, Weckwerth 2001
Zn	
Diesel fuel	Weckwerth 2001, Harrison et al. 2003
Lubricating oil	Laschober et al. 2004
Brake wear	Laschober et al. 2004
Carriage wear	Laschober et al. 2004
Tire wear	Weckwerth 2001, Harrison et al 2003

[a] From Kelly et al. 2011b.

[b] Wear on the body of the vehicle.

Measuring PM Oxidative Activity

The oxidative potential of PM was determined using the validated RTLF model (Zielinski et al. 1999; Mudway et al. 2004) that measures the degree to which PM can oxidize a range of protective antioxidant molecules present at the surface of the lung. These determinations were made by incubating PM suspensions derived from TEOM filter extractions in the RTLF at a final particle concentration of 50 µg/mL. Full details of the extraction and resuspension protocols used are outlined in Appendix C and were identical to the

Table 4. PM_{10} and $PM_{2.5}$ TEOM Filters Extracted and Analyzed from Sites in the London Metropolitan Area[a]

Site	Code	Filter Archive Collection Period (Start Date–End Date)	Classification	PM_{10} Filters (*n*)	$PM_{2.5}$ Filters (*n*)
Wandsworth—A3	A30	Jan. 5–May 4, 2006	Roadside	4	
Barnet—Tally Ho Corner	BN1	Jan. 11, 2005–Sept. 15, 2006	Roadside	8	
Bexley—Thames Road North	BX7	Aug. 16, 2005–Sept. 26, 2006	Roadside	15	
		Aug. 16–29, 2005			16
Bexley—Thames Road South	BX8	July 22, 2005–July 3, 2006	Roadside	13	
		June 21, 2005–Aug. 29, 2006			15
Bloomsbury—Russell Square	BL0	July 13, 2005–Sept. 13, 2006	Background	14	
		July 13, 2005–Sept. 13, 2006			14
Brent—Kingsbury	BT1	Sept. 5, 2005–Sept. 26, 2006	Background	8	
Brent—Ikea	BT4	Dec. 21, 2005–Aug. 25, 2006	Roadside	9	
		May 22–Sept. 13, 2006			4
Camden—Swiss Cottage	CD1	Aug. 2, 2005–Aug. 15, 2006	Roadside	17	
Camden—Shaftesbury Avenue	CD3	Aug. 2, 2005–Aug. 30, 2006	Roadside	14	
Croydon—George Street	CR4	Jan. 6–July 7, 2006	Roadside	3	
Crystal Palace—Crystal Palace Parade	CY1	Jan. 4–July 12, 2006	Roadside	4	
Ealing—Acton Town Hall	EA2	Dec. 7, 2005–June 29, 2006	Roadside	12	
		Jan. 10–Sept. 26, 2006			6
Ealing—Southall	EA7	Dec. 13, 2005–Mar. 14, 2006	Background	3	
Greenwich—Eltham	GR4	Aug. 10, 2005–July 21, 2006	Background	6	
Greenwich—Woolwich Flyover	GR8	Jan. 5–Sept. 7, 2006	Roadside	13	
		May 23–Sept. 7, 2006			4
Greenwich—Westhorne Avenue	GR9	April 27–June 14, 2006	Roadside	1	
		April 27–June 14, 2006			1
Greenwich Bexley—Falconwood	GB6	Dec. 20, 2005–Sept. 27, 2007	Roadside	11	
		Dec. 20, 2005–Sept. 7, 2006			10
H & F—Hammersmith Broadway	HF1	July 5, 2005–Sept. 28, 2007	Roadside	28	
H & F—Brook Green	HF2	July 12, 2005–Sept. 15, 2006	Background	11	
Haringey—Town Hall	HG1	Sept. 9, 2005–Sept. 13, 2007	Roadside	9	
Harrow—North Harrow	HR2	Jan. 5–Sept. 20, 2006	Roadside	11	
Havering—Romford	HV3	Jan. 16–June 16, 2006	Roadside	5	
Hillingdon—Hillingdon Hospital	HI2	Dec. 21, 2005–Jan. 26, 2006	Roadside	1	
Hounslow—Brentford	HS5	Jan. 1–June 29, 2006	Roadside	6	
Islington—Upper Street	IS1	Dec. 21, 2005–Sept. 28, 2006	Roadside	13	
K & C—North Kensington	KC1	July 6, 2005–Sept. 28, 2006	Background	14	
K & C—Cromwell Road	KC2	July 26, 2005–Sept. 12, 2006	Roadside	33	
Lewisham—New Cross	LW2	July 29, 2005–June 12, 2006	Roadside	9	
Westminster—Marylebone Road	MY1	July 20, 2005–Sept. 27, 2006	Roadside	56	
		July 18, 2005–Sept. 22, 2006			24
Richmond—Castelnau	RI1	July 19, 2005–July 10, 2006	Roadside	11	
Southwark—Elephant & Castle	SK1	July 29, 2005–Aug. 24, 2006	Background	10	
Southwark—Old Kent Road	SK2	July 29, 2005–April 20, 2006	Roadside	14	
Sutton—Wallington	ST4	Dec. 30, 2005–June 30, 2006	Roadside	8	
Tower Hamlets—Poplar	TH1	Dec. 16, 2005–June 22, 2006	Background	6	
Waltham Forest—Dawlish Road	WL1	Jan. 4, 2006–Sept. 7, 2006	Background	5	
Waltham Forest—Chingford	WL3	Jan. 16, 2006–Sept. 7, 2006	Roadside	5	

[a] No filters were obtained from the Tower Hamlets—Blackwall Tunnel (TH4) site over the study period.

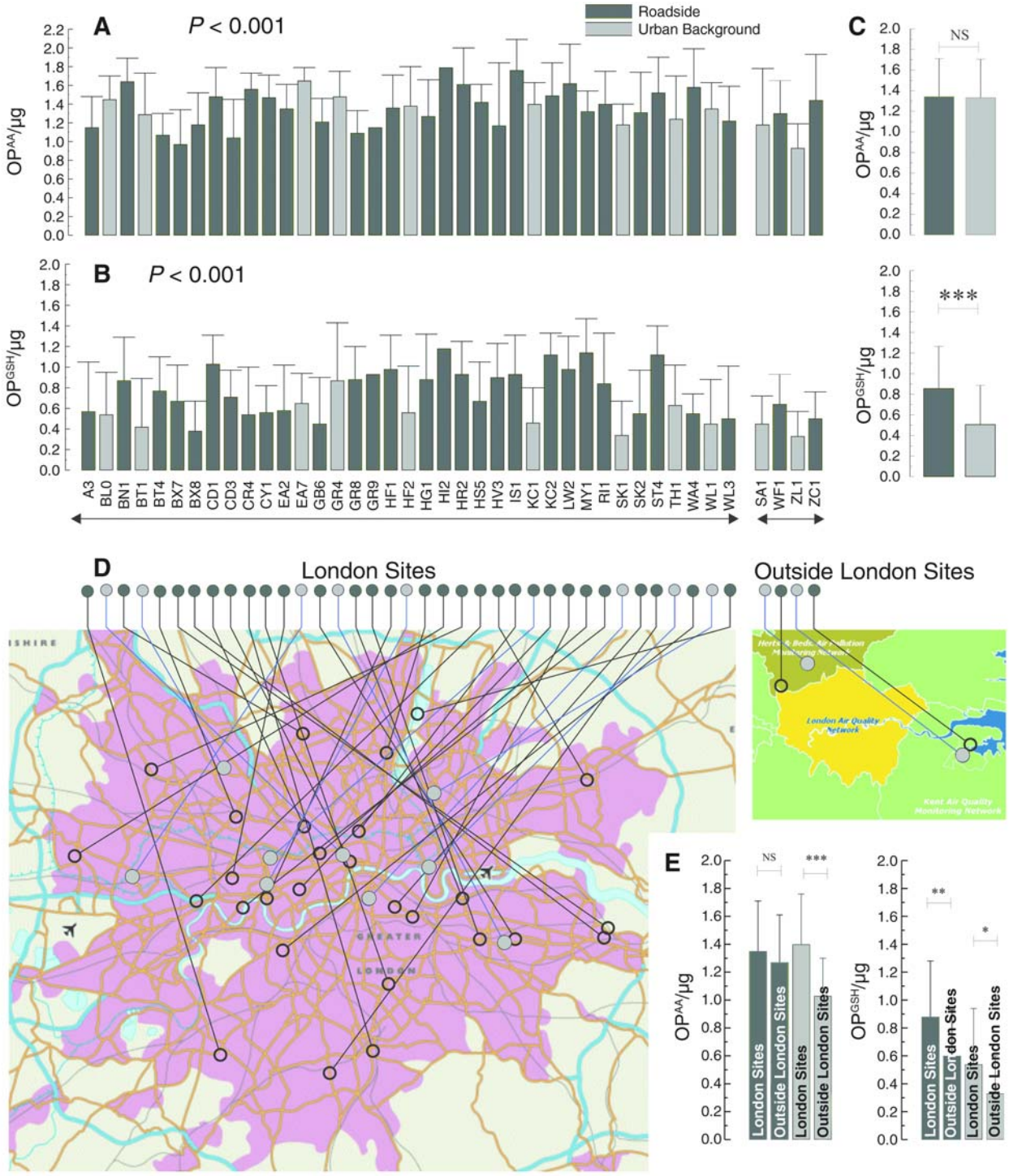

Figure 8. Summary of OP^{AA}/µg (A) and OP^{GSH}/µg (B) for PM_{10} for the 41 sites studied. Results are grouped to show site locations (in London or outside London). The numbers of filter samples in each group are given in Table 1 (for sites in London) and Table 2 (for sites outside London). *P* values are the results of an ANOVA examination of site-specific contrasts in the data set. **(C)** OP^{AA}/µg and OP^{GSH}/µg for all roadside filters (31 sites, 362 samples) and all urban background filters (11 sites, 94 samples), expressed as means ± 1 SD. Comparisons between roadside and urban background results were performed using a two-tailed unpaired *t* test (assuming unequal group variances). **(D)** Locations of the sites. **(E)** Comparison of the OP metrics at the roadside and urban background sites, within and outside of London, expressed as means ± 1 SD. NS = nonsignificant difference, *** = $P < 0.001$, ** = $P < 0.01$, and * = $P < 0.05$. See Appendix E for site codes and names.

methods employed in our previous HEI-funded study investigating the impact of the introduction of London Congestion Charging Zone (Kelly et al. 2011b). The only major deviation from our previous study was that prior to extraction filter reflectance measurements were performed using an EEL Model 43 analogue reflectometer to provide a surrogate measure for black smoke (elemental carbon). This methodology is presented in detail in Appendix C, together with derivation of the absorption coefficient. The RTLF solutions used contained equimolar concentrations (the starting concentration was 200 μM) of the antioxidants AA, urate, and reduced GSH. PM and antioxidants were co-incubated for 4 hours at 37°C at pH 7. Reactions were then quenched by acidification of the sample (using metaphosphoric acid at a final concentration of 5%), and particles were removed by centrifugation (13,000 rpm for 60 minutes at 4°C) before determining the remaining antioxidant concentrations in the supernatant. To ensure intra-assay standardization between experiments, control PM samples were also run. These consisted of a particle-free control (auto-oxidation), residual oil fly ash (used as the positive control), and the inert carbon black particle M120 (used as the negative control). The details of the composition of these control particles have been published previously (Miller et al. 1998; Zielinski et al. 1999). All incubations were performed in triplicate. AA and urate concentrations were determined using reverse-phase high-pressure liquid chromatography with electrochemical detection in the amperometric mode (Iriyama et al. 1984). Reduced and oxidized GSH were measured using the enzyme recycling method of Tietze modified for use on a plate reader (Baker et al. 1990). A full description of these methods is given in Appendix C.

Statistics

Oxidative potential measurements and PM absorbance were normally distributed and are described throughout as mean ± 1 SD. The significance of variation of means across monitoring sites was tested by ANOVA, with post hoc testing using the Games–Howell test to provide robustness against unequal within-site variances, given the different sample sizes for each site. All PM metal data were nonparametric and are summarized throughout this report as median concentrations with interquartile range and 95% confidence intervals. The significance of differences in concentrations between sites was established using Kruskal–Wallis ANOVA. Comparisons of roadside and urban background oxidative potentials and PM metal concentrations were performed using a *t* test (two-way, assuming unequal variances) and Mann–Whitney U test, respectively, initially using all filters, irrespective of clustering by site, then using only those filters from sites with measurements covering at least 60% of the study period, and finally using the site means over the study interval. The significance of associations between site means for all variables was assessed using the Spearman Rank Order test. Multiple linear regression was used to assess the association between PM metals with measures of oxidative potential using a backward-deletion approach.

RESULTS

Five hundred TEOM filters (358 for PM_{10} and 142 for $PM_{2.5}$) were extracted, and the recovered PM was analyzed (in 21 batches) for its capacity to deplete AA, urate, and GSH from synthetic RTLF during a 4-hr incubation period (37°C, pH 7). The raw data outlining the extent of the AA, urate, and GSH depletion observed with each of these PM extracts are illustrated and discussed briefly in Appendix C.

For a more accessible representation of the capacity of PM extracts to oxidize physiologic antioxidants, the data were expressed as a percentage depletion per μg of PM_{10} or $PM_{2.5}$ (i.e., assuming a linear dose–function relationship [Ayres et al. 2008]) relative to the particle-free control — thereby obtaining a metric for oxidative potential that was scalable from 0 to 2. To specify whether this metric was derived from the capacity of PM to deplete AA or GSH, the superscripts AA and GSH were used. Having derived unitary expressions for PM oxidative potential per unit mass, we next derived expressions for PM oxidative activity per m^3 ambient air dependent on AA and GSH. The subsequent descriptions of the results in this report are based on these derived expressions of PM oxidative potential.

Of the 500 samples examined, 83 were excluded (35 for PM_{10} and 48 for $PM_{2.5}$) from the analysis of the spatial variability of oxidative potential and soluble metal components. The reasons for excluding these samples were the following: the period of filter collection occurred outside the designated study period, i.e., before September–October 2005 (56 samples, largely of $PM_{2.5}$ from Bloomsbury—Russell Square, Bexley—Thames Road North, Bexley—Thames Road South, and Westminster—Marylebone Road); the samples came from sites not designated in the original contract (23 samples from Bexley—Slade Green, Bexley—Belvedere, Bexley—Erith, and Bexley—Thames Road North); and the sampling dates were sufficiently ambiguous that the calculation of reliable masses was impossible (4 filters). The LEZ data set of PM samples was supplemented with 135 PM_{10} samples from the CCS data set, which overlapped with the time period of the current study, to give a total of 456 PM_{10} and 96 $PM_{2.5}$ filter extracts. These filter extracts were derived predominately

Table 5. PM_{10} and $PM_{2.5}$ TEOM Filters Extracted and Analyzed from Sites Outside the London Metropolitan Area

Site	Code	Filter Archive Collection Period (Start Date–End Date)	Classification	PM_{10} Filters (n)	$PM_{2.5}$ Filters (n)
Chatham Roadside—A2	ZC1	Jan. 3–June 26, 2006	Roadside	11	—
Luton—Background	ZL1	Jan. 3–June 26, 2006	Background	10	—
Saint Albans—Fleetville	SA1	Dec. 13, 2005–Dec. 7, 2006	Background	7	—
Watford—Roadside	WF1	Dec. 14, 2005–Nov. 9, 2006	Roadside	5	—

from sites within Greater London (Table 4) but also included PM_{10} samples derived from four sites outside the city (Table 5). It should be noted that, by the end of the study, filters had been analyzed up to July–August 2006 and that an archive of unextracted samples is now maintained for future examination. Of the key LEZ indicator sites, only a single set of PM_{10} and $PM_{2.5}$ filters was available from Greenwich—Westhorne Avenue, and no ratified filters were available from Hackney—Old Street. Good time-series data were available for all other sites, especially Westminster—Marylebone Road (56 PM_{10} 7-day filter collections and 24 $PM_{2.5}$ 14-day filter collections) over the 12-month period covered by the study.

Location-Dependent Differences in PM Oxidative Potential

Clear evidence of differences between sites examined in the present study was observed (one-way ANOVA, $P < 0.001$) for both AA- and GSH-dependent oxidative potential per unit mass of extracted PM (OP^{AA}/μg and OP^{GSH}/μg, respectively) (Figure 8A and B). The geographic locations of these sites within and outside London are shown in Figure 8D. When the samples were grouped into roadside (362 PM_{10} samples from 30 sites) and urban background sites (94 PM_{10} samples from 11 sites), with no correction for clustering by site, no difference in OP^{AA}/μg was noted (Figure 8C). In contrast, roadside sites showed markedly increased OP^{GSH}/μg ($P < 0.0001$) compared with samples obtained from background locations, consistent with our earlier observations (Kelly et al. 2011a,b). Although these results were based on all the filters collected from the roadside and urban background sites, these observations were robust when only sites with at least 60% coverage of the study period were used in the analysis or when only site means were used: for OP^{AA}/μg the values were 1.36 ± 0.21 (10 urban background sites) versus 1.35 ± 0.21 (31 roadside sites) ($P = 0.98$); for OP^{GSH}/μg the values were 0.53 ± 0.16 (10 urban background sites) versus 0.77 ± 0.23 (31 roadside sites) ($P = 0.002$). To examine whether there was an increment in OP^{AA} and OP^{GSH} per μg of PM attributable to London, filters from 4 sites (18 filter extracts from 2 roadside sites and 17 filter extracts from 2 urban background sites) outside London were compared with those located within the metropolitan area (344 filter extracts from 28 roadside sites and 77 filter extracts from 9 urban background sites). For the roadside locations, only OP^{AA}/μg was elevated within the city compared with the sites outside London. In contrast, both OP^{AA}/μg and OP^{GSH}/μg were significantly elevated at urban background sites within greater London ($P < 0.001$ and $P < 0.05$, respectively) compared with those outside of the city (Figure 8E). A similar pattern was apparent when OP^{AA} and OP^{GSH} measurements were expressed per m^3 of ambient air (Figure 9E). Clear site-dependent differences in both OP^{AA}/m^3 and OP^{GSH}/m^3 were apparent (Figure 9A and B) with a greater activity associated with the roadside sampling sites for both metrics when all PM samples were considered (Figure 9C). As described above, the difference between roadside and urban background sites was robust when the analyses were restricted to those sites with the most comprehensive filter archives as well as when the analyses were restricted to the site means over the study period: OP^{AA}/m^3 of 26.28 ± 5.32 (10 urban background sites) versus 33.90 ± 8.42 (31 roadside sites) ($P = 0.002$); OP^{GSH}/m^3 of 10.35 ± 3.16 (urban background sites) versus 19.22 ± 8.39 (roadside sites) ($P < 0.001$). In addition, OP^{GSH} was found to be elevated at London roadside and urban background locations compared with the equivalent site types outside the city (Figures 8E and 9E). Although this city increment in OP^{GSH} was apparent at both types of sites and for the metric expressed, both per unit PM_{10} mass or m^3, for OP^{AA}/μg this higher activity was only apparent at the background sites (Figure 8E).

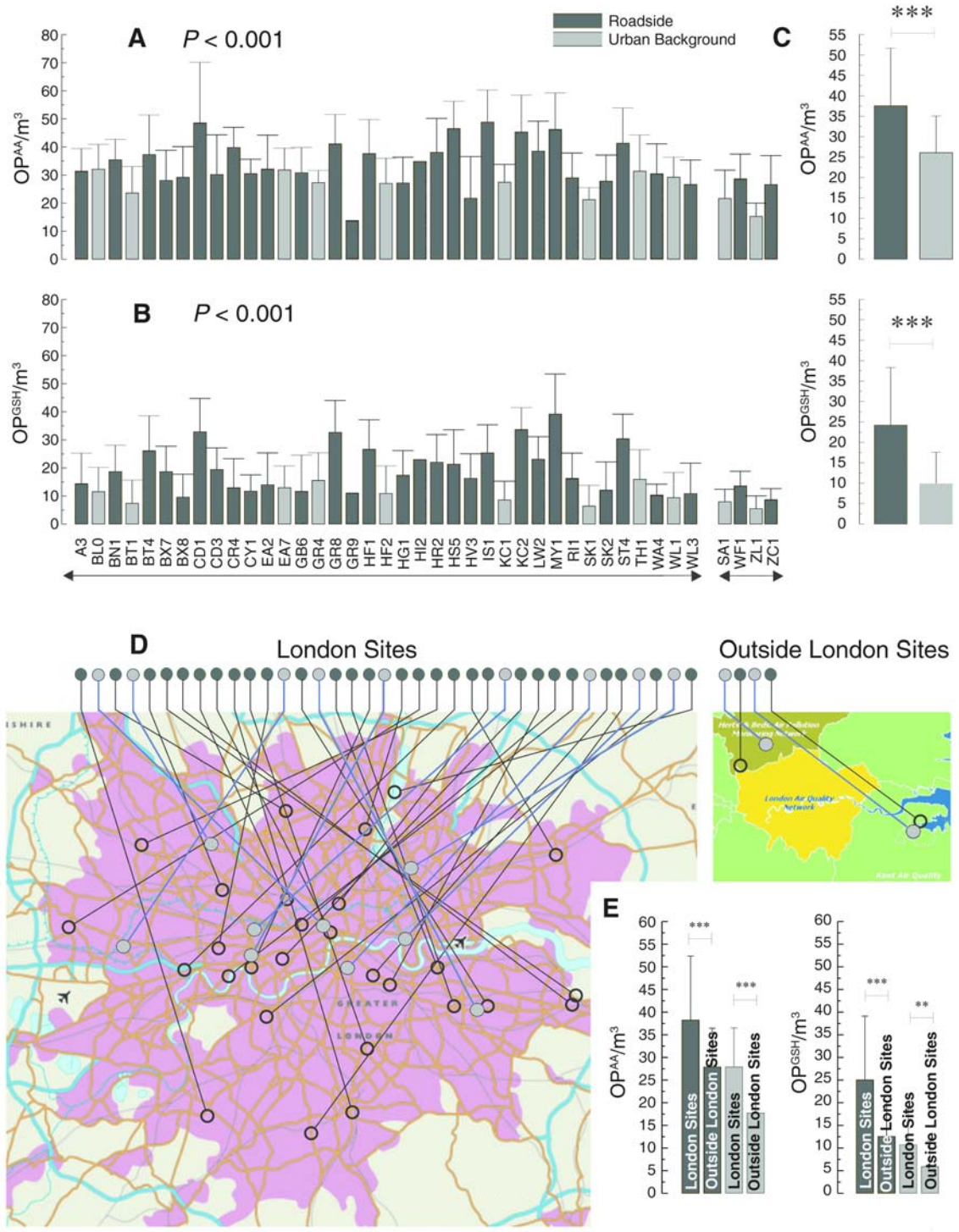

Figure 9. Summary of OP^{AA}/m^3 (A) and OP^{GSH}/m^3 (B) for PM_{10} for the 41 sites studied. Results are grouped to show site locations (in London or outside London). The numbers of filter samples in each group are given in Table 1 (for sites in London) and Table 2 (for sites outside London). *P* values are the results of an ANOVA examination of site-specific contrasts in the data set. **(C)** OP^{AA}/m^3 and OP^{GSH}/m^3 for all roadside filters (31 sites, 362 samples) and all urban background filters (11 sites, 94 samples), expressed as means ± 1 SD. Comparisons between roadside and urban background results were performed using a two-tailed unpaired *t* test (assuming unequal group variances). **(D)** Locations of the sites. **(E)** Comparison of the OP metrics at the roadside and urban background sites within and outside London, expressed as means ± 1 SD. NS = nonsignificant difference, *** = $P < 0.001$, ** = $P < 0.01$, and * = $P < 0.05$. See Appendix E for site codes and names.

$PM_{2.5}$ TEOM filters were available from 9 sites (1 urban background and 8 roadside), all of which were located within Greater London. The mean site values for OP^{AA} and OP^{GSH} expressed per unit mass of extracted PM and per m^3 of ambient air are shown in Figure 10. As with the PM_{10} oxidative potential determinations, significant site-dependent differences were observed, though these were more marked for OP^{GSH}; $PM_{2.5}$ from the roadside sites showed significantly elevated oxidative activity (Figure 10F). Although this finding agreed with the PM_{10} finding, the comparison was limited by the availability of filters from only a single urban background site. For the nine sites from which both PM_{10} (144 samples) and $PM_{2.5}$ (95 samples) data were available over the study period, we observed clear evidence for OP^{AA}/μg (1.24 ± 2.29 for PM_{10} versus 1.14 ± 0.32 for $PM_{2.5}$ [$P < 0.05$]) and for OP^{GSH}/μg (0.79 ± 0.47 for PM_{10} versus 0.56 ± 0.39 for $PM_{2.5}$ [$P < 0.001$]). Because the concentration of $PM_{2.5}$ was lower at each site, all measures of PM_{10} oxidative potential were significantly greater when expressed per volume of sampled air: the OP^{AA}/m^3 for PM_{10} was 36.8 ± 14.5 versus 19.5 ± 8.1 for $PM_{2.5}$ ($P < 0.001$), and the OP^{GSH}/m^3 for PM_{10} was 25.2 ± 17.7 versus 9.8 ± 7.8 for $PM_{2.5}$ ($P < 0.001$); the difference between samples was consistent across all sites.

Metal-Dependent and Metal-Independent Oxidative Potential

To attempt to determine the relative contributions of metal and non-metal components to the observed PM oxidative activity, experiments were performed in the AA-only model with and without the addition of the metal chelator DTPA. The data from these experiments are presented in full in Appendix C. However, comparison of the rates of AA depletion observed in this simplified model with the OP^{AA}/μg values of individual PM extracts (both PM_{10} and $PM_{2.5}$) determined in the full RTLF model revealed significant associations (Spearman rank order correlation) with both the total ($\rho = 0.54$, $P < 0.001$) and

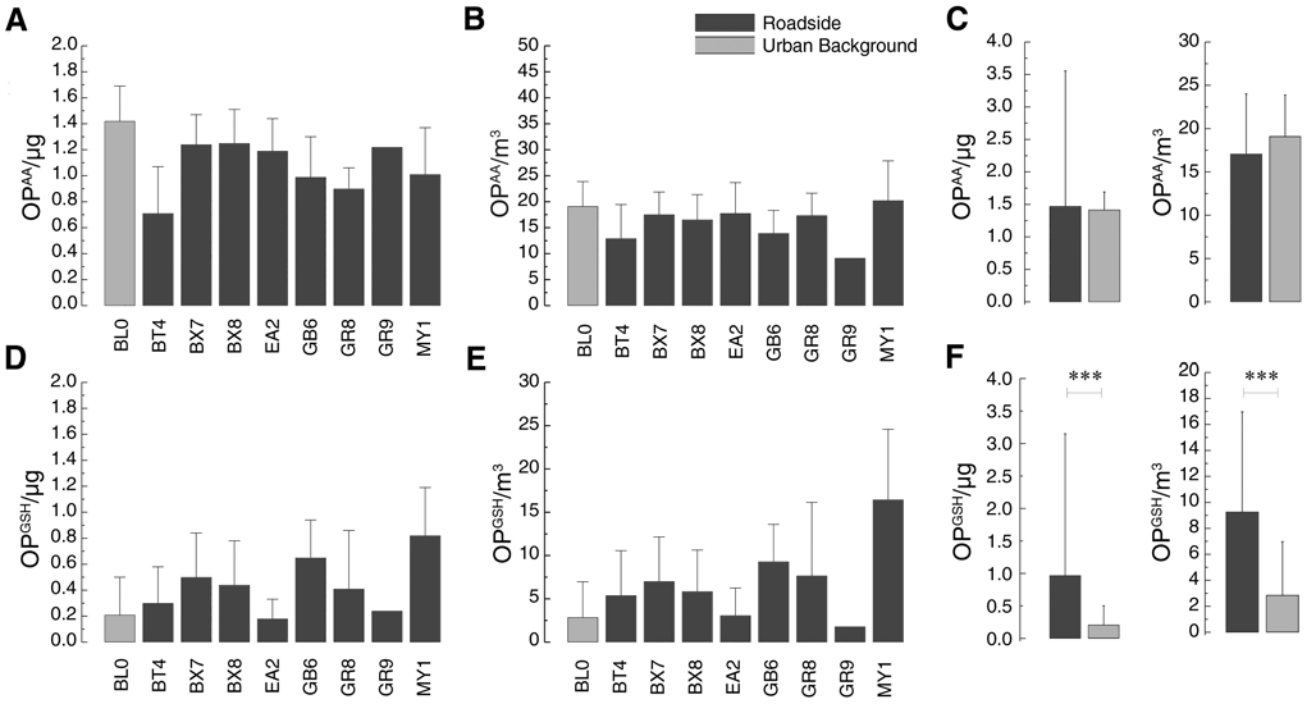

Figure 10. Summary of OP^{AA} metrics (A and B) and OP^{GSH} metrics (D and E) for $PM_{2.5}$ for the 9 sites from which $PM_{2.5}$ was obtained. The numbers of filter samples in each group are given in Table 1 (for sites in London) and Table 2 (for sites outside London). **(C** and **F)** Comparison of the OP metrics for roadside filters (1 site [Bloomsbury—Russell Square], 14 samples) and urban background filters (8 sites, 82 samples), expressed as means ± 1 SD. The comparisons between the roadside and urban background were performed using a two-tailed unpaired *t* test (assuming unequal group variances). *** = $P < 0.001$. Note that some of the *y*-axis scales vary from panel to panel. See Appendix E for site codes and names.

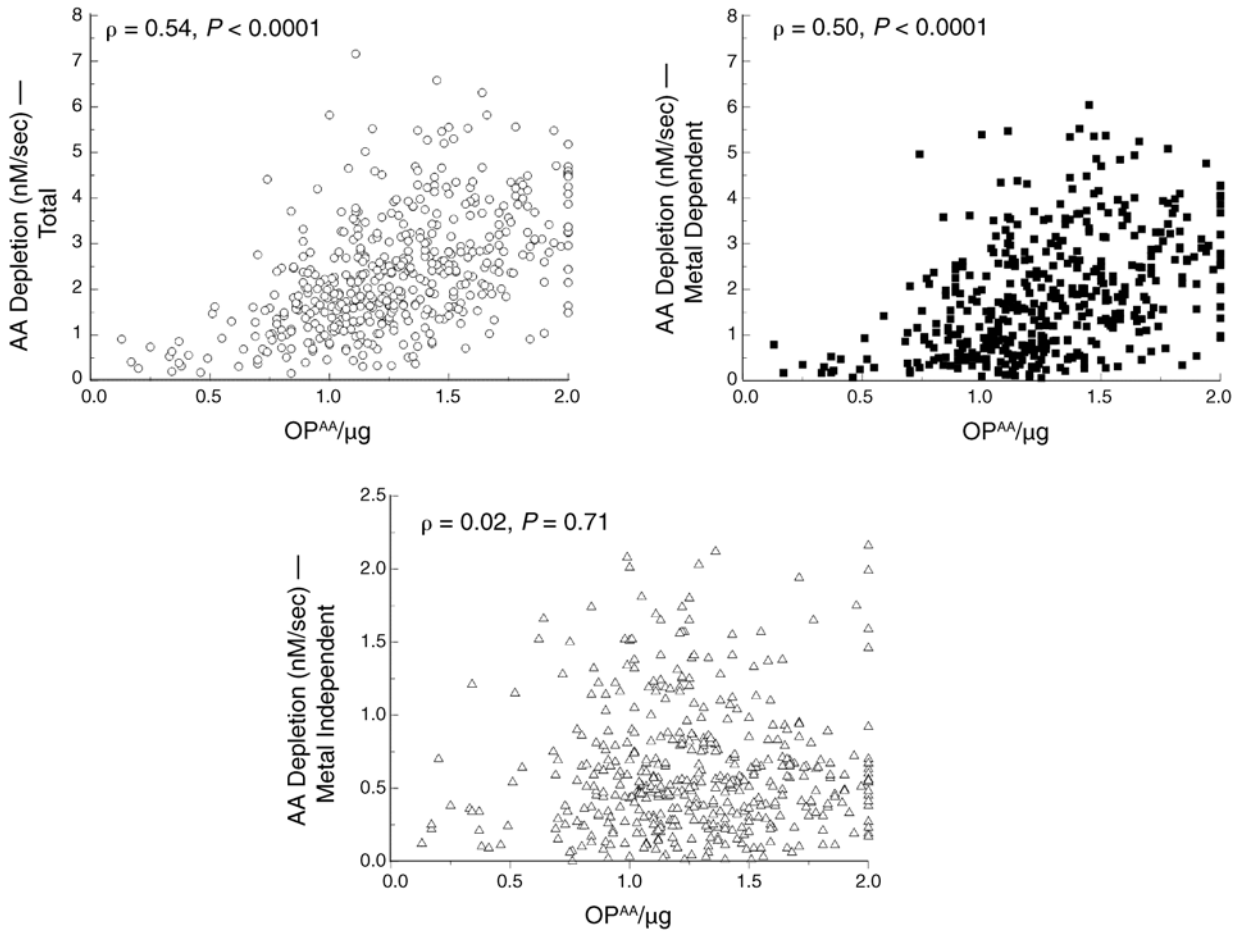

Figure 11. The relationship (Spearman rank correlation) between AA-dependent oxidative potential (OP^{AA}/µg) and measured AA depletion rates (total, metal-dependent, and metal-independent) obtained with the same samples. The metal-dependent and metal-independent rates were derived from the total rate of PM-induced AA oxidation through co-incubation with the synthetic metal chelator DTPA, with the residual activity being attributed to non-metal sources. The Spearman correlation (ρ) and the level of significance (*P*) are illustrated for each comparison.

metal-dependent rates (ρ = 0.50, $P < 0.001$), but not with the metal-independent signal (ρ = 0.02, $P = 0.71$) (Figure 11). In contrast, weaker and negative associations were observed between the total (ρ = −0.27, $P = 0.001$) and metal-dependent (ρ = −0.26, $P = 0.001$) rates with the individual PM-extract OP^{GSH}/µg values (Figure 12).

Correlation Analysis

Correlation analyses were performed between all oxidative potential metrics (both per µg and per m^3), including AA depletion rates with the soluble metal and bioavailable Fe content of the PM_{10} samples. The soluble and bioavailable metal data are presented and discussed in Appendix C. To limit the influence of temporal autocorrelation and clustering of data by site, the analysis was restricted to the use of site means over the 12-month period covered in this study ($n = 41$, see Table 6). A similar approach was not taken with $PM_{2.5}$, for which only nine sites were available. The correlation analyses demonstrated that OP^{AA}/µg was significantly associated with the soluble aluminum (Al) (ρ = 0.37, $P < 0.05$), Cu (ρ = 0.35, $P < 0.05$), Mo (ρ = 0.55, $P < 0.01$), and Zn (ρ = 0.45, $P < 0.01$) concentrations found in PM_{10}, whereas no positive association was apparent between OP^{GSH}/µg and any of the soluble metals measured. OP^{GSH}/µg only showed a significant positive correlation when BPS Fe was considered (ρ = 0.69, $P < 0.01$). When correlations were performed using the mean site values for OP per m^3, the OP^{AA}/m^3 was found to be significantly positively associated with PM Ba (ρ = 0.54, $P < 0.01$),

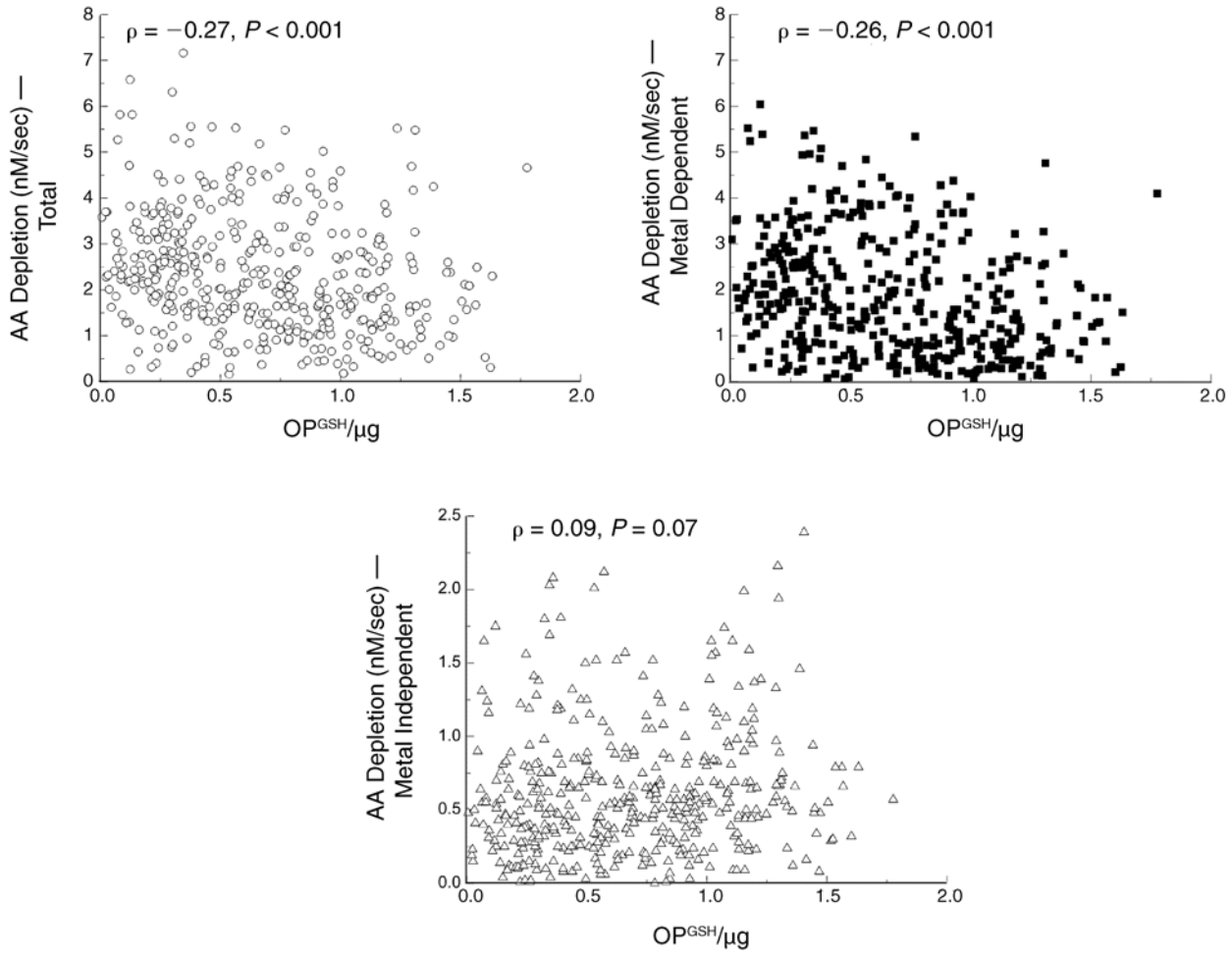

Figure 12. The relationship (Spearman rank correlation) between GSH-dependent oxidative potential (OP^{GSH}/µg) and measured AA depletion rates (total, metal-dependent, and metal-independent) obtained with the same samples. Spearman correlation (ρ) and the level of significance (*P*) are illustrated for each comparison. Note that some of the *y*-axis scales vary from panel to panel.

Cu (ρ = 0.39, $P < 0.01$), Mo (ρ = 0.44, $P < 0.01$), and BPS Fe (ρ = 0.69, $P < 0.01$) concentrations, whereas OP^{GSH}/m^3 was again only significantly associated with BPS Fe (ρ = 0.73, $P < 0.01$). In contrast, no strong associations were seen with the total ascorbate depletion rate, and the metal-dependent oxidative rate was only weakly associated with soluble Mn concentrations (ρ = 0.33, $P < 0.05$).

To further clarify these relationships, multiple linear regression analyses were performed using a backward-deletion approach and the mean site data for the period of the study. The model data for each of the endpoints examined are summarized below and include the standardized beta coefficients (in parentheses) for the metals retained in the model as well as the adjusted r^2 values:

- For OP^{AA}/µg, inclusion of arsenic (As) (β coefficient 0.24), Mo (0.57), Al (0.35), and vanadium (V) (−0.45) in the model yielded an adjusted r^2 of 0.59.
- When OP^{AA}/m^3 was used as the dependent variable, inclusion of BPS Fe (0.50), Mo (0.35), Al (0.22), and V (−0.30) yielded a model with an adjusted r^2 of 0.65.
- For OP^{GSH}/µg, a model including Mo (0.38), Mn (−0.34), V (−0.28), Fe (−0.44), Cu (0.46), Pb (0.33), and BPS Fe (0.33) yielded an adjusted r^2 of 0.64.
- When OP^{GSH}/m^3 was used as the dependent variable, a model including BPS Fe (0.37), Cd (0.80), Cu (−0.30), Ba (0.40), and V (0.30) yielded an adjusted r^2 of 0.51.

Table 6. Association Matrix for All Parameters Investigated in the Current Research Project [a]

	OP^{AA}/m^3	$OP^{GSH}/\mu g$	OP^{GSH}/m^3	AA^{Total}	AA^{Metal}	$AA^{Non\text{-}metal}$	Al	As	Ba	Cd	Cu	Fe	Mn	Mo	Ni	Pb	V	Zn	BPS Fe	Reflectance
$OP^{AA}/\mu g$	0.515 **	0.347 *	0.260	0.533 **	0.487 **	−0.058	0.371 *	0.190	0.093	0.187	0.354 *	0.219	0.076	0.533 **	−0.004	0.126	−0.028	0.449 **	0.214	−0.034
OP^{AA}/m^3		0.570 **	0.781 **	0.162	0.105	−0.027	0.008	−0.279	0.538 **	−0.322 *	0.386 *	0.020	0.044	0.439 **	−0.189	−0.422 **	−0.361 *	0.143	0.694 **	−0.096
$OP^{GSH}/\mu g$			0.899 **	0.080	0.052	−0.003	−0.217	−0.108	0.257	−0.177	0.208	−0.370 *	−0.359 *	0.307	−0.428 **	−0.242	−0.539 **	0.176	0.659 **	−0.074
OP^{GSH}/m^3				−0.053	−0.077	−0.055	0.228	−0.240	0.451 **	−0.344 *	0.298	−0.290	−0.255	0.331 *	−0.383 *	−0.430 **	−0.542 **	0.090	0.728 **	−0.100
AA^{Total}					0.964 **	−0.035	0.055	0.083	0.030	0.136	0.038	0.098	0.283	0.275	0.053	0.155	0.088	0.149	0.156	−0.092
AA^{Metal}						−0.243	0.133	0.091	0.003	0.112	0.054	0.160	0.323 *	0.284	0.139	0.158	0.206	0.149	0.111	−0.054
$AA^{Non\text{-}metal}$							−0.274	−0.090	0.163	0.153	−0.246	−0.292	−0.123	−0.096	−0.288	−0.136	−0.324 *	−0.206	0.039	0.053
Al								0.374 *	−0.089	0.336 *	0.362 *	0.694 **	0.468 **	0.337 *	0.547 **	0.42	−0.559 **	0.461 **	−0.275	0.067
As									−0.486 **	0.398 *	−0.172	0.102	−0.021	−0.014	0.184	0.697 **	0.351 *	0.196	−0.473 **	0.249
Ba										−0.433 **	0.482	0.082	0.428 **	0.350 *	0.149	−0.660 **	−0.262	−0.096	0.530	−0.301
Cd											−0.095	0.309 *	0.053	0.114	0.149	0.756 **	0.322 *	0.367 *	−0.511 **	0.280
Cu												0.530 **	0.289	0.390 *	0.437 **	−0.208	0.019	0.539 **	0.411 **	−0.301
Fe													0.556 **	0.352 *	0.641 **	0.297	0.618 **	0.452 **	−0.214	0.006
Mn														0.250	0.486 **	0.067	0.404 *	0.107	−0.150	−0.107
Mo															0.294	−0.038	0.222	0.297	0.220	0.068
Ni																0.103	0.577 **	0.248	−0.200	−0.053
Pb																	0.485 **	0.280	−0.692 **	0.411 **
V																		0.085	−0.551 **	0.140
Zn																			−0.018	0.099
BPS Fe																				−0.252

[a] Spearman correlations based on the site mean ($n = 41$) for the 12-month study period. Spearman's ρ (ρ) values, with associated P value ($^*P < 0.05$ or $^{**}P < 0.01$) are shown for each pair of comparisons. The AA depletion rate associated with each PM sample incubated in 200 μM AA is described as AA^{Total}, the rate obtained during co-incubations with the metal chelator DTPA as $AA^{Non\text{-}metal}$, and AA^{Total} minus $AA^{Non\text{-}metal}$ as the metal-dependent rate AA^{Metal}. All rates were expressed as nM/sec. The units of measurement for each parameter were as follows: soluble metals (ng/μg PM), BPS Fe (μM/mg) and reflectance (derived absorbance 10^{-5}/m). The OP metrics were defined as outlined previously (Kelly et al. 2011b), expressed per μg of extracted PM_{10}, or per m^3 of ambient air. As the OP metrics were derived from the percentage loss of antioxidants from the synthetic RTLF at a particle concentration of 50 μg/mL, all expressions per unit mass were scaled between 0 (no loss) and 2 (complete antioxidant depletion).

- For the total AA depletion rate, a model including BPS Fe (0.37), Cd (0.80), Ba (0.40), Cu (−0.30), and V (0.25) yielded an adjusted r^2 value of 0.49.
- The best model for the metal-dependent AA rate included BPS Fe (0.26), Cd (0.64), and Mn (0.25) and yielded an adjusted r^2 value of 0.32.
- When the metal-independent AA depletion rate was used as the dependent variable, a model including Mn (−0.27), Cu (−0.35), Cd (0.76), and Ba (0.72) yielded an adjusted r^2 value of 0.59.

Characterizing the Mechanism of PM-Induced Ascorbate Oxidation

The mechanisms driving the oxidative depletion of AA by PM were investigated in the AA-only model through co-incubation experiments with a panel of free-radical scavengers and metal chelators. The PM samples used (two PM_{10} and two $PM_{2.5}$ samples) were selected from two of the key LEZ indicator sites, Westminster—Marylebone Road and Bexley—Thames Road North, based on the observation that the total AA depletion rate of these samples was similar in magnitude to the overall mean rate of samples collected from these sites over the study period. The results of these PM–inhibitor co-incubation experiments are summarized in Figure 13 and showed significant decreases in AA depletion with the chelators DTPA and desferroximine (DFO). In contrast, in three of the four samples AA depletion rates were increased by co-incubation with ethylenediaminetetraacetic acid (EDTA). Co-incubation with EDTA in the sample from Westminster—Marylebone Road conversely decreased the observed depletion rate. Although both DTPA and DFO inhibited PM-induced AA depletion, the rates were not reduced to particle-free control levels with DTPA, indicating the presence of residual non-metal activity. In contrast, DFO reduced the depletion rate to below that observed in the particle-free controls, implying that its presence in the reaction mixture was reducing background auto-oxidation in the samples. Because of the propensity of both quinones (Roginsky et al. 1999, 2000) and transition metals to redox cycle in reducing environments (Buettner and Jurkiewicz 1996) and to generate superoxide radical ($O^{-\bullet}$) we also used the enzymatic antioxidants Cu,Zn–superoxide dismutase and catalase (SOD/CAT; see Figure 13) to assess the extent to which the generation of $O^{-\bullet}$ would lead to a secondary oxidation of

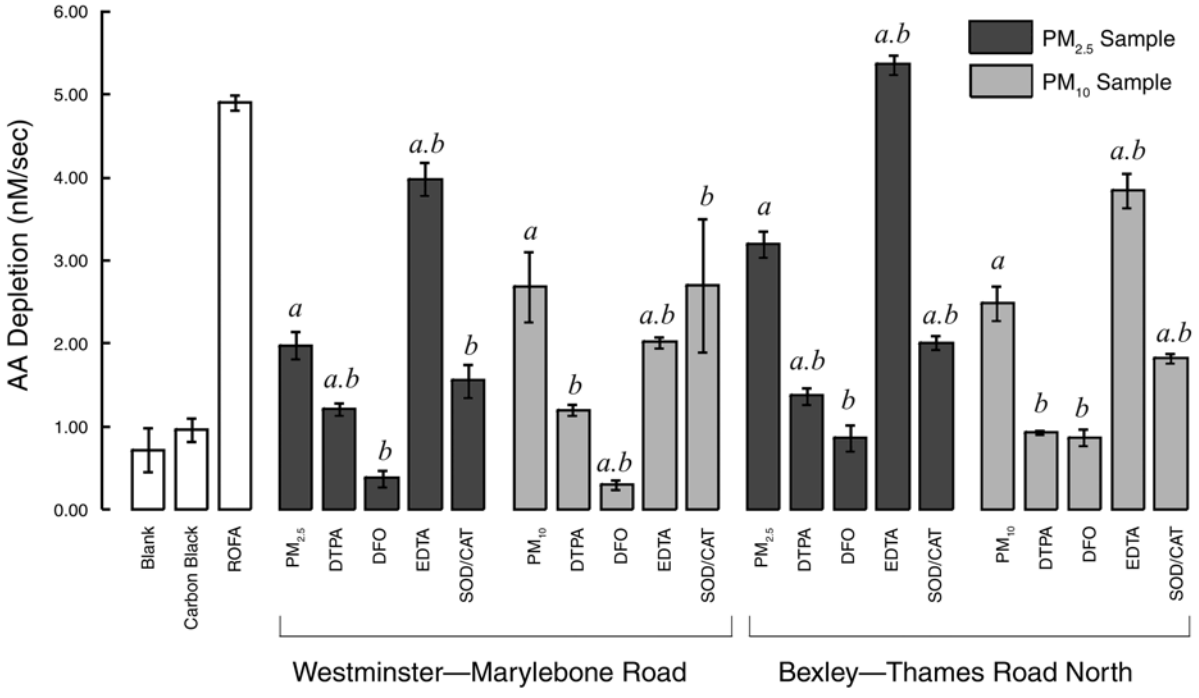

Figure 13. Effects of metal chelation and antioxidant treatment on PM_{10}- and $PM_{2.5}$-induced AA-depletion rates. Results expressed as means ± 1 SD of triplicate incubations. DTPA (200 µM); DFO (200 µM); EDTA (200 µM); and SOD/CAT (150 U/mL and 50 U/mL, respectively). The comparisons of the treatment groups for each of the four PM samples were performed using a one-way ANOVA with post hoc testing using the Games–Howell test: *a* = significant difference ($P < 0.05$) between the concentrations in the treatment groups and the particle-free 4-hr control (i.e., the blank); *b* = significant difference between the concentrations in the treatment groups and the untreated PM_{10} sample. Samples are from the Westminster—Marylebone Road and Bexley—Thames Road North monitoring sites.

AA. In three of the four samples, co-incubation with both of these antioxidants resulted in a 20% to 30% reduction of the PM-induced AA-depletion rate. Notably, the only instance where no protection was observed with the SOD/CAT treatment was in the Westminster—Marylebone Road PM_{10} sample, which had demonstrated protection with EDTA.

Data for soluble-metal content of all PM extracts as well as data from experiments undertaken to identify whether metals or organic radicals dominated PM oxidative potential are reported in Appendix C.

DISCUSSION

In this study we assessed the capacity of ambient PM_{10} and $PM_{2.5}$ samples, collected over a 12-month period, both within and outside Greater London, to drive the oxidation of antioxidants in a range of simple model systems, based on reactions likely to occur when inhaled particles interact with components of RTLF. The models were developed to provide a quantitative and potentially physiologically relevant measure of the oxidative potential of inhaled pollutants. The first pollutants studied were the oxidant gases O_3 and NO_2 (Kelly and Tetley 1997; Mudway and Kelly 1998); subsequently three types of particulate pollutants were studied, model particles (residual oil fly ash, carbon black), vehicle-derived PM (exhaust from diesel- and gasoline-powered vehicles), and ambient PM samples (Zielinski et al. 1999; Mudway et al. 2004; Künzli et al. 2006). The focus on the quantification of oxidative potential has arisen from the hypothesis that the capacity of particles to elicit oxidative stress at the air–lung interface, as well as systemically, is linked to the pathophysiologic responses observed in populations exposed to elevated concentrations of ambient PM (Shi et al. 2003; Borm et al. 2007) Under this hypothesis, particles introduce redox-active compounds, such as transition metals (Aust et al. 2002; Greenwell et al. 2002) and quinones (Nel et al. 2001; Squadrito et al. 2001; Xia et al. 2004; Cho et al. 2005), into the lung and thus promote the formation of reactive oxygen species (Buettner and Jurkiewicz 1996; Roginsky et al. 1999, 2000), which in turn shift the extracellular and intracellular compartments from reducing to oxidizing environments. This shift, referred to as an oxidative insult, triggers the formation of redox-sensitive transcription factors, which initially induce protective adaptations, but if the duration or magnitude of the oxidative insult is sufficient, it will ultimately promote inflammation and cell death (Li et al. 2003; Nel 2005). Although this paradigm describes acute responses to an oxidative insult, it is believed that recurrent exposures result in structural changes and functional impairment of the lung, which manifest as the health effects reported in the epidemiologic literature. It should be noted at this time that, although clear location-dependent differences in PM oxidative potential have been demonstrated (Künzli et al. 2006), to date there are no robust data demonstrating whether this metric is predictive of health effects at the level of populations, largely because there is a paucity of data.

In addition to acting as vectors for the introduction of redox-active materials into the lung, inhaled PM can also induce oxidative stress through indirect pathways. These pathways include the processes of xenobiotic metabolism of polyaromatic hydrocarbons to reactive intermediates (Bonvallot et al. 2001), disruption of mitochondrial function (Xia et al. 2004), endotoxin-induced inflammation (Monn et al. 2003), or induction of particle phagocytosis and the oxidative burst (Becker and Soukup 1998). The sum of all these processes can be considered as the "total" oxidative potential of ambient PM. However the assessment of oxidative stress occurring through these indirect pathways would require the use of cell or tissue models, which are not amenable to the high-throughput screening procedures necessary for the approach adopted in the current study. Rather, we have modeled the intrinsic oxidizing properties of PM, which provide an integrative summary of the activity of the redox-active components associated with PM. The use of the synthetic RTLF and AA-only models and the transition-metal chelator DTPA allowed us to dissect out the relative contributions of metals and organic radicals to PM's oxidative potential.

In this study we used both of these models to examine the oxidative potential of ambient PM_{10} and $PM_{2.5}$ within London, with a specific focus on the contribution of traffic-derived components. Numerous studies have demonstrated increased rates of respiratory or allergic illnesses and impaired lung growth in children living in homes or attending schools near high-traffic sites and indicated that these associations were particularly marked near roads with a high proportion of diesel-powered heavy-goods vehicles (Brunekreef et al. 1997; Janssen et al. 2003; Gauderman et al. 2007). Consistent with these epidemiologic observations, we have shown that $PM_{2.5}$ samples from traffic sites showed elevated oxidative activities compared with samples from background sites (Künzli et al. 2006) when compared on an equal mass basis. In addition, and consistent with the oxidative stress paradigm, exposure of human subjects to controlled diesel exhaust challenges has been shown to induce pulmonary and systemic inflammation (Salvi et al. 1999) through the induction of redox-sensitive pathways (Pourazar et al. 2005). Assuming the validity of the link between traffic-derived contributions to particulate pollution and the observed health impacts, strategies aimed at reducing traffic levels or emissions should provide measurable health benefits and could result in

reduced PM concentrations or alterations in PM composition. Some support for this expectation has been reported in studies where reductions in respiratory symptoms have been observed in response to short-term traffic management schemes (Friedman et al. 2001) or to long-term reductions in particulate pollution (Bayer-Oglesby 2005). The introduction in February 2008 of the London LEZ, which aimed to reduce emissions from the most-polluting vehicles over the entirety of the Greater London area, provided a unique opportunity to examine the impact of such targeted regulation on air quality as well as on the magnitude of the possible health dividend.

We hypothesized that the reduction in the number of heavy-goods vehicles (as well as light-goods vehicles at a later date in the LEZ scheme's timetable) entering London, combined with tighter emission controls, would change the composition of ambient PM_{10} and $PM_{2.5}$ such that their oxidative potential would decrease, and, thereby lead to beneficial health outcomes in populations with high roadside exposures. To maximize observation of these changes after the introduction of the LEZ scheme, we embarked on a detailed pre-implementation measurement campaign. This assessment of PM oxidative potential prior to the implementation of the LEZ also afforded us the opportunity to examine how this metric, as well as PM soluble metals, varied geographically across London, between urban background and roadside sites, as well as between sites within and outside the city.

The results from the present study demonstrated that PM from the London airshed, particularly that from roadside sites, displayed considerable oxidative activity, in many cases greater than the residual oil fly ash we employed as our positive control particle. There was clearly marked geographical variation in PM oxidative potential throughout the city, with clear increments at roadside locations, especially when the data were expressed per m^3 of ambient air. These findings therefore both confirm and extend our preliminary observations made in our earlier CCS study (Kelly et al. 2011b). Overall the capacity of particles to deplete AA from the synthetic RTLF model, on which the measure was based, was greater than for the depletion of GSH, though notably there was little correlation between the two measures. Despite a lower overall activity, the OP^{GSH} measurements yielded more pronounced site differences than the equivalent OP^{AA} measurements when the data were expressed on a per unit mass basis, with a significant difference in activity between the roadside and urban background sites. When the data were expressed per m^3, the site-location difference was apparent for both the OP^{AA} and OP^{GSH}, reflecting the increased particle concentrations at the roadside locations. Although our data on $PM_{2.5}$ was more limited than for PM_{10}, from the sites where both were available there was evidence that PM_{10} displayed the greater OP^{AA} and OP^{GSH}, expressed both per unit mass and m^3 of ambient air. This was suggestive of an enrichment of redox-active components in the coarse fraction, $PM_{2.5–10}$.

The lack of association between OP^{AA} and OP^{GSH} indicates that these two antioxidants display differential sensitivity to different PM components. Although we have preliminary data demonstrating the basis of these discrepancies (Ayres et al. 2008) — specifically a higher sensitivity of GSH to Cu-catalyzed oxidation — at the time it was not clear whether one metric should take precedence over the other or indeed whether OP^{AA} and OP^{GSH} should be summed to provide a total "intrinsic" activity. We believe that the ultimate test of the value of these metrics is how predictive they are of health effects in exposed populations, which we aim to address in later studies using this data set. In this report both metrics are provided and should be considered to be of equal weight.

To investigate the relative contributions of metals and organic radicals to overall oxidative potential, we used an AA-only model, with and without DPTA. Initial experiments used a panel of quinones (1,2-naphthoquinone and 9,10-phenanthroquinone) and redox-active metals (Fe and Cu) to investigate both the concentration of DTPA required to suppress metal-catalyzed oxidation in the PM suspensions at a concentration of 10 µg/mL and the specificity of DTPA for metal-dependent oxidative depletion of AA. These experiments demonstrated that adding an excess of DTPA inhibited metal-catalyzed losses of AA but had no impact on quinone-driven losses. On this basis we examined the capacity of all of the PM samples collected in the current LEZ study to deplete AA, with or without the presence of an excess of DTPA (200 µM), so that we could derive rates indicative for their total, metal-dependent, and -independent oxidative potential. Using this simplified model we observed that a major proportion (60% to 70%) of the total activity, measured as an AA depletion rate, could be attributed to metals, although this proportion varied widely between samples. It was notable, however, that although site differences were apparent for total, metal-dependent, and metal-independent oxidative potential, they were less pronounced with the metal-independent values, suggesting that much of the variation in PM oxidative potential in London reflects local differences in metal emissions. No difference in the rate of AA depletion was noted between roadside and urban background sites in samples examined on an equal-mass basis, consistent with the earlier OP^{AA}/µg result obtained in the RTLF model. The pattern was somewhat different for the $PM_{2.5}$ samples for which there was evidence of increased AA depletion rates at the single background site examined, compared

with the eight roadside samples examined. However, generalizing from this observation to samples from other urban background sites is questionable from this limited analysis.

To investigate the relationship between measures of particle oxidative potential and metal content, a panel of metals was measured in aqueous extracts from each of the PM samples collected. We used water-soluble metals rather than total acid extracts because previous observations indicated that metal availability in water is similar to (and strongly correlated with) that observed after incubation in synthetic RTLF (Kelly et al. 2011b) We therefore concluded that the soluble-metal content of ambient PM was a better predictor of the concentrations likely to be released from the particle surface in vivo and hence to promote damaging biologic oxidative reactions. It should be noted that in the previous study we observed metal mobilization (i.e., the displacement of metal from the PM's surface) by AA but found that mobilization was inhibited in the presence of both urate and GSH. The metals examined in the aqueous extracts were chosen to reflect known traffic sources related to vehicle-exhaust emissions and non-exhaust vehicle emissions (tire, brake, and carriage wear) (de Miguel et al. 1997; Onianwa 2001; Weckwerth 2001; Manoli et al. 2002; Harrison et al. 2003; Laschober et al. 2004; Zechmeister et al. 2005). As with the oxidative potential measurements, we observed marked site-dependent contrasts in all of the soluble-metal concentrations (expressed per unit mass of extracted PM) in PM_{10} samples, and between Al, As, Cu, Fe, Mn, Pb, V, and Zn in $PM_{2.5}$ samples. As with the previous analysis of the impact of the CCS, we found that PM_{10} samples from roadside locations were enriched with Ba, Cu, and Mo, whereas the concentrations of the water-soluble metals Al, As, Cd, Fe, Ni, Pb, V, and Zn were higher in samples from the urban background sites. It was notable that although Ba, Cu, and Mo concentrations were higher in PM_{10} samples from roadside locations compared with urban background sites, a similar pattern was not apparent in the $PM_{2.5}$ samples, where no contrast between the two site types was apparent. This discrepancy between the two PM fractions strongly supports the contention that the higher concentrations of Ba, Cu, and Mo in PM_{10} reflect contributions in the coarse fraction of $PM_{2.5–10}$. In contrast, Al, Fe, Pb, V, and Zn concentrations were higher in both PM_{10} and $PM_{2.5}$ samples from urban background sites.

Many of these metals reflect non-exhaust motor-vehicle sources, such as brake and tire wear or the resuspension of road dust (Thorpe and Harrison 2008; Kleeman and Cass 1998; Jaecker-Voirol and Pelt 2000; Harrison et al. 2001). Although the contribution of non-exhaust PM to ambient air at roadside locations has been widely acknowledged, relatively few studies have investigated their contribution to the toxicity of ambient PM. Of these non-exhaust sources, tire wear is believed to be the largest source (Lükewille et al. 2001), with emission rates of 100 μg/vehicle km (Boulter 2006) and even higher rates for heavy-goods vehicles (Legret and Pagotto 1999). Because Zn has been used as a marker for tire wear (Fauser 1999), in the current study we expected that elevated Zn concentrations would be associated with PM from the study's roadside sites, but the opposite was observed. In contrast, both Ba and Cu, used as markers of brake wear (Sternbeck et al. 2002; Boulter 2006), were clearly elevated in PM_{10} despite lower emission factors of 10 to 20 μg/vehicle km (Legret and Pagotto 1999; Garg et al. 2000). Even though brake-wear emissions from heavy-goods vehicles have been estimated to be double these values (Kennedy et al. 2002), these data either suggest that there is an additional source of Cu or Ba at these locations or that the published emission rates have dramatically underestimated the contribution of brake wear to the ambient PM at roadsides. It was also notable from our analysis that increases in the concentrations of these metals in PM at roadside sites appeared to be largely attributable to $PM_{2.5–10}$, which is consistent with earlier reports that most of the mass of brake-wear particles was associated with this fraction (Berdowski et al. 1997).

Although we have argued that for metals, their water-soluble concentration represents an effective surrogate for their bioavailability in human respiratory tract lining fluid, Fe presents unique difficulties because it is not very soluble in water. Fe exists in a number of forms, two of which, hematite and magnetite, appear to be relatively inert. On the other hand, ferric oxyhydroxides and Fe associated with silicates have been shown to be catalytically active once rendered bioavailable through the use of low-molecular-weight ligands, such as citrate (Veranth et al. 2000). An understanding of the size of the pool of Fe likely to become bioavailable in vivo, in both intracellular and extracellular compartments, is therefore critical for understanding the potential toxicity of this metal (Smith et al. 1998; Aust et al. 2002). To assess the size of this bioavailable pool in PM samples we used the chromogenic chelator BPS, which shows a binding affinity for Fe of 1×10^{22}, comparable to transferrin ($1 \times 10^{22–28}$) and greater than that of citrate (1×10^{16}). BPS is therefore able to bind Fe associated with the surface of the particle, resulting in its liberation into solution as a Fe-BPS complex. Using this compound we found, in complete contrast to the results for water-soluble Fe, that concentrations of BPS Fe were high in PM_{10} roadside samples. This observation agreed with our previous findings (Kelly et al. 2011b). In contrast,

no difference in BPS Fe concentrations were observed between roadside and urban background sites in the $PM_{2.5}$ samples examined. The source of the insoluble Fe in $PM_{2.5-10}$ at roadside sites is not clear at this time, but Fe silicates associated with either road surface erosion or brake linings (Hildemann et al. 1991) might be potential sources.

Of the metals examined, those most consistently associated with the observed oxidative potential measurements were Al, Cu, Fe, Ba, Mo, and BPS Fe for OP^{AA}/μg and OP^{AA}/m^3; only BPS Fe was associated with OP^{GSH}/μg and OP^{GSH}/m^3. This analysis was based on the site means for the 12-month study period and was restricted to the PM_{10} samples, as the number of sites available for $PM_{2.5}$ sampling were insufficient to warrant this approach. Three of these metals — Cu, Fe (in either soluble or mobilized form), and Mo — are known to catalyze the oxidation of biologic reductants (Buettner and Jurkiewicz 1996), which is consistent with the observed associations, although Al and Ba most likely provide information on the potential emission sources. It was notable from the correlation analysis that none of the soluble metals or BPS Fe was strongly associated with any of the rates obtained from the AA-depletion model. As stated earlier, although the pool of water-soluble metals is broadly equivalent to that seen after samples have been incubated in the RTLF model, certain metals are mobilized by AA, and this might account for the discrepancy.

The contribution of metals to the measured oxidative potential, assessed in the AA-depletion model, was also investigated in inhibitor studies using an extensive panel of chelators and the antioxidant enzymes Cu,Zn–SOD/CAT. These studies confirmed that much of the oxidation of AA observed in this model could be attributed to metals, because co-incubation with both metal chelators, DTPA and DFO, inhibited AA depletion. These experiments also highlighted the importance of the mobilizable Fe pool, as co-incubation with EDTA actually promoted AA depletion in three of four samples examined. This result was interpreted as reflecting the binding of EDTA to surface Fe, permitting its mobilization yet still allowing its participation in reduction–oxidation reactions. This paradox exists because the EDTA molecule does not completely encapsulate the Fe molecule; as a result the Fe is held in an "open basket" position, where it is capable of existing as both Fe^{2+} and Fe^{3+} and is free to participate in oxidative reactions (Liu and Hider 2002). Co-incubation with the free radical scavengers SOD/CAT inhibited AA depletion (approximately 20% to 30%) illustrating the involvement of the superoxide ion in some of the depletion observed.

In conclusion, we have produced the first data set that describes in detail the oxidative potential of a major city's airshed using novel metrics based on the synthetic RTLF model. We have shown clear location-dependent differences in oxidative potential within London with evidence that OP^{GSH} (expressed both per unit mass and per m^3) is enhanced in roadside $PM_{2.5}$ and PM_{10} compared with samples from urban background sites. In the PM_{10} samples this increased oxidative potential appeared to be related to increased content of Cu, Ba, and BPS Fe in the roadside PM, whereas in the roadside $PM_{2.5}$ samples no simple association could be drawn, suggesting other unmeasured components were driving the increased oxidative potential in this size fraction. These data suggest that Cu and BPS Fe (Ba being redox inactive but a good marker of brake wear) contributed to the oxidative potential of the $PM_{2.5-10}$ collected at the roadside sites and that an unidentified redox catalyst affected the oxidative potential of $PM_{2.5}$.

It is important to note that the data derived from this baseline study confirmed all the key observations made in the more limited spatial mapping exercise described in our earlier HEI report on the introduction of the CCS in London (Kelly et al. 2011a,b).

Although the data generated in this study provided robust baseline information on the oxidative potential and metal content of PM in the London airshed before the implementation of the LEZ, the findings that $PM_{2.5-10}$ had considerable oxidative potential and that brake wear is apparently related to the components in $PM_{2.5-10}$ that affect oxidative potential raise important issues about the optimal design of traffic-management schemes designed to improve health. For example, the LEZ is designed to target tailpipe emissions and thus might have a smaller impact on PM oxidative potential than originally expected.

At one level this study provided a unique opportunity to test the validity of the PM oxidative potential metric. As has been stated previously, although the current study demonstrated location-dependent contrasts in PM oxidative potential, the value of this metric as a predictor of health effects has not been firmly established. Should a marked health dividend be observed in the future in populations living in high-traffic microenvironments in London after the introduction of the LEZ in the absence of a change in PM oxidative potential, this would strongly argue against the usefulness of the oxidative potential metric and the contribution to the observed health effects of metals derived from brake and tire wear. On the other hand, if no health dividend is observed after the implementation of the LEZ's tightening of tailpipe emission regulations, then

the regulation of non-tailpipe sources of traffic emissions should be included in future traffic management schemes.

At the time this report was prepared, the sample archive included samples collected through the third quarter of 2006, a full archive of samples from the sites outlined in this report are still collected. When these analyses are completed they will provide valuable information on the impact of the introduction of this major traffic management scheme on the composition and toxicity of PM in a major urban airshed.

DEVELOPMENT OF METHODS TO EVALUATE THE IMPACT OF THE LEZ ON MORBIDITY

INTRODUCTION

An evaluation of the health outcomes of large-scale interventions affecting mobile-source pollution, such as the London LEZ, ideally requires data that meet the following criteria: (1) relevance to the cause–effect relationship, (2) linkage of subjects to estimates of changes in exposure, (3) sufficient numbers of health outcomes in the area studied, (4) availability of data on relevant spatial and temporal confounding factors, and (5) continuity over the time course of the environmental intervention. When many factors affecting both environment and health outcomes are changing over time, the specific health effects of individual environmental policies can be very difficult to discern because it is often difficult to allow convincingly for confounding factors (HEI Accountability Working Group 2003). The evaluation of stepwise changes in ambient air pollution that result from the rapid implementation of abatement policies is important because confounding factors are unlikely to change over such a short time scale. Further, if the potential effects of confounding over time are allowed for by using an appropriate control population, the problem associated with continuity over time, the fourth criterion, is largely addressed.

For the purposes of studying the temporal and spatial changes in health outcomes in such large-scale interventions, it is fortunate that most large cities in developed countries maintain complete records of mortality data, which include information on age, sex, cause and place of death, and home address. In London, for example, we had access to data that gave us the capacity to analyze the location of deaths at the level of a postcode, which corresponds to approximately 15 addresses. This degree of detail enabled us to aggregate mortality data at a scale that is appropriate for the gradations of traffic pollution concentrations generally found in cities. Mortality data have been used to evaluate the effect of interventions affecting whole cities or sections of cities (Pope 1989; Clancy et al. 2002; Hedley et al. 2002). However, the potential of mortality data to be used to evaluate interventions affecting relatively small areas of cities, as was the case with the London CCS study, or to evaluate the effects of policies directed toward line sources on populations living near roads is limited by the relatively low number of expected deaths. On the other hand, the availability of within-city temporal control data provides a good way to control for time-related confounders, as shown by Hedley and colleagues (2002). Another source of health data relates to an individual's admission to a hospital. The U.K. is one of the few countries to have a hospital admissions data system that covers most of the population at risk (although the system is more comprehensive for emergency admissions than elective admissions, some of which relate to surgery in the private sector). In comparison with mortality data, hospital admissions data have the benefits of more data pertaining to higher rates of admissions, diagnoses that relate to the immediate cause of admission rather than the underlying cause, a higher quality of diagnosis, and greater representation of children. Both mortality and hospital admissions can be linked to postcode of residence for research purposes, given the appropriate ethics approvals, but both suffer from considerable lags in availability.

Data from primary-care use have several potential advantages over mortality and hospital admissions data. Owing to the fact that the proportion of the population using primary-care services is much greater than that for hospital admissions, these data have more statistical power for studying effects in very limited areas, such as areas in proximity to line sources (i.e., roads). Furthermore, primary-care data include a wide range of chronic and acute morbidities not captured by mortality or hospital admissions data. The U.K. is one of very few countries with extensive, computerized primary-care databases. Our study explored the potential for using such data for air quality outcome research in the context of evaluating the London LEZ.

Of crucial importance, there is abundant evidence that ambient air pollution is associated with the prevalence of symptoms that might be reflected in the use of primary-care services. These include respiratory symptoms of irritative origin, such as cough, and to a lesser extent symptoms of asthma, such as wheezing (Dockery et al. 1989; Braun-Fahrlander et al. 1997; Peters et al. 1999; Zemp et al. 1999; Binková et al. 2005; World Health Organization [WHO] 2007). Of particular relevance to the current report are studies of the relationship between proximity to vehicle pollution and the prevalence of lower respiratory symptoms (Studnicka et al. 1997; Ciccone et al. 1988; Hirsch et al. 1999; Nakai et al. 1999; Venn et al. 2001; Brauer et al. 2002b; Shima et al. 2003), and upper respiratory symptoms (Brauer

et al. 2006). A number of cohort studies have observed intra-urban variations in mortality associated with air pollution (Hoek et al. 2002; Finkelstein et al. 2004; Nafstad et al. 2004; Jerrett et al. 2005; Gehring et al. 2006), and three of these relate specifically to proximity to traffic (Hoek et al. 2002; Finkelstein et al. 2004; Gehring et al. 2006). Little is known about the mechanism behind mortality associations such as these, but if there were associated morbidity as well, then an increase in health service usage would be expected. In the city of Duisburg, Germany, an association between exposure to traffic and coronary atherosclerosis was recently reported (Hoffmann et al. 2007). If real, this association would provide a link to cardiovascular mortality and might be reflected in greater morbidity from coronary heart disease.

There is also abundant evidence that day-to-day variations in air pollution are associated with symptoms and various physiological indicators relating to the respiratory and cardiovascular systems (Health Effects Institute 2001, 2002; Department of Health Committee on Medical Effects of Air Pollution 2006; WHO 2006); these associations might also be reflected in data on primary-care use. Daily time-series studies have demonstrated that primary-care use is a sensitive marker of short-term effects of air pollution on upper and lower respiratory disease in the community. In London, when using primary-care databases of the same type used in the present study, short-term associations were observed for asthma and other lower respiratory symptoms (Hajat et al. 1999), upper respiratory diseases (Hajat et al. 2001), and allergic rhinitis (Hajat et al. 2002). Furthermore, the associations were quite large. For lower respiratory diseases (excluding asthma), an increase in PM_{10} from the 10th to 90th percentile concentration was associated with a 3.7% increase in consultations in the $\geq$ 65-year group (lag 2 days, $P < 0.03$). For asthma, the same increase in PM_{10} was associated with a 6.3% increase in the 15–64-year group (cumulative lag 0–3 days, $P < 0.006$). For upper respiratory conditions, for example, in the 1–14-year group, a 10th to 90th percentile change in PM_{10} was associated with a 17% increase in consultations for allergic rhinitis (cumulative lag 0–6 days, $P < 0.001$), and in the $\geq$ 65-year group, the same increase in PM_{10} was associated with a 10% increase in consultations for upper respiratory disease (most significant lag, $P < 0.001$). Associations with primary-care outcomes have also been reported using data on house calls made in Paris (Medina et al. 1997), on unscheduled outpatient visits in Beijing (Xu et al. 1995), on visits to general practitioners in Hong Kong (Wong et al. 2002), on clinic visits in Taiwan (Hwang and Chan 2002), and on the sale of prescription drugs in Le Havre, France (Zeghnoun et al. 1999).

In Britain, 98% of the population is registered with a doctor in a "general practice" or community health care center which is contracted by the local health authority to provide primary care free of charge. Although general practitioners are independent contractors, many procedures and recording systems are mandatory and may be linked to remuneration through the setting of targets by the central government. Prescriptions are free for the young and elderly and limited to a fixed cost for those of working age. Furthermore, drugs such as low-dose aspirin, used for prevention of cardiovascular events, bought over the counter without prescription are likely to be recorded in general-practice systems for medico-legal reasons. Virtually all practices now use a computerized system for recording consultations and prescriptions, because general-practice income is dependent on meeting targets that are assessed by interrogating these systems. There is therefore a good argument for using primary-care records when evaluating interventions that might affect exposure to air pollution and the consequent health effects. This report describes the development of this idea in London, with the specific aim of applying it to the evaluation of the LEZ.

Aims and Objectives

The aim of the work described in this section of the report was to develop a method for using primary-care databases to evaluate the health effects of regulatory interventions within the context of the London LEZ.

Our objectives were the following:

1. To develop a method of classifying patients according to exposure to traffic pollution and to predicted changes resulting from the LEZ, while protecting anonymity. This would include obtaining the approval of research ethics committees, organizations that control the databases, and the general practices themselves.
2. Depending on the outcome of the first objective, to carry out cross-sectional analyses of the associations between health outcomes and exposure to primary traffic pollution. This would include investigation of the availability of data on potential confounders, namely smoking and socioeconomic deprivation, and the sensitivity of estimates to the control of these variables.
3. To investigate the power of primary-care databases to evaluate changes in health outcomes associated with the introduction of traffic schemes such as the LEZ.
4. To develop a strategy for recruiting appropriate general practices and procuring the necessary data for evaluating the LEZ in an efficient and acceptable manner.

METHODS

Databases Used in This Study

Three medical-records software systems produced by Egton Medical Information Systems Ltd (EMIS; Leeds, U.K.; *www.emis-online.com*), In Practice Systems (Cegedim; London, U.K.; *www.inps4.co.uk*), and iSOFT (Banbury, U.K.; *www.isofthealth.com*) dominate the market. Three research databases are designed to download data from each of the systems: Qresearch (using EMIS), General Practice Research Database (using In Practice Systems), and Doctors' Independent Network (DIN) (using iSOFT). The types of data in these systems are essentially the same.

Doctors' Independent Network The Division of Community Health Sciences at St. George's, University of London, has a research program using primary-care databases and a collaborative arrangement with the DIN, which provides access to the database without requiring visits to practices to download data. The DIN database has the additional advantage of containing socioeconomic indicators based on postcode linkages (Carey et al. 2004). Prevalence rates for a wide range of conditions, including coronary heart disease (De Wilde et al. 2003), diabetes (de Lusignan et al. 2005), atrial fibrillation (De Wilde et al. 2006), and common childhood diagnoses (Bremner et al. 2003; De Wilde et al. 2004), have been shown to compare well with other national data sources.

A mechanism has been set up allowing the linkage of data at the postcode level to an individual's electronic record. A postcode includes 15 households on average and typically represents one side of a road. In order to maintain anonymity, the postcodes are not available to the researchers directly, but information relating to relevant postcodes can be uploaded to practices and linked to individual patient records by the practice's computer system. The patient record, minus the postcode but including the relevant socioeconomic or other characterizations, is then downloaded and added to the DIN database. Thus far, the linkage has been restricted to socioeconomic data. In particular, we have linked in the "A Classification of Residential Neighborhoods" (ACORN) classification based on census data as well as other small-area statistics, including income data (*www.caci.co.uk*) and the English Index of Multiple Deprivation in 2004 (Index of Multiple Deprivation 2004), which is a measure of socioeconomic status in 2004 at the small-area level (*www.odpm.gov.uk/stellent/groups/odpm_control/documents/contentservertemplate/odpm_index.hcst?n=4610&l=3*). The Index of Multiple Deprivation is made up of various deprivation domains, including income, employment, health and disability, education and training, housing and services, crime, and living environment. Whereas ACORN is available at the postcode level, the Index of Multiple Deprivation 2004 (and Index of Multiple Deprivation in subsequent years) is available at the super output area level (super output areas average 400 households and 1,500 residents and were designed to provide information for areas of compact shape and social homogeneity). Super output areas have an advantage over postcodes because anonymity can be better preserved (*http://neighbourhood.statistics.gov.uk/SOAFAQ.asp*). Because we can link postcodes to modeled air pollution data and to distance from roads, the same technique can in principle be used to assign exposure categories to patients while preserving anonymity.

After recruitment into the DIN database an initial tape download of the medical-records data takes place at the practice. Subsequently, data from each practice are downloaded daily by modem to a remote computer. This ensures that the centrally held data are up to date with the corresponding data at each practice. Failure to download on one day is dealt with by automatic re-download of that data the following day. The three most important components of the database downloaded are the "Register" file (containing patient registration information), the "Notes" file, and the "Issues" file. The "Notes" file contains diagnoses, symptoms, administration, medical history, vaccinations, and prescriptions other than repeats. The "Issues" file contains more detailed prescribing data on all prescriptions, including repeats. For research purposes, "Notes" and "Issues" are combined into one file.

We identified 152 DIN practices that had continuous good-quality recording for the period from 2000 to 2005. We have previously described our methods for identifying good-quality data in DIN (Carey et al. 2004), and this method was used here. In 13 of the 152 practices, the majority of patients were registered with a London address inside the boundary created by the M25 motorway. This report used the data from these 13 DIN practices for linking air pollution data to patients' medical data.

Lambeth DataNet The Lambeth DataNet is a primary-care data set for the inner London Borough of Lambeth (population 250,000) that comprises 29 practices with a combined list of about 200,000 patients. This data set originated as a service development project created to investigate and address inequalities by adding data on ethnicity, religion, and language, obtained by patient questionnaire, to the existing patient records. In October 2006, a team from the Division of Community Health Sciences at St. George's visited each of the 29 practices and downloaded anonymous but postcoded data for a range of conditions for all registered patients. Most of the conditions were not relevant here (e.g., psychosis or Alzheimer disease) but did

include an "ever" diagnosis of asthma or ischemic heart disease, together with smoking and Index of Multiple Deprivation data, as described by van Vlymen and de Lusignan (2005) and van Vlymen and colleagues (2005). The data were stored securely at the Division of Community Health Sciences. Independently a file was next prepared that contained NO_x values, postcode, and a deprivation indicator (Index of Multiple Deprivation). This file was then linked by postcode with the patient's primary-care clinical data file, and then the postcode was removed to create a file of clinical data containing NO_x values and no postcode.

Classification of Reasons for Consultation and Actions Taken

Various classifications have been developed for assigning a reason for a patient consultation. These include not only diagnoses that can be mapped to the WHO's International Classification of Disease codes, but also undifferentiated symptoms. This is important because in a primary-care setting patients might present many conditions in a mild or early stage of a disease process. Respiratory conditions, for example, usually present with symptoms like cough, runny nose, or wheezing. The classification currently most used in the U.K. is that developed by Read (*www.connectingforhealth.nhs.uk/systemsandservices/data/uktc/readcodes*) specifically for primary care. The combination of diagnostic Read codes and prescriptions provides a database from which it is possible to reliably estimate changes in disease patterns and their presentation over time and between different areas (De Wilde et al. 2004; de Lusignan et al. 2005). Depending on the goal of the analysis, various measures of disease occurrence can be obtained, such as (1) the lifetime prevalence of any consultation for a particular diagnosis (e.g., asthma) (useful for comparing the prevalence of chronic diseases and reflects cumulative incidence over time); (2) the incidence of consultations or prescriptions over a defined period (e.g., one year) can be obtained and this may be persons or spell-based and (3) the incidence over a defined period of the first diagnosis of a disease (e.g., asthma).

The practices in the Lambeth and DIN datasets both used 5-byte Read codes. (A complete list of the Read codes for definitions of the outcomes used in this report is in Tables D.1 to D.4 of Appendix D, which is available on HEI's Web site). We chose to focus on the following conditions: asthma, chronic obstructive pulmonary disease, wheeze, hay fever, respiratory tract infections, ischemic heart disease, heart failure, and atrial fibrillation. For respiratory tract infections our intention was to separate upper respiratory infections from lower respiratory infections, but there were some coding issues that limited diagnostic certainty (De Wilde et al. 2004). In Read coding, precise codes for "upper respiratory tract infection" are not as readily apparent as for other conditions, and many general practices in DIN were not making a consistent clinical distinction between upper and lower respiratory tract infections but instead used a higher-level code ("H1" for acute respiratory infections).

We chose to measure lifetime prevalence to the end of 2005 for each condition, indicated by any Read code in the record up to that point in time. This "ever" type outcome would indicate incidence of chronic diseases, such as chronic obstructive pulmonary disease or asthma, depending on the time period specified, and also serve as a denominator for measuring the risk of exacerbations over specified time periods. In order to investigate the incidence of outcomes that could be located in a defined time period and that might reflect exacerbations, we chose five outcomes, all restricted to 2005. These were respiratory tract infection and prescriptions for asthma drugs, loop diuretics (prescribed for heart failure), nitrates (prescribed for angina, a manifestation of ischemic heart disease), and asthma drugs written in 2005 for those with a diagnosis of asthma made through the end of 2004.

Assigning Exposures to Clinical Records

NO_x and PM_{10} concentrations were modeled at a 20 × 20–m grid resolution (see below). The modeled outputs were then used to assign an annual average for NO_x and PM_{10} to each London postcode by way of an intermediary program that mapped each postcode. The centroids of the 20 × 20–m grids were matched to the postcodes, and the values for those within a postcode were averaged. 176,965 London postcodes were assigned pollutant concentrations for NO_x, NO_2, and PM_{10} based on the 2005 model in 2006. Any postcodes that were "vertical streets" (i.e., single premises such as tower blocks) and were included in the initial allocation (i.e., contained within one of the 20 × 20–m grid squares) were excluded from the assignment of exposures to clinical records. The list of 176,965 postcodes, then, was based only on postcodes with a horizontal component. About 6% of postcodes could not be allocated a pollution value, because they were vertical streets, corresponding to a single grid reference without a polygon. This is about average for the country as a whole (*www.statistics.gov.uk/geography/nspd.asp*).

We had pollutant concentrations for NO_x, NO_2, and PM_{10} for each postcode and found that a large number of postcodes could easily be identified because they had a unique permutation of these pollutants. This remained the case even when we chose a less precise value for each pollutant concentration (rounded to fewer decimal places,

such as tenths). Because this was a feasibility study — and to avoid the possibility of contravening the agreements with the ethics committees about confidentiality — we decided to use the concentration, rounded to the nearest thousandth for only one pollutant, NO_x. NO_x was chosen because it was the best indicator of exposure to vehicle emissions and was highly correlated with the other pollutants. Each of the 176,965 postcodes was assigned a value of 0 to 999 to correspond to its thousandth percentile of the distribution of all NO_x values. The file of NO_x concentrations was then linked to all patients with one of these postcodes without identifying the postcode itself. This process follows the methods outlined for linking in ACORN (described above). We estimated an approximate population distribution of NO_x exposures for the population of London by linking the NO_x data to postcode head-count data from the 2001 census (*www.statistics.gov.uk/census2001/product_pc_headcounts.asp*) and then calculating the relative proportion of the population with the given categories of exposure.

To characterize variability in the predicted NO_x concentrations in the Borough of Lambeth, the model concentration estimates, made at the 20 × 20–m grid resolution, were extracted from the 2005-model grid for Greater London and plotted in graphic form across a straight-line transect.

Analysis

Logistic regressions were used to investigate the cross-sectional associations between NO_x pollution concentrations and disease and drug outcomes for 2005. The final evaluation will be a longitudinal analysis, but we did this cross-sectional analysis at the time to ensure that we understood the processes of categorization of outcomes and their frequency, the nature of potential confounders, and the best way of handling a practice as a variable. For presentation purposes, NO_x was further summarized as deciles (tenths of the overall distribution) in the tables in this report. In Lambeth, there were insufficient numbers of patients with NO_x exposures in the four lowest deciles, reflecting Lambeth's inner-city location; the analysis was therefore restricted to the remaining six deciles. Because the distribution of NO_x in the Lambeth and DIN practices was very different, choosing the baseline decile for NO_x was problematic. The decision was made to use the upper decile with the highest number of patients exposed as the baseline for each database (the sixth decile in DIN and the eighth decile in Lambeth).

The data were analyzed separately by five age groups (1–4, 5–14, 15–44, 45–64, ≥ 65 years). Within each age group, the models were further adjusted for the effect of age. In addition, adjustments were made for sex, ethnicity (Lambeth only), smoking (for patients more than 15 years old only) and Index of Multiple Deprivation. Index of Multiple Deprivation values, referred to as Index of Multiple Deprivation fifths, are scores ranging from 1 to 5, which represented fifths of the national ranking of Index of Multiple Deprivation scores (1 = most deprived). In Lambeth, which is on average a more deprived area, there were few patients in the least deprived category (Index of Multiple Deprivation = 5), and the top two categories (Index of Multiple Deprivation = 4 and Index of Multiple Deprivation = 5) were therefore combined in the analyses. In the DIN analyses only, regressions were carried out adjusting for ACORN as well as for Index of Multiple Deprivation; in this report, however, we present regressions adjusting for Index of Multiple Deprivation only in order to provide consistency with the approach in Lambeth and because Index of Multiple Deprivation would be the measure used in a later evaluation. For all Lambeth DataNet practices, information on ethnicity had been obtained by self-completed questionnaires. Ethnicity was categorized as White, Asian/Asian British, Black/Black British, Chinese/Other, and Mixed.

The effect of practice was investigated in three ways. First, the models were corrected for all the confounding factors described above but were not adjusted for practice. Second, practice was adjusted for as a fixed effect (fitting a dummy variable to represent each practice). Third, practice was adjusted for as a random effect allowing for clustering within practices. These three analyses represent a spectrum of degrees of control for otherwise uncontrolled risk factors that might vary between practices. Broadly, inclusion of a practice fixed effect gives the most stringent control, but with potential loss of precision. Omitting any term for practice maximizes precision but leaves potential for confounding bias and spuriously narrow confidence intervals. Inclusion of practice as a random effect provides an intermediate trade-off between these two degrees of control. Further sensitivity analyses were performed with and without Index of Multiple Deprivation and smoking as variables.

Permissions and Ethics Approvals

Approvals were obtained from separate Ethics Committees for the anonymous linking of the clinical records in DIN (Wandsworth Local Research Ethics Committee; REC reference number 07/Q0803/28) and the Lambeth DataNet (Bexley and Greenwich Local Research Ethics Committee; REC reference number 05/Q0707/41) with pollution data by way of patient postcodes.

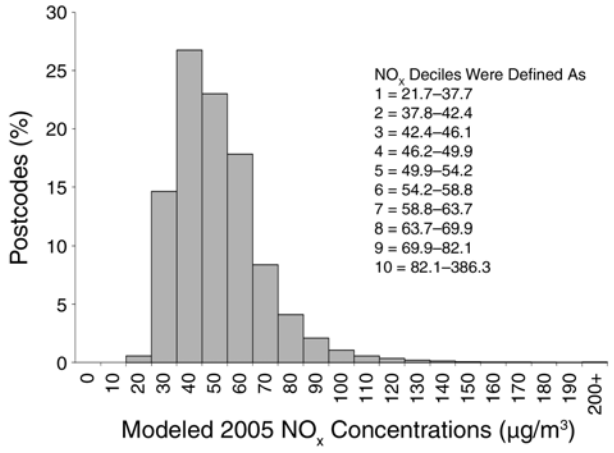

Figure 14. Frequency distribution of modeled 2005 NO_x concentrations by percentage of 158,493 London postcodes.

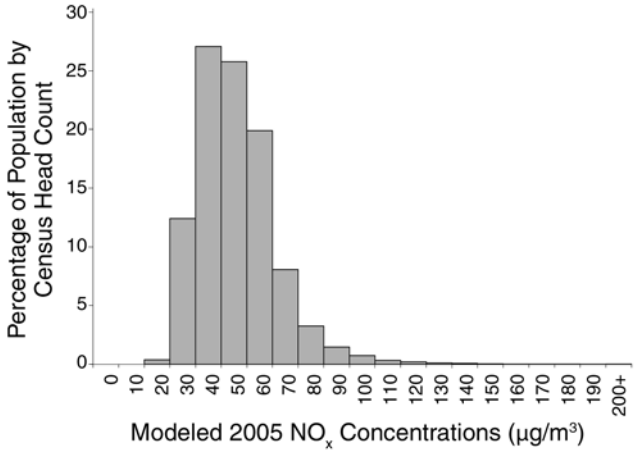

Figure 15. Frequency distribution of modeled 2005 NO_x concentrations by percentage of population.

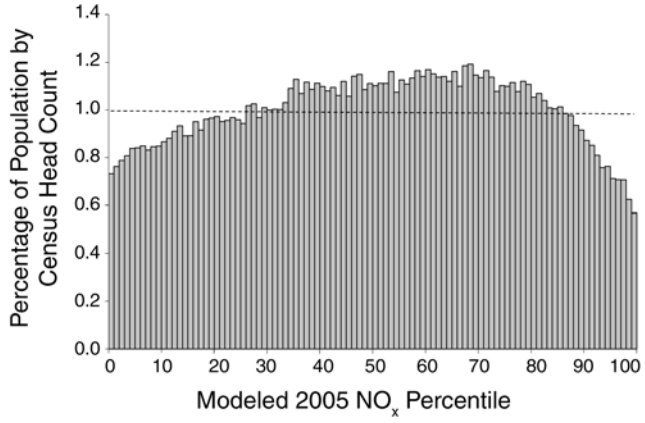

Figure 16. Distribution of modeled 2005 NO_x concentration percentiles by percentage of population.

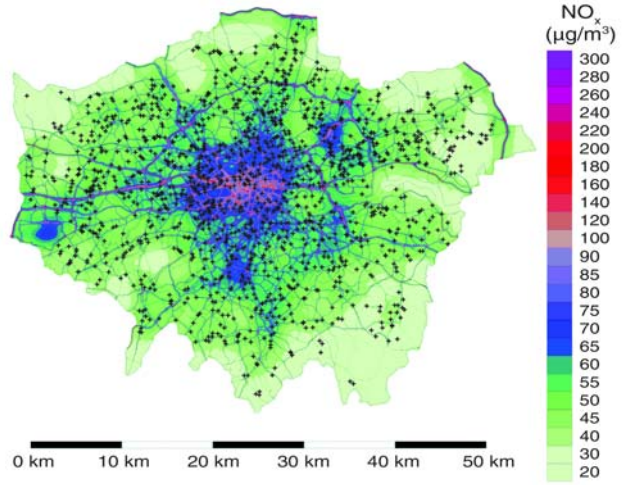

Figure 17. London contour map of modeled 2005 NO_x concentrations. Black dots indicate locations of general practices.

RESULTS

Pollution Exposure

The London postcodes that were available for linkage with census headcounts are shown in Figure 14. The distribution of concentrations ranged from 21.7 to 386.3 µg/m^3 and was skewed to the right, with a median of 54.2 µg/m^3. By linking these data with postcode head-count data (see Methods section), we calculated the relative proportions of the population with the given categories of exposure (Figure 15). Only a small percentage of the population was exposed to less than 30 µg/m^3; only about 5% of the population was exposed to more than 80 µg/m^3. The relative proportions of the population exposed to different percentiles of modeled NO_x are shown in Figure 16. The 30th to 85th percentiles were overrepresented up to about 1.2%, and the lower and upper percentiles were underrepresented, as low as about 0.8% and 0.6% for the lower and upper percentiles, respectively.

A contour map of modeled London NO_x concentrations for 2005 is shown in Figure 17. As expected, concentrations were higher centrally and along roads. The distribution of the NO_x percentiles for patients within each of the 13 DIN practices is shown in Figure 18 and it is clear that the distribution varied greatly. Practice 285, for example, had a narrow range of exposures at the lowest percentiles and

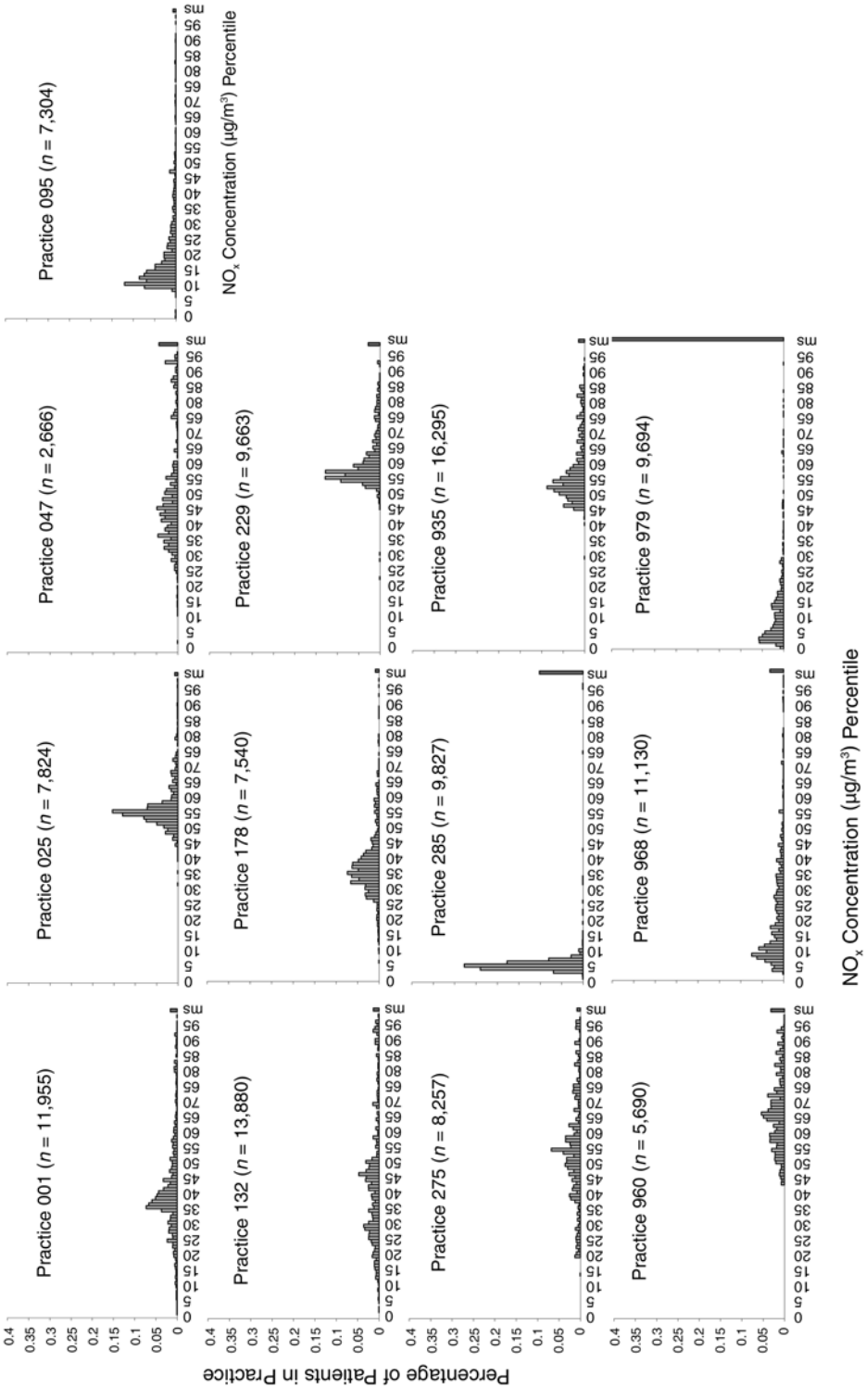

Figure 18. Distribution of modeled 2005 NO_x concentration percentiles for patients in the 13 DIN practices. On the *x* axis, "ms" (missing) indicates that no pollution value was assigned to the patient record because (1) of an invalid postcode caused by absence, error, or a location outside of London, or (2) a pollution value could not be assigned to a valid postcode because the postcode had no spatial dimension (being probably a single building, such as a tower block).

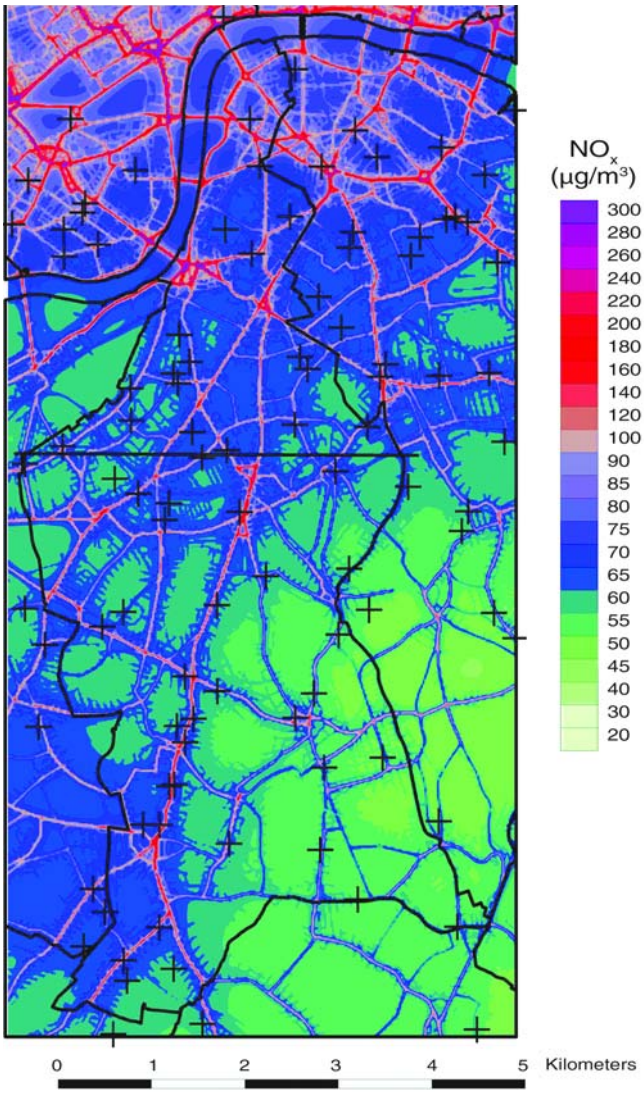

Figure 19. Lambeth contour map of modeled 2005 NO_x concentrations. Locations of general practices (crosses) and an east–west transect (black horizontal line) are shown.

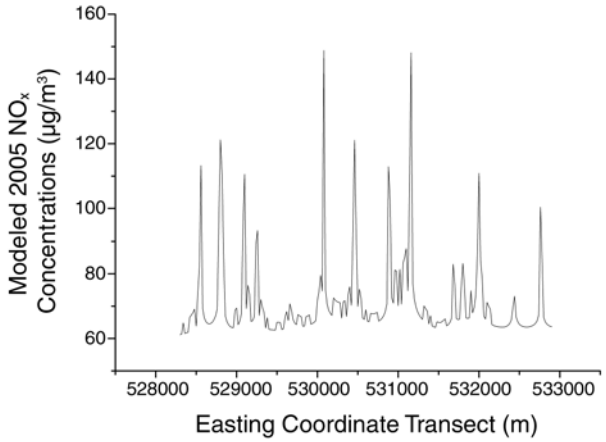

Figure 20. Modeled 2005 NO_x concentrations along an east–west transect of Lambeth.

most of its population was exposed to less than the 10th percentile of NO_x. In contrast, practice 229 had few patients exposed to less than the 50th percentile.

A contour map of the Borough of Lambeth is shown in Figure 19, with the practices indicated by crosses and an east–west transect indicated by a horizontal black line. The map corresponds to the southeast part of the center of the London map shown in Figure 17, an area to the south of and bordering on, the River Thames. The NO_x concentrations across the transect are shown in Figure 20. The concentrations show marked variation, from a baseline of 60 to 70 µg/m^3 between main roads up to as high as 150 µg/m^3. Few practices were in a low-exposure location, reflecting the higher urban background concentrations in this inner-city environment. This point is further illustrated in Figure 21, which shows the percentage distribution of NO_x percentiles (based on the whole of London) in the 29 Lambeth practices studied. In contrast with the 13 London DIN practices, there was less variation between Lambeth practices. No practice had patients exposed to the lower NO_x percentiles, and most had some patients with high exposures. The number of patients with missing NO_x data varied considerably for a number of reasons, including patients who had no postcode linkage to their medical record (postcode absent or invalid) and patients with postcodes but no linkage to NO_x. The main reason for the latter was that the postcode did not have a spatial dimension (as is the case with some tower blocks) or was situated out of London.

Figure 22 shows a map of London that predicts for 2010 the difference in annual concentrations of NO_x between the base case (i.e., from a model run without the impact of an LEZ scenario) and the preferred LEZ scenario (i.e., LEZ Scenario 6, in which a Euro IV emissions standard for PM and NO_x emissions is imposed on heavy-goods vehicles

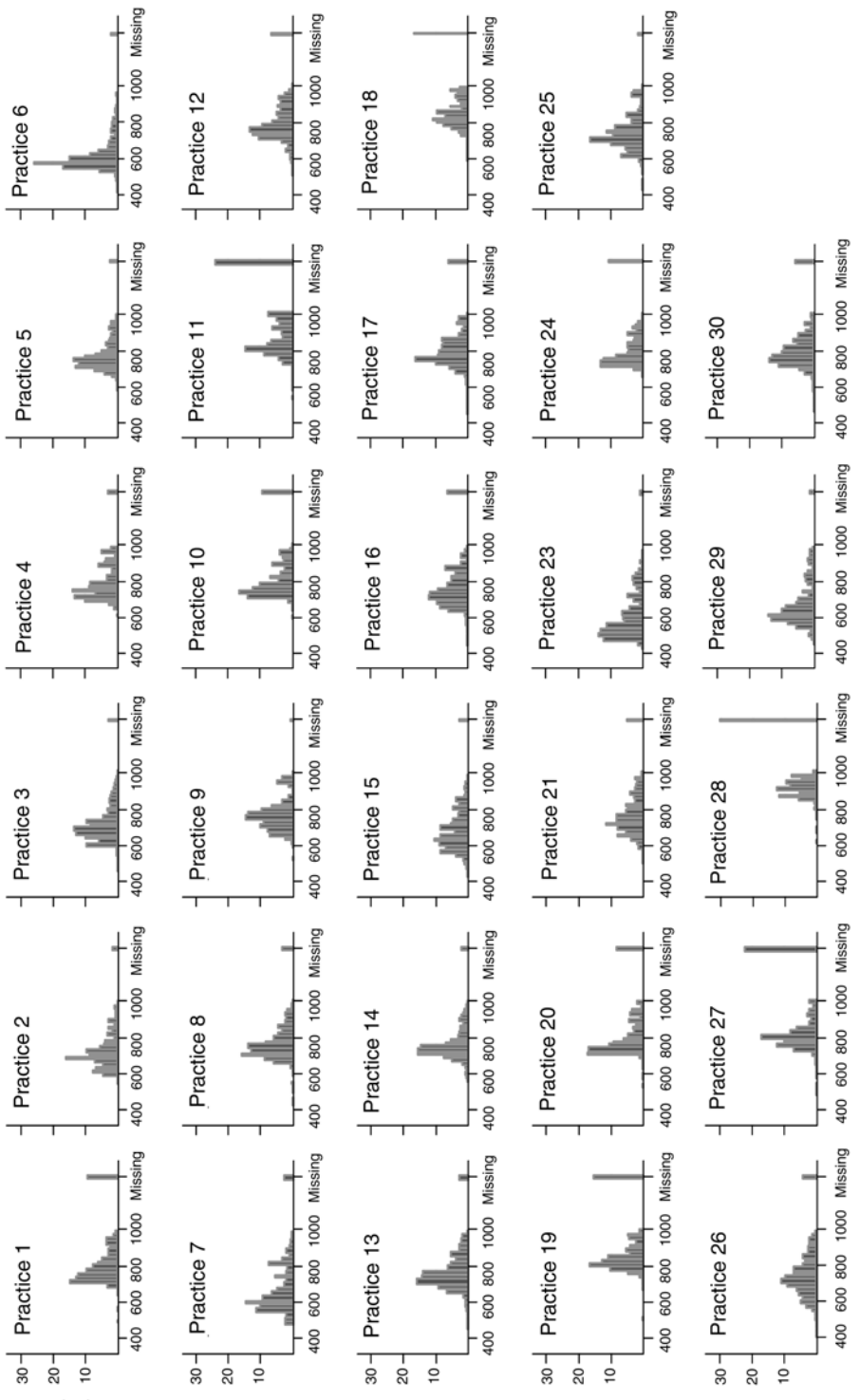

Figure 21. Distribution of modeled 2005 NO_x concentration percentiles (for London as a whole) in the 29 Lambeth practices. On the *x* axis, "Missing" indicates that no pollution value was assigned to the patient record because (1) of an invalid postcode caused by absence, error, or a location outside of London or (2) a pollution value could not be assigned to a valid postcode because the postcode had no spatial dimension (being probably a single building, such as a tower block).

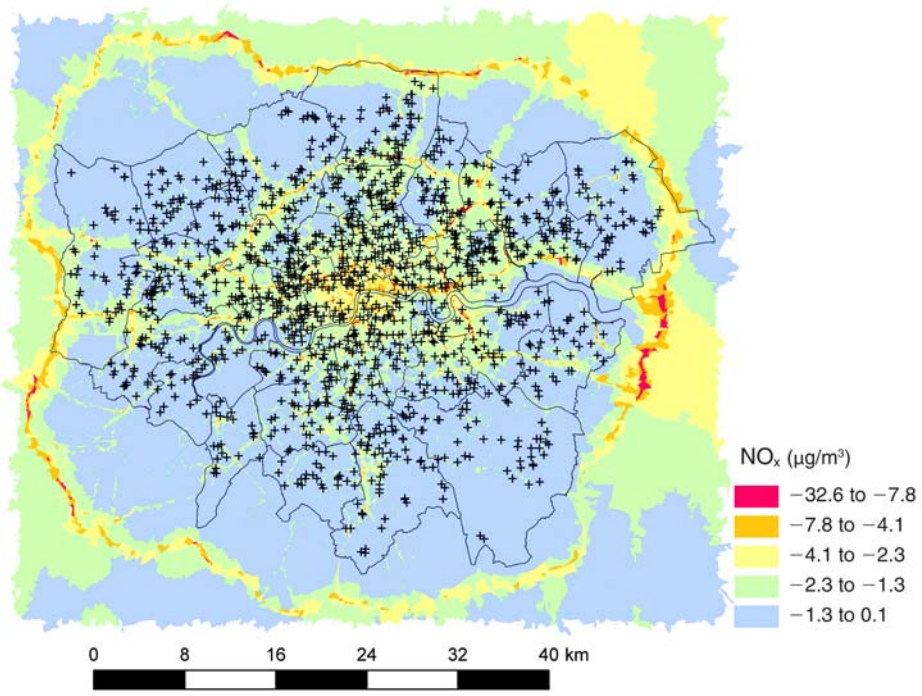

Figure 22. Annual mean NO_x concentration difference plot for the 2010 base case and LEZ Scenario 6. Crosses indicate locations of practices. The color scale represents the difference between the base case (without LEZ) and the LEZ Scenario 6. The metric is annual mean NO_x concentrations (µg/m^3) and the year is 2010.

and coaches). This information will guide the planning of the future evaluation of the impact of the LEZ on air quality and on health outcomes using primary-care records (see Discussion).

Associations Between NO_x Exposures and Smoking and Indicators of Socioeconomic Status

Smoking and socioeconomic status are important potential confounders of any cross-sectional relationship between proximity to traffic and health outcomes, so they are taken into account in this baseline study of the DIN and Lambeth practices. However, we expect that these factors will be less important in our future analysis of the LEZ because that will be a longitudinal, not cross-sectional analysis. For the DIN practices, we investigated the relationship between NO_x exposure at the postcode level and smoking status (as recorded in the clinical record for patients registered in the 13 DIN practices in 2005 [Figure 23]). For all practices combined, there was little evidence of an association with smoking status. Within practices there was also little evidence of a relationship with smoking status, and any patterns that did exist were not consistent. In contrast, there was a clear positive gradient of NO_x exposure associated with increasing deprivation — amounting to a twofold increase between the least and most deprived categories of the Index of Multiple Deprivation (Figure 24). At the level of individual practices, there were variations in overall NO_x exposure, and most of the practices showed evidence of higher exposure in patients living in more deprived areas. Nevertheless, there were variations in the within-practice patterns. Two practices had a high level of exposure and no differential by Index of Multiple Deprivation category. In contrast, one practice with low exposure had very few patients classified as living in more deprived areas. The distribution of exposures across ACORN categories within individual practices showed some variation in pattern. However, for all practices combined, it can be seen that exposure in the "wealthy achievers" category was lower than in the "hard pressed" category (Figure 25).

The relationship, in the DIN practices, between NO_x deciles and sex, age group, smoking, Index of Multiple Deprivation, and ACORN categories is analyzed in detail in Table 7. In total there were 121,063 patients, 94% of whom were assigned to a NO_x decile, with percentages tailing off toward the higher deciles. There was no obvious difference in exposure between the sexes. Among the age groups, there was some evidence that increasing percentages of the 15–44-year age group fell within the upper

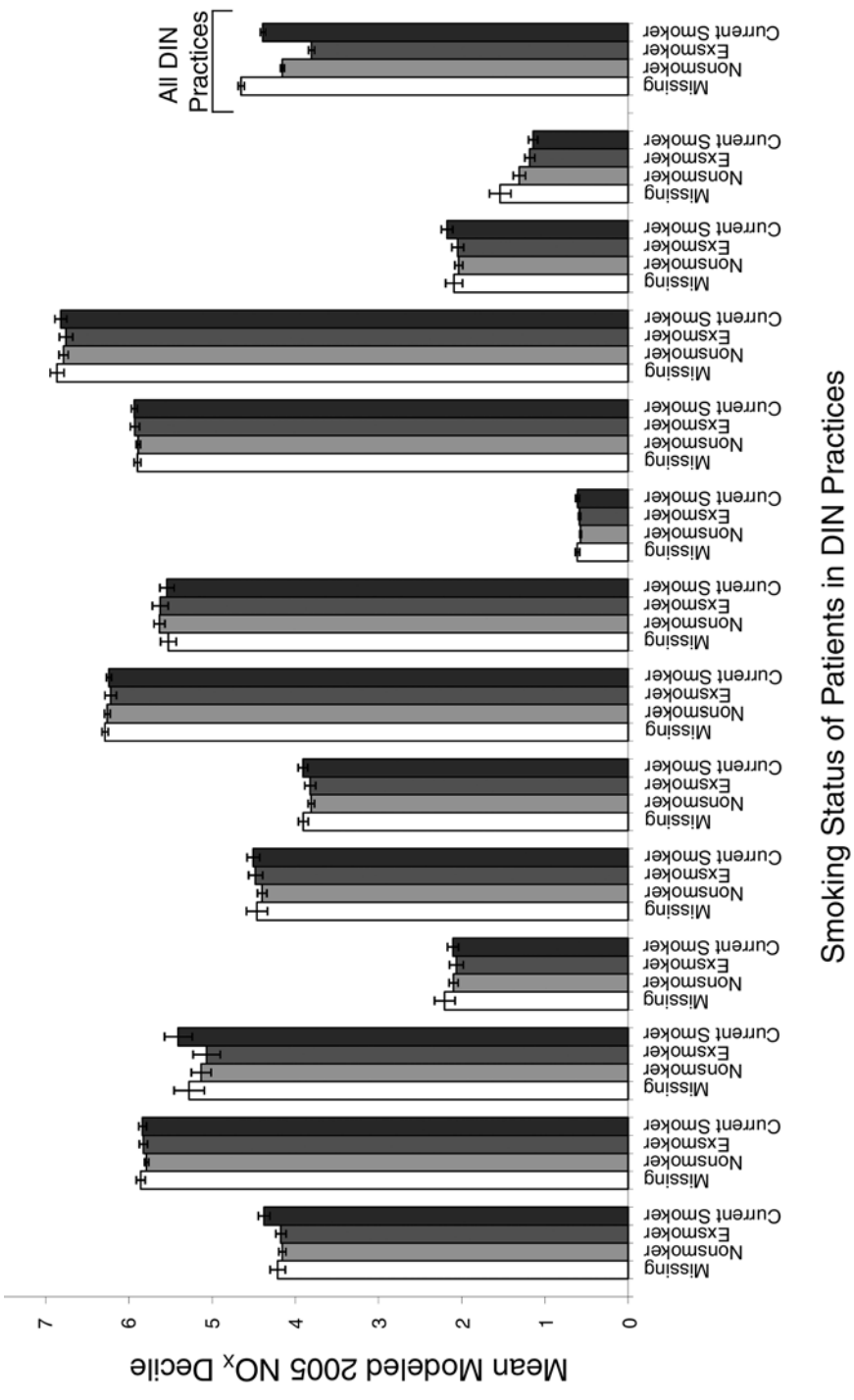

Figure 23. Mean deciles of modeled 2005 NO_x distribution by smoking status of patients registered in 2005 in the 13 DIN practices and for all 13 practices as a whole. On the *x* axis, "Missing" indicates that no pollution value was assigned to the patient record because (1) of an invalid postcode caused by absence, error, or a location outside of London or (2) a pollution value could not be assigned to a valid postcode because the postcode had no spatial dimension (being probably a single building, such as a tower block).

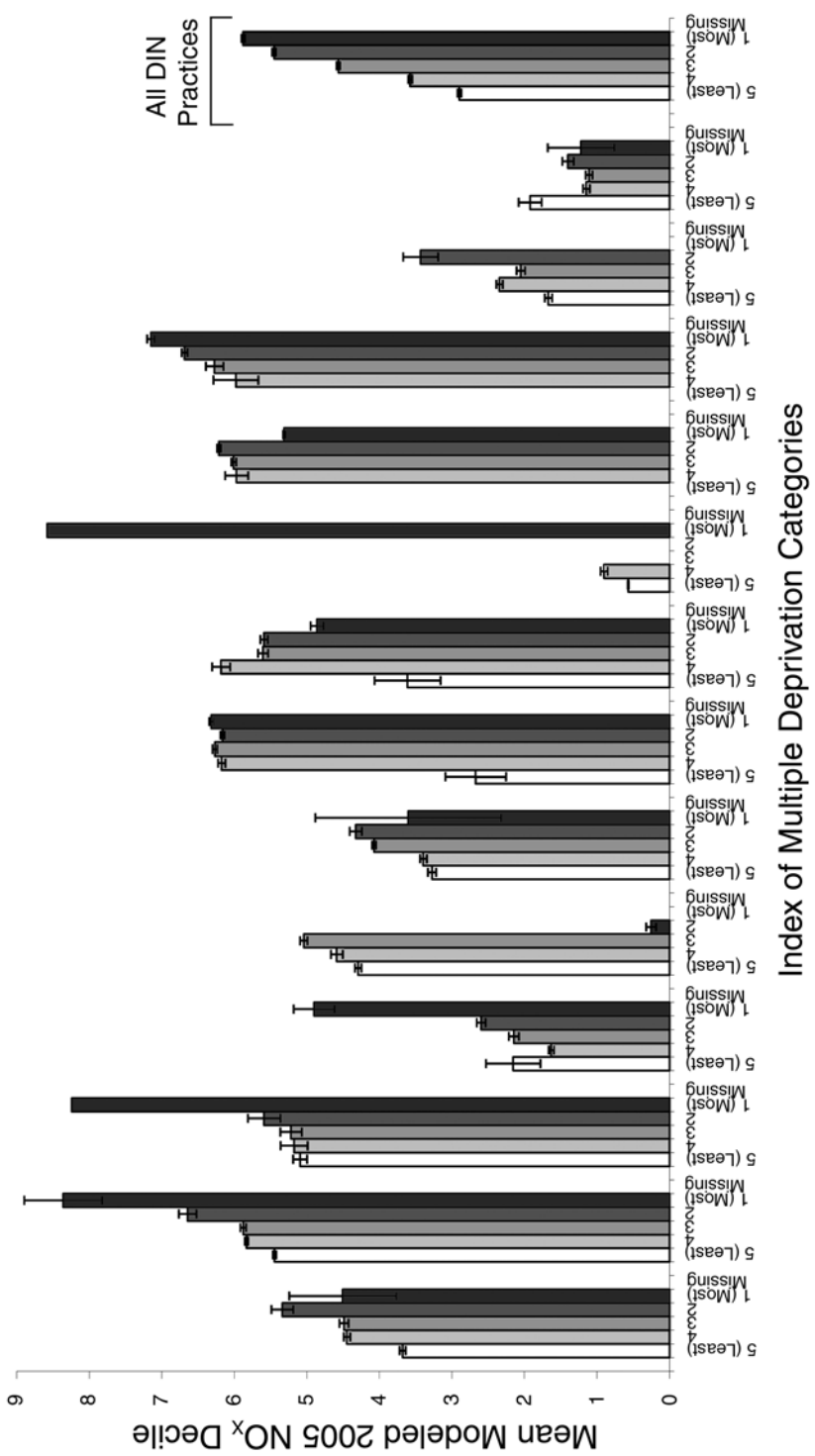

Figure 24. Mean deciles of modeled 2005 NO_x distribution by Index of Multiple Deprivation scores for patients registered in 2005 in the 13 DIN practices and for all 13 practices as a whole. Index of Multiple Deprivation scores range from 5 (least deprived) to 1 (most deprived). On the *x* axis, "Missing" indicates that no pollution value was assigned to the patient record because (1) of an invalid postcode caused by absence, error, or a location outside of London or (2) a pollution value could not be assigned to a valid postcode because the postcode had no spatial dimension (being probably a single building, such as a tower block).

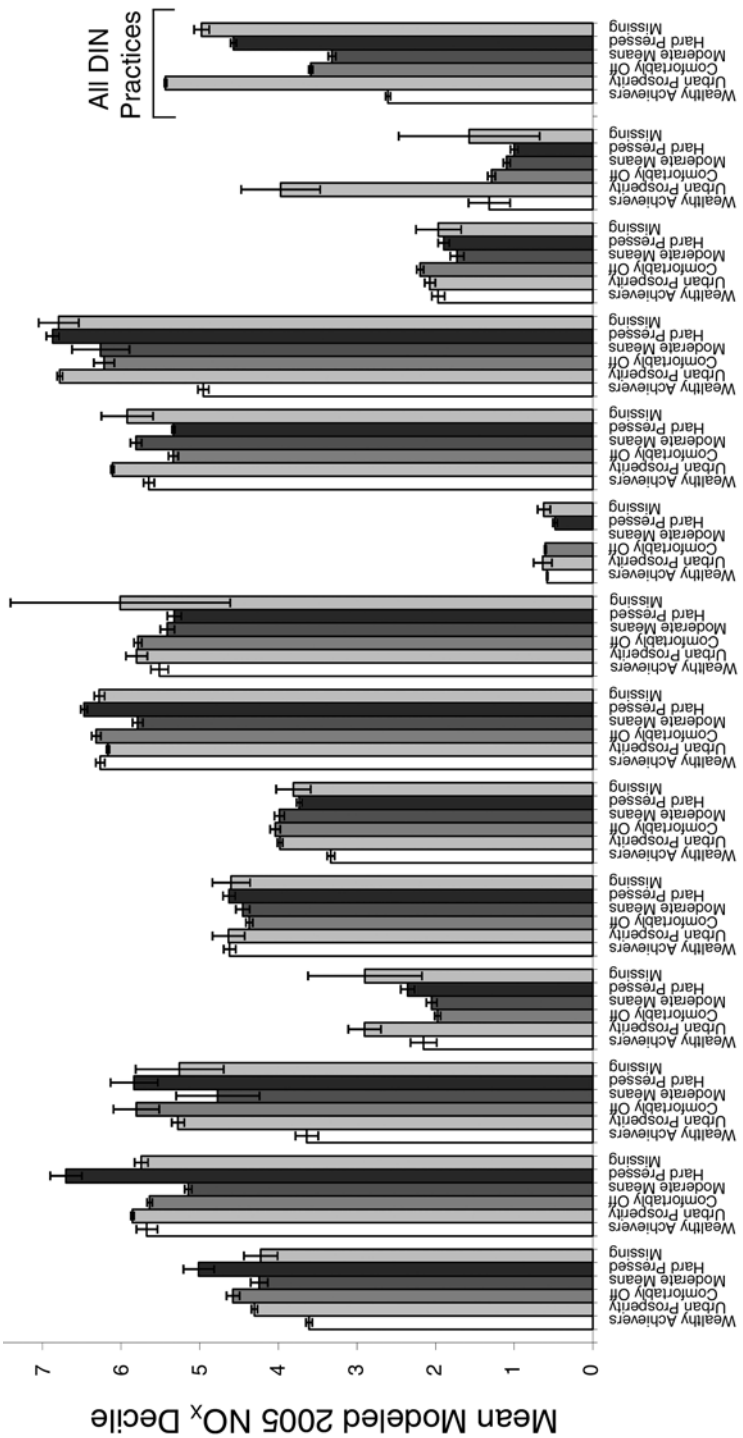

Figure 25. Mean deciles of modeled 2005 NO_x distribution by ACORN category for patients registered in 2005 in the 13 DIN practices and for all 13 practices as a whole. On the x axis, "Missing" indicates that no pollution value was assigned to the patient record because (1) of an invalid postcode caused by absence, error, or a location outside of London or (2) a pollution value could not be assigned to a valid postcode because the postcode had no spatial dimension (being probably a single building, such as a tower block).

Table 7. The Relationship of NO_x Concentration Deciles to Data on Age, Sex, Smoking, Index of Multiple Deprivation Score, and ACORN Category for Patients in DIN Practices

			NO_x Concentration (μg/m³) Deciles									
Patient Groups[a]	All	Missing[b]	**1** (21.7–37.7)	**2** (37.8–42.4)	**3** (42.4–46.1)	**4** (46.2–49.9)	**5** (49.9–54.2)	**6** (54.2–58.8)	**7** (58.8–63.7)	**8** (63.7–69.9)	**9** (69.9–82.1)	**10** (82.1–386.3)
All Patients (*N*)	121,063	6,663	15,407	11,087	9,463	14,054	14,602	27,912	10,219	5,611	3,745	2,300
Percent		5.5	12.7	9.2	7.8	11.6	12.1	23.1	8.4	4.6	3.1	1.9
Sex												
Males (*n*)	60,030	3,407	7,531	5,479	4,631	7,009	7,159	13,855	5,071	2,780	1,902	1,206
Percent	49.6	51.1	48.9	49.4	48.9	49.9	49.0	49.6	49.6	49.5	50.8	52.4
Females (*n*)	61,033	3,256	7,876	5,608	4,832	7,045	7,443	14,057	5,148	2,831	1,843	1,094
Percent	50.4	48.9	51.1	50.6	51.1	50.1	51.0	50.4	50.4	50.5	49.2	47.6
Age Group (yr)												
1–4 (*n*)	6,115	124	753	636	454	721	769	1,503	568	292	178	117
Percent	5.1	1.9	4.9	5.7	4.8	5.1	5.3	5.4	5.6	5.2	4.8	5.1
5–14 (*n*)	14,264	705	2,033	1,566	1,146	1,647	1,716	3,151	1,032	639	377	252
Percent	11.8	10.6	13.2	14.1	12.1	11.7	11.8	11.3	10.1	11.4	10.1	11.0
15–44 (*n*)	53,746	2,693	5,520	4,973	4,065	6,033	6,575	13,133	5,055	2,723	1,832	1,144
Percent	44.4	40.4	35.8	44.9	43.0	42.9	45.0	47.1	49.5	48.5	48.9	49.7
45–64 (*n*)	29,496	1,918	4,241	2,521	2,331	3,528	3,346	6,675	2,262	1,277	859	538
Percent	24.4	28.8	27.5	22.7	24.6	25.1	22.9	23.9	22.1	22.8	22.9	23.4
≥ 65 (*n*)	17,442	1,223	2,860	1,391	1,467	2,125	2,196	3,450	1,302	680	499	249
Percent	14.4	18.4	18.6	12.5	15.5	15.1	15.0	12.4	12.7	12.1	13.3	10.8
Smoking												
Men (≥ 15 yr)												
Nonsmoker/never (*n*)	17,079	585	2,305	1,489	1,522	2,198	2,090	3,954	1,367	717	490	362
Percent	34.5	19.6	37.9	34.3	39.3	38.1	35.4	34.5	32.2	31.1	30.6	35.1
Exsmokers (*n*)	8,941	675	1,554	889	797	1,172	1,054	1,519	553	317	219	192
Percent	18.4	22.6	25.6	20.5	20.6	20.3	17.8	13.3	13.0	13.7	13.7	18.6
Current (*n*)	12,876	835	1,294	1,335	927	1,327	1,574	2,968	1,213	657	475	271
Percent	26.5	28.0	21.3	30.8	24.0	23.0	26.6	25.9	28.6	28.5	29.6	26.3
Missing (*n*)	10,678	887	921	624	624	1,075	1,189	3,005	1,109	618	419	207
Percent	22.0	29.7	15.2	14.4	16.1	18.6	20.1	26.3	26.1	26.8	26.1	20.1
Women (≥ 15 yr)												
Nonsmoker/never (*n*)	24,494	719	3,241	2,135	2,070	3,112	3,093	5,796	2,036	1,144	759	389
Percent	47.9	25.2	49.5	46.9	51.8	52.6	49.8	49.1	46.5	48.3	47.8	43.3
Exsmokers (*n*)	9,413	785	1,552	940	766	1,125	1,180	1,640	624	358	239	204
Percent	18.4	27.5	23.7	20.7	19.2	19.0	19.0	13.9	14.3	15.1	15.1	22.7
Current (*n*)	11,774	736	1,131	1,212	840	1,135	1,381	2,929	1,169	607	410	224
Percent	23.0	25.8	17.3	26.7	21.0	19.2	22.2	24.8	26.7	25.6	25.8	24.9
Missing (*n*)	5,429	612	623	261	317	542	556	1,447	548	262	179	82
Percent	10.6	21.5	9.5	5.7	7.9	9.2	9.0	12.3	12.5	11.1	11.3	9.1

Table continues next page

[a] Percentages in table were calculated within each group.

[b] Missing indicates that no pollution value was assigned to the patient record because (1) of an invalid postcode caused by absence, error, or a location outside of London or (2) a pollution value could not be assigned to a valid postcode because the postcode had no spatial dimension (being probably a single building, such as a tower block).

deciles of NO_x concentrations. Smoking data were missing in 22% of men and 11% of women; 27% of men and 23% of women were current smokers. There was no obvious relationship between smoking and NO_x exposure. Index of Multiple Deprivation data were available for 96% of patients, and overall there was a clear trend toward increasing exposure in the more deprived and less exposure in the less deprived.

The ACORN data showed something similar with higher proportions of "wealthy achievers" in the lower versus higher exposure groups. Although the pattern was less clear in the other groups, it is important to note that the ACORN data are not a graded scale of deprivation. An example of this is the "urban prosperity" category, the category adjacent to "wealthy achievers," in which the trend was toward higher NO_x exposure.

Table 7 (*continued*). The Relationship of NO_x Concentration Deciles to Data on Age, Sex, Smoking, Index of Multiple Deprivation Score, and ACORN Category for Patients in DIN Practices

			NO_x Concentration (μg/m³) Deciles									
Patient Groups[a]	All	Missing[b]	**1** (21.7–37.7)	**2** (37.8–42.4)	**3** (42.4–46.1)	**4** (46.2–49.9)	**5** (49.9–54.2)	**6** (54.2–58.8)	**7** (58.8–63.7)	**8** (63.7–69.9)	**9** (69.9–82.1)	**10** (82.1–386.3)
Index of Multiple Deprivation Score Fifths												
5(least deprived) (*n*)	31,413	818	10,626	2,157	3,992	4,968	3,519	2,975	476	545	482	855
Percent	25.9	12.3	69.0	19.5	42.2	35.4	24.1	10.7	4.7	9.7	12.9	37.2
4 (*n*)	24,984	298	2,471	5,312	2,835	3,881	2,823	4,565	1,456	624	433	286
Percent	20.6	4.5	16.0	47.9	30.0	27.6	19.3	16.4	14.2	11.1	11.6	12.4
3 (*n*)	26,342	244	1,769	2,032	1,336	4,002	4,600	7,409	2,347	1,222	1,030	351
Percent	21.8	3.7	11.5	18.3	14.1	28.5	31.5	26.5	23.0	21.8	27.5	15.3
2 (*n*)	22,690	221	518	1,584	1,286	1,133	1,706	8,005	4,139	1,997	1,452	649
Percent	18.7	3.3	3.4	14.3	13.6	8.1	11.7	28.7	40.5	35.6	38.8	28.2
1 (most deprived) (*n*)	10,908	356	23	2	14	70	1,954	4,958	1,801	1,223	348	159
Percent	9.0	5.3	0.2	0.0	0.1	0.5	13.4	17.8	17.6	21.8	9.3	6.9
Missing (*n*)	4,726	4,726	0	0	0	0	0	0	0	0	0	0
Percent	3.9	70.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
ACORN Categories												
Wealthy achievers (*n*)	20,036	819	8,151	1,027	2,082	3,549	1,503	1,334	607	461	229	274
Percent	16.6	12.3	52.9	9.3	22.0	25.3	10.3	4.8	5.9	8.2	6.1	11.9
Urban prosperity (*n*)	41,110	566	524	1,109	1,531	4,517	4,721	15,885	6,237	2,972	2,305	743
Percent	34.0	8.5	3.4	10.0	16.2	32.1	32.3	56.9	61.0	53.0	61.5	32.3
Comfortably off (*n*)	33,210	2,027	4,222	5,796	3,920	3,882	4,219	5,362	1,437	805	679	861
Percent	27.4	30.4	27.4	52.3	41.4	27.6	28.9	19.2	14.1	14.3	18.1	37.4
Moderate means (*n*)	8,990	1,280	1,112	1,782	719	1,131	1,124	1,198	156	305	163	20
Percent	7.4	19.2	7.2	16.1	7.6	8.0	7.7	4.3	1.5	5.4	4.4	0.9
Hard pressed (*n*)	15,278	1,151	1,275	1,303	1,089	843	2,850	3,587	1,510	979	317	374
Percent	12.6	17.3	8.3	11.8	11.5	6.0	19.5	12.9	14.8	17.4	8.5	16.3
Missing (*n*)	2,439	820	123	70	122	132	185	546	272	89	52	28
Percent	2.0	12.3	0.8	0.6	1.3	0.9	1.3	2.0	2.7	1.6	1.4	1.2

[a] Percentages in table were calculated within each group.

[b] Missing indicates that no pollution value was assigned to the patient record because (1) of an invalid postcode caused by absence, error, or a location outside of London or (2) a pollution value could not be assigned to a valid postcode because the postcode had no spatial dimension (being probably a single building, such as a tower block).

The relationships between NO_x exposure and sex, age, ethnicity, smoking, and Index of Multiple Deprivation in the Lambeth practices is shown in Table 8. Of 205,462 patients, 93% were assigned to a NO_x decile. Because Lambeth is an inner-city borough, most of the population's estimated exposure fell in the sixth or higher deciles ($\geq$ 54.2 μg/m³). There was some evidence of trends toward lower exposures in the 1–4-year and 5–14-year age groups and higher exposures in the 15–44-year age group. Information on ethnicity was available for 52% of patients. The percentage of patients for whom data on ethnicity was missing declined with increasing exposure. Of the total, including the missing, 32.4% were "White"; there was a slight tendency for this group to be more exposed but overall these ethnic groups showed similar patterns of exposure. Smoking status was available for 77% of men. There was no obvious association between NO_x exposure and current smokers. However, a trend toward fewer exsmokers in the more exposed categories was seen. Smoking status was available for 90% of women, and there was no association with NO_x exposure. Strong relationships between Index of Multiple Deprivation and NO_x exposure were seen, with the least-deprived categories (Index of Multiple Deprivation 3–5) showing a negative relationship with NOx exposure and the more deprived (Index of Multiple Deprivation 1–2) showing a positive relationship.

Associations Between NO_x Exposures and Health Outcomes

The univariate associations between the health outcomes in the DIN database are shown in Appendix Tables D.5, D.6, and D.7. There are 36 comparisons relating to 12 health outcomes. Because the results of logistic regression analyses, which adjusted for potential confounding factors, are presented elsewhere in this report, only the salient points from these tables are commented on here. Results are presented for seven "ever" outcomes — asthma ever (five age groups), ischemic heart disease ever (two age groups), chronic obstructive pulmonary disease ever ($\geq$ 65-year age group),

Table 8. The Relationship of NO_x Concentration Deciles to Data on Age, Sex, Ethnicity, Smoking, and Index of Multiple Deprivation Score for Patients in Lambeth Practices

			NO_x Concentration ($\mu g/m^3$) Deciles									
Patient Groups[a]	All	Missing[b]	**1** (21.7–37.7)	**2** (37.8–42.4)	**3** (42.4–46.1)	**4** (46.2–49.9)	**5** (49.9–54.2)	**6** (54.2–58.8)	**7** (58.8–63.7)	**8** (63.7–69.9)	**9** (69.9–82.1)	**10** (82.1–386.3)
All Patients (*N*)	205,462	13,555	0	0	0	0	1,418	16,494	37,848	74,874	40,514	20,759
Percent		6.6	0.0	0.0	0.0	0.0	0.7	8.0	18.4	36.4	19.7	10.1
Sex												
Males (*n*)	105,799	7,040	0	0	0	0	755	8,078	19,313	38,392	21,085	11,136
Percent	51.5	51.9	—	—	—	—	53.2	49.0	51.0	51.3	52.0	53.6
Females (*n*)	99,663	6,515	0	0	0	0	663	8,416	18,535	36,482	19,429	9,623
Percent	48.5	48.1	—	—	—	—	46.8	51.0	49.0	48.7	48.0	46.4
Age Group (yr)												
1–4 (*n*)	9,693	734	0	0	0	0	74	940	2,003	3,370	1,817	755
Percent	4.7	5.4	—	—	—	—	5.2	5.7	5.3	4.5	4.5	3.6
5–14 (*n*)	20,353	1,465	0	0	0	0	144	2,161	4,106	7,334	3,639	1,504
Percent	9.9	10.8	—	—	—	—	10.2	13.1	10.8	9.8	9.0	7.2
15–44 (*n*)	119,355	7,786	0	0	0	0	764	7,870	20,811	44,647	24,071	13,406
Percent	58.1	57.4	—	—	—	—	53.9	47.7	55.0	59.6	59.4	64.6
45–64 (*n*)	39,268	2,580	0	0	0	0	303	3,711	7,649	13,751	7,602	3,672
Percent	19.1	19.0	—	—	—	—	21.4	22.5	20.2	18.4	18.8	17.7
≥65 (*n*)	16,793	990	0	0	0	0	133	1,812	3,279	5,772	3,385	1,422
Percent	8.2	7.3	—	—	—	—	9.4	11.0	8.7	7.7	8.4	6.9
Ethnicity												
White (*n*)	66,512	3,815	0	0	0	0	414	4,680	10,745	25,630	13,948	7,280
Percent	32.4	28.1	—	—	—	—	29.2	28.4	28.4	34.2	34.4	35.1
Mixed (*n*)	4,987	285	0	0	0	0	38	396	950	1,793	989	536
Percent	2.4	2.1	—	—	—	—	2.7	2.4	2.5	2.4	2.4	2.6
Asian/Asian British (*n*)	4,511	330	0	0	0	0	34	370	810	1,476	847	644
Percent	2.2	2.4	—	—	—	—	2.4	2.2	2.1	2.0	2.1	3.1
Black/Black British (*n*)	26,824	2,505	0	0	0	0	122	1,579	4,965	10,092	5,392	2,169
Percent	13.1	18.5	—	—	—	—	8.6	9.6	13.1	13.5	13.3	10.4
Chinese/Other (*n*)	5,473	599	0	0	0	0	22	256	696	1,834	1,197	869
Percent	2.7	4.4	—	—	—	—	1.6	1.6	1.8	2.5	3.0	4.2
Not recorded (*n*)	97,155	6,021	0	0	0	0	788	9,213	19,682	34,049	18,141	9,261
Percent	47.3	44.4	—	—	—	—	55.6	55.9	52.0	45.5	44.8	44.6

Table continues next page

[a] Percentages in table were calculated within each group.

[b] Missing indicates that no pollution value was assigned to the patient record because (1) of an invalid postcode caused by absence, error, or a location outside of London or (2) a pollution value could not be assigned to a valid postcode because the postcode had no spatial dimension (being probably a single building, such as a tower block).

heart failure ever (≥ 65-year age group), atrial fibrillation ever (≥ 65-year age group), hay fever ever (four age groups), wheeze ever (five age groups) — as well as respiratory tract infection in 2005 (five age groups), prescriptions for asthma drugs in 2005 (five age groups), loop diuretics in 2005 (≥ 65-year age group), and nitrates in 2005 (≥ 65-year age group). Results are also presented for prescriptions for asthma drugs in 2005 in patients with a history of asthma ever (five age groups). Overall, there appeared to be no evidence of consistent positive associations between any of the outcomes and deciles of NO_x. Instead, the tendency was generally toward negative associations throughout,

Table 8 (*continued*). The Relationship of NO_x Concentration Deciles to Data on Age, Sex, Ethnicity, Smoking, and Index of Multiple Deprivation Score for Patients in Lambeth Practices

			NO_x Concentration (μg/m^3) Deciles									
Patient Groups[a]	All	Missing[b]	**1** (21.7–37.7)	**2** (37.8–42.4)	**3** (42.4–46.1)	**4** (46.2–49.9)	**5** (49.9–54.2)	**6** (54.2–58.8)	**7** (58.8–63.7)	**8** (63.7–69.9)	**9** (69.9–82.1)	**10** (82.1–386.3)
Smoking												
Men (≥ 15 yr)												
Nonsmoker/never (*n*)	32,651	2,180	0	0	0	0	225	1,964	5,423	12,372	6,788	3,699
Percent	36.1	19.2	—	—	—	—	35.5	30.4	33.5	37.6	37.1	37.0
Exsmoker (*n*)	12,479	726	0	0	0	0	123	1,134	2,285	4,553	2,469	1,189
Percent	13.8	6.4	—	—	—	—	19.4	17.5	14.1	13.8	13.5	11.9
Current (*n*)	24,761	1,589	0	0	0	0	149	1,730	4,571	8,789	5,084	2,849
Percent	27.4	14.0	—	—	—	—	23.5	26.7	28.2	26.7	27.8	28.5
Missing (*n*)	20,574	1,442	0	0	0	0	137	1,642	3,918	7,233	3,951	2,251
Percent	22.7	12.7	—	—	—	—	21.6	25.4	24.2	22.0	21.6	22.5
Women (≥ 15 yr)												
Nonsmoker/never (*n*)	44,003	2,983	0	0	0	0	326	3,071	7,636	16,600	8,791	4,596
Percent	51.8	55.0	—	—	—	—	57.6	44.4	49.1	53.2	52.4	54.0
Exsmoker (*n*)	13,135	663	0	0	0	0	91	1,429	2,656	4,695	2,478	1,123
Percent	15.5	12.2	—	—	—	—	16.1	20.6	17.1	15.0	14.8	13.2
Current (*n*)	18,853	1,114	0	0	0	0	106	1,618	3,546	6,715	3,854	1,900
Percent	22.2	20.6	—	—	—	—	18.7	23.4	22.8	21.5	23.0	22.3
Missing (*n*)	8,960	659	0	0	0	0	43	805	1,704	3,213	1,643	893
Percent	10.5	12.2	—	—	—	—	7.6	11.6	11.0	10.3	9.8	10.5
Index of Multiple Deprivation Score Fifths												
4 or 5 (least deprived) (*n*)	7,563	34	0	0	0	0	200	3,108	1,433	1,517	714	557
Percent	3.7	0.3	—	—	—	—	14.1	18.8	3.8	2.0	1.8	2.7
3 (*n*)	22,839	4	0	0	0	0	766	5,156	7,832	5,803	2,052	1,226
Percent	11.1	0.0	—	—	—	—	54.0	31.3	20.7	7.8	5.1	5.9
2 (*n*)	79,118	2	0	0	0	0	152	4,659	12,566	34,887	17,535	9,317
Percent	38.5	0.0	—	—	—	—	10.7	28.2	33.2	46.6	43.3	44.9
1 (most deprived) (*n*)	82,438	11	0	0	0	0	300	3,571	16,017	32,667	20,213	9,659
Percent	40.1	0.1	—	—	—	—	21.2	21.7	42.3	43.6	49.9	46.5
Missing	13,504	13,504	0	0	0	0	0	0	0	0	0	0
Percent	6.6	99.6	—	—	—	—	0.0	0.0	0.0	0.0	0.0	0.0

[a] Percentages in table were calculated within each group.

[b] Missing indicates that no pollution value was assigned to the patient record because (1) of an invalid postcode caused by absence, error, or a location outside of London or (2) a pollution value could not be assigned to a valid postcode because the postcode had no spatial dimension (being probably a single building, such as a tower block).

with disease outcomes being less frequent in the higher NO_x deciles (e.g., wheeze ever in 5–14 year olds, for which patients in the lower deciles had period prevalences ranging from 10% to 16% and those in the higher deciles had prevalences of the study period in the 6% to 8% range).

The univariate associations between outcomes and NO_x deciles in the Lambeth data set are shown in Appendix Table D.8 for asthma ever (five age groups) and ischemic heart disease ever (two age groups). No obvious trends were seen, except, as was seen in the DIN analysis, a negative relationship between NO_x decile and asthma ever in the 15–44-year age group.

The results of logistic regression analyses for the DIN asthma ever data are shown in Table 9. For each age group,

Table 9. Summary of Regression Analyses for Asthma Ever from the DIN Practices[a]

	Ages 1–4 yr (N = 5,991)						Ages 5–14 yr (N = 13,559)					
		+ Age, Sex, and Practice			+ Age, Sex, Practice, and IMD			+ Age, Sex, and Practice			+ Age, Sex, Practice, and IMD	
	n	OR	L95	U95	OR	L95	U95	n	OR	L95	U95	OR	L95	U95
NO_x Decile[b]														
1	753	1.03	0.51	2.08	1.30	0.68	2.46	2,033	0.89	0.79	1.00	0.98	0.85	1.13
2	636	1.04	0.48	2.27	1.19	0.53	2.66	1,566	0.99	0.84	1.16	1.09	0.93	1.27
3	454	0.65	0.38	1.11	0.76	0.45	1.30	1,146	1.02	0.82	1.27	1.09	0.86	1.37
4	721	0.64	0.38	1.08	0.77	0.45	1.31	1,647	0.84	0.75	0.95	0.89	0.78	1.03
5	769	1.35	0.88	2.07	1.45	0.90	2.32	1,716	1.05	0.95	1.17	1.07	0.97	1.19
6	1,503	1			1			3,151	1			1		
7	568	1.46	0.95	2.26	1.44	0.99	2.10	1,032	0.87	0.70	1.08	0.86	0.69	1.08
8	292	1.65	0.76	3.63	1.59	0.76	3.30	639	1.06	0.86	1.30	1.04	0.84	1.28
9	178	1.12	0.32	3.95	1.16	0.33	4.14	377	0.70	0.57	0.84	0.70	0.59	0.84
10	117	0.54	0.15	1.96	0.59	0.15	2.27	252	0.99	0.87	1.13	1.01	0.84	1.21
Test for trend[c]		P = 0.27			P = 0.73				P = 0.72 (neg)			P = 0.15 (neg)		
Sex														
Male	3,072	1			1			6,959	1			1		
Female	2,919	0.60	0.42	0.87	0.61	0.42	0.88	6,600	0.66	0.60	0.72	0.66	0.60	0.72
Age Subgroup[d]														
1	1,585	1			1			2,860	1			1		
2	1,511	1.84	1.22	2.78	1.81	1.21	2.72	2,763	1.54	1.33	1.77	1.53	1.33	1.76
3	1,477	2.70	1.60	4.56	2.69	1.60	4.50	2,705	1.95	1.73	2.20	1.96	1.74	2.20
4	1,418	4.92	3.00	8.06	4.88	2.97	8.01	2,652	2.34	1.90	2.87	2.34	1.91	2.87
5								2,579	2.67	2.39	2.98	2.68	2.41	2.98
6														
Smoking Status														
Never smoker														
Exsmoker														
Current smoker														
Missing[e]														
Index of Multiple Deprivation Score														
5 (least deprived)	1,413				1			3,674				1		
4	1,228				1.63	1.11	2.38	2,657				0.98	0.83	1.17
3	1,334				1.15	0.71	1.87	3,025				1.07	0.88	1.30
2	1,293				1.74	0.96	3.15	2,777				1.36	1.11	1.68
1 (most deprived)	723				2.02	1.10	3.72	1,426				1.34	1.04	1.72

Table continues on next page

[a] For each age group, the results from two models are shown. The first model "+Age, Sex, and Practice" controlled for age (within age group), sex, and practice (random-effects model). The second model "+Age, Sex, Practice, and IMD" controlled for age (within age group), sex, practice, Index of Multiple Deprivation, and — for the age groups older than 15 years — smoking. Note that practice is fitted as a random effect in both models. OR indicates odds ratio, L95 indicates lower 95 percent confidence limit, and U95 indicates upper 95 percent confidence limit.

[b] See Table 6 for ranges of NO_x concentrations ($\mu g/m^3$) in each decile.

[c] P value for test for NO_x trend indicates positive trend unless indicated; neg indicates negative trend.

[d] Subgroups for ages 1–4 yr are 1 = 1 yr, 2 = 2 yr, 3 = 3 yr, 4 = 4 yr; for ages 5–14 yr, 1 = 5–6 yr, 2 = 7–8 yr, 3 = 9–10 yr, 4 = 11–12 yr, 5 = 13–14 yr; for ages 15–44 yr, 1 = 15–19 yr, 2 = 20–24 yr, 3 = 25–29 yr, 4 = 30–34 yr, 5 = 35–39 yr, 6 = 40–44 yr; for ages 45–64 yr, 1 = 45–49 yr, 2 = 50–54 yr, 3 = 55–59 yr, 4 = 60–64 yr; and for ages ≥ 65 yr, 1 = 65–69 yr, 2 = 70–74 yr, 3 = 75–79 yr, 4 = 80–84 yr, 5 = ≥ 85 yr.

[e] Missing indicates that no pollution value was assigned to the patient record because (1) of an invalid postcode caused by absence, error, or a location outside of London or (2) a pollution value could not be assigned to a valid postcode because the postcode had no spatial dimension (being probably a single building, such as a tower block).

Table 9 (*continued*). Summary of Regression Analyses for Asthma Ever from the DIN Practices[a]

	Ages 15–44 yr (N = 51,053)							Ages 45–64 yr (N = 27,578)						
		+ Age, Sex, and Practice			+ Age, Sex, Practice, Smoking, and IMD				+ Age, Sex, and Practice			+ Age, Sex, Practice, Smoking, and IMD		
	n	OR	L95	U95	OR	L95	U95	n	OR	L95	U95	OR	L95	U95
NO_x Decile[b]														
1	5,520	1.10	0.92	1.32	1.12	0.80	1.56	4,241	1.03	0.87	1.22	1.09	0.92	1.29
2	4,973	1.17	1.01	1.35	1.18	0.90	1.55	2,521	1.11	0.93	1.31	1.15	0.99	1.33
3	4,065	1.16	1.02	1.32	1.17	0.94	1.46	2,331	1.03	0.88	1.19	1.08	0.93	1.25
4	6,033	1.06	0.94	1.19	1.06	0.89	1.26	3,528	1.03	0.87	1.21	1.06	0.91	1.24
5	6,575	1.07	0.96	1.18	1.06	0.93	1.20	3,346	1.05	0.87	1.26	1.03	0.86	1.25
6	13,133	1			1			6,675	1			1		
7	5,055	0.92	0.82	1.02	0.91	0.81	1.02	2,262	1.00	0.85	1.18	0.97	0.81	1.16
8	2,723	0.86	0.75	0.99	0.87	0.74	1.02	1,277	0.89	0.71	1.12	0.87	0.69	1.08
9	1,832	0.99	0.85	1.16	0.99	0.81	1.21	859	0.84	0.69	1.02	0.86	0.69	1.06
10	1,144	1.02	0.84	1.24	1.00	0.95	1.05	538	1.14	1.01	1.29	1.12	0.99	1.26
Test for trend[c]		P = 0.006 (neg)			P = 0.003 (neg)				P = 0.15 (neg)			P = 0.02 (neg)		
Sex														
Male	25,632	1			1			14,094	1			1		
Female	25,421	1.01	0.95	1.06	0.89	0.85	0.95	13,484	1.43	1.30	1.58	1.33	1.21	1.47
Age Subgroup[d]														
1	6,297	1			1			8,400	1			1		
2	5,914	0.83	0.75	0.91	0.68	0.62	0.76	6,995	0.95	0.85	1.07	0.95	0.85	1.06
3	8,299	0.63	0.58	0.70	0.48	0.43	0.53	6,958	0.91	0.81	1.02	0.89	0.79	1.00
4	9,930	0.59	0.53	0.64	0.42	0.39	0.47	5,225	0.87	0.78	0.97	0.83	0.74	0.93
5	10,543	0.53	0.48	0.58	0.38	0.35	0.42							
6	10,070	0.49	0.44	0.53	0.35	0.32	0.39							
Smoking Status														
Never smoker	21,817				1			11,743				1		
Exsmoker	5,593				1.44	1.32	1.57	5,858				1.36	1.14	1.62
Current smoker	13,536				1.22	1.14	1.30	6,800				1.25	0.95	1.63
Missing[e]	10,107				0.39	0.36	0.43	3,177				0.22	0.16	0.30
Index of Multiple Deprivation Score														
5 (least deprived)	11,977				1			8,422				1		
4	11,435				1.02	0.93	1.12	5,992				1.01	0.90	1.12
3	11,803				1.05	0.94	1.16	6,239				1.12	1.05	1.20
2	10,538				1.05	0.93	1.20	4,913				1.22	1.01	1.47
1 (most deprived)	5,300				1.06	0.91	1.23	2,012				1.64	1.42	1.89

Table continues on next page

[a] For each age group, the results from two models are shown. The first model "+Age, Sex, and Practice" controlled for age (within age group), sex, and practice (random-effects model). The second model "+Age, Sex, Practice, and IMD" controlled for age (within age group), sex, practice, Index of Multiple Deprivation, and — for the age groups older than 15 years — smoking. Note that practice is fitted as a random effect in both models. OR indicates odds ratio, L95 indicates lower 95 percent confidence limit, and U95 indicates upper 95 percent confidence limit.

[b] See Table 6 for ranges of NO_x concentrations ($\mu g/m^3$) in each decile.

[c] P value for test for NO_x trend indicates positive trend unless indicated; neg indicates negative trend.

[d] Subgroups for ages 1–4 yr are 1 = 1 yr, 2 = 2 yr, 3 = 3 yr, 4 = 4 yr; for ages 5–14 yr, 1 = 5–6 yr, 2 = 7–8 yr, 3 = 9–10 yr, 4 = 11–12 yr, 5 = 13–14 yr; for ages 15–44 yr, 1 = 15–19 yr, 2 = 20–24 yr, 3 = 25–29 yr, 4 = 30–34 yr, 5 = 35–39 yr, 6 = 40–44 yr; for ages 45–64 yr, 1 = 45–49 yr, 2 = 50–54 yr, 3 = 55–59 yr, 4 = 60–64 yr; and for ages ≥ 65 yr, 1 = 65–69 yr, 2 = 70–74 yr, 3 = 75–79 yr, 4 = 80–84 yr, 5 = ≥ 85 yr.

[e] Missing indicates that no pollution value was assigned to the patient record because (1) of an invalid postcode caused by absence, error, or a location outside of London or (2) a pollution value could not be assigned to a valid postcode because the postcode had no spatial dimension (being probably a single building, such as a tower block).

Table 9 (*continued*). Summary of Regression Analyses for Asthma Ever from the DIN Practices[a]

		Ages ≥ 65 yr (N = 16,219)					
		+ Age, Sex, and Practice			+ Age, Sex, Practice, Smoking, and IMD		
	n	OR	L95	U95	OR	L95	U95
NO_x Decile[b]							
1	2,860	0.79	0.68	0.91	0.87	0.78	0.98
2	1,391	0.91	0.73	1.15	0.91	0.70	1.20
3	1,467	0.75	0.60	0.94	0.82	0.67	1.00
4	2,125	0.81	0.70	0.92	0.89	0.78	1.03
5	2,196	0.86	0.74	0.99	0.90	0.77	1.06
6	3,450	1			1		
7	1,302	0.86	0.70	1.04	0.80	0.64	1.01
8	680	0.96	0.80	1.15	0.90	0.73	1.12
9	499	1.04	0.81	1.34	1.07	0.85	1.33
10	249	0.68	0.44	1.07	0.70	0.47	1.04
Test for trend[c]			P = 0.19			P = 0.62	
Sex							
Male	6,866	1			1		
Female	9,353	1.28	1.13	1.46	1.40	1.24	1.59
Age Subgroup[d]							
1	4,399	1			1		
2	3,817	0.90	0.76	1.07	0.88	0.74	1.04
3	3,257	0.92	0.81	1.05	0.89	0.78	1.02
4	2,529	0.93	0.75	1.15	0.92	0.74	1.14
5	2,217	0.73	0.60	0.88	0.79	0.66	0.95
6					1		
Smoking Status							
Never smoker	6,709				1.72	1.52	1.95
Exsmoker	5,443				1.55	1.17	2.04
Current smoker	2,743				0.26	0.15	0.44
Missing[e]	1,324				1		
Index of Multiple Deprivation Score							
5 (least deprived)	5,109				0.96	0.80	1.15
4	3,374				1.04	0.90	1.19
3	3,697				1.28	1.04	1.57
2	2,948				1.35	1.18	1.54
1 (most deprived)	1,091						

[a] For each age group, the results from two models are shown. The first model "+Age, Sex, and Practice" controlled for age (within age group), sex, and practice (random-effects model). The second model "+Age, Sex, Practice, and IMD" controlled for age (within age group), sex, practice, Index of Multiple Deprivation, and — for the age groups older than 15 years — smoking. Note that practice is fitted as a random effect in both models. OR indicates odds ratio, L95 indicates lower 95 percent confidence limit, and U95 indicates upper 95 percent confidence limit.

[b] See Table 6 for ranges of NO_x concentrations ($\mu g/m^3$) in each decile.

[c] P value for test for NO_x trend indicates positive trend unless indicated; neg indicates negative trend.

[d] Subgroups for ages 1–4 yr are 1 = 1 yr, 2 = 2 yr, 3 = 3 yr, 4 = 4 yr; for ages 5–14 yr, 1 = 5–6 yr, 2 = 7–8 yr, 3 = 9–10 yr, 4 = 11–12 yr, 5 = 13–14 yr; for ages 15–44 yr, 1 = 15–19 yr, 2 = 20–24 yr, 3 = 25–29 yr, 4 = 30–34 yr, 5 = 35–39 yr, 6 = 40–44 yr; for ages 45–64 yr, 1 = 45–49 yr, 2 = 50–54 yr, 3 = 55–59 yr, 4 = 60–64 yr; and for ages ≥ 65 yr, 1 = 65–69 yr, 2 = 70–74 yr, 3 = 75–79 yr, 4 = 80–84 yr, 5 = ≥ 85 yr.

[e] Missing indicates that no pollution value was assigned to the patient record because (1) of an invalid postcode caused by absence, error, or a location outside of London or (2) a pollution value could not be assigned to a valid postcode because the postcode had no spatial dimension (being probably a single building, such as a tower block).

the results from two models are shown. The first model controlled for age (within age group), sex, and practice (random-effects model). The second model controlled for age (within age group), sex, practice, Index of Multiple Deprivation, and — for the age groups older than 15 years — smoking. The sixth NO_x decile was the base for the odds ratios and the significance tests for trends across the NO_x deciles. The table also shows the odds ratios for the outcomes in relation to sex, age (within age group), smoking, and Index of Multiple Deprivation. The main purpose of this analysis was to see if the results had epidemiologic credibility in relation to these risk factors. In the 15–44-year and 45–64-year age groups, in the fully adjusted model (i.e., the second model), there was a trend toward a higher prevalence of asthma with lower exposure to NO_x, $P = 0.003$ and $P = 0.02$ for the two groups, respectively, and there appeared to be an increase in prevalence in the more deprived groups. None of the other age groups showed a significant trend. The relationships with sex, age, and smoking were in the directions expected from known epidemiologic data.

The results for the prevalence of asthma ever in the Lambeth data set are shown in Table 10. The models controlled for the same variables as the DIN analysis with the addition of ethnicity. There was a significant negative association in both models between the prevalence of asthma ever and NO_x in the 15–44-year age group. There was some association with ethnicity, but this was not consistent across the age groups. As found for the DIN practices, there was an increased risk of asthma in ex-smokers, followed by current smokers. In all but the 15–44-year age group, there was a positive association between asthma prevalence and deprivation score.

Similar analyses were done for the prevalence of consultations for other respiratory outcomes, prescription medications, and ischemic heart disease. The results are shown in Appendix Tables D.9 to D.17. The results of all of these analyses are summarized in Table 11. Most relevant to future evaluations of the LEZ are outcomes that measure incidence of consultations or prescriptions over a defined period. These included respiratory tract infections in one year (2005), asthma, cardiac failure or angina drugs in one year (2005), and prescriptions for asthma drugs in 2005 in those with a history of asthma. Again, the various cross-sectional results will not be detailed here, because our aim was to establish the feasibility of obtaining, classifying, and analyzing these data for a future longitudinal analysis rather than to carry out a cross-sectional analysis. However, it was generally found that the associations between these outcomes and age, sex, smoking, and deprivation were consonant with known epidemiologic data, thus providing internal validation for the method. For example, compared with White groups, ischemic heart disease was more prevalent among Asian or Asian British groups and less prevalent among Black or Black British groups. Many outcomes (e.g., acute respiratory infections, wheeze, asthma treatment, chronic obstructive pulmonary disease, and heart failure) showed a positive relationship with increasing deprivation; this was not observed for hay fever. Mostly there was no association or a negative association with NO_x decile.

For asthma ever and ischemic heart disease ever, the sensitivity of the results to adjustment for practice and for random-effects versus fixed-effects models were examined (Table 12). Generally, the results were fairly robust to the method of adjustment, but there were exceptions. In the DIN practices, for example, the association with ischemic heart disease in the $\geq$ 65-year age group ranged from significantly negative when controlled only for age and sex to nonsignificantly positive when adjusted for practice, Index of Multiple Deprivation, and smoking.

Table 10. Summary of Regression Analyses for Asthma Ever from the Lambeth Practices[a]

	Ages 1–4 yr (N = 8,810)[b]							Ages 5–14 yr (N = 18,888)						
	+ Age, Sex, Ethnicity, and Practice				+ Age, Sex, Ethnicity, Practice, and IMD			+ Age, Sex, Ethnicity, and Practice				+ Age, Sex, Ethnicity, Practice, and IMD		
	n	OR	L95	U95	OR	L95	U95	n	OR	L95	U95	OR	L95	U95
NO_x Decile[c]														
5	74	0.61	0.05	6.92	0.73	0.07	8.00	144	1.03	0.55	1.91	1.13	0.66	1.95
6	937	1.35	0.93	1.97	1.51	0.96	2.38	2,161	1.12	0.98	1.28	1.21	1.07	1.35
7	1,973	1.22	0.94	1.59	1.25	0.94	1.67	4,106	0.94	0.80	1.10	0.95	0.81	1.12
8	3,296	1			1			7,334	1			1		
9	1,788	0.99	0.69	1.43	0.98	0.68	1.42	3,639	0.98	0.88	1.10	0.98	0.87	1.09
10	742	0.95	0.56	1.61	0.95	0.56	1.59	1,504	0.93	0.79	1.09	0.92	0.78	1.09
Test for trend[d]		P = 0.108 (neg)			P = 0.079 (neg)				P = 0.358 (neg)			P = 0.063 (neg)		
Sex														
Male	4,535	1			1			9,609	1			1		
Female	4,275	0.46	0.33	0.65	0.46	0.33	0.65	9,279	0.69	0.64	0.75	0.69	0.64	0.75
Age Subgroup[e]														
1	1,838	0.03	0.00	0.20	0.03	0.00	0.20	3,992	1			1		
2	2,428	0.48	0.27	0.85	0.48	0.27	0.85	3,816	1.49	1.29	1.73	1.49	1.28	1.74
3	2,281	1			1			3,752	1.99	1.70	2.33	1.99	1.69	2.33
4	2,263	3.18	2.28	4.43	3.16	2.27	4.39	3,714	2.28	1.91	2.72	2.28	1.91	2.72
5								3,614	2.73	2.29	3.26	2.72	2.28	3.25
6														
Ethnicity[f]														
W	1,050	1			1			2,489	1			1		
M	304	1.28	0.66	2.47	1.27	0.64	2.49	685	1.25	0.95	1.65	1.23	0.93	1.63
AB	92	1.70	0.67	4.34	1.72	0.68	4.39	317	1.39	0.90	2.16	1.39	0.91	2.13
BB	812	1.60	1.02	2.50	1.53	0.97	2.41	2,320	1.06	0.91	1.24	1.01	0.86	1.19
C	121	1.02	0.26	4.09	1.01	0.25	4.09	345	0.92	0.59	1.44	0.89	0.57	1.38
NA	6,431	0.73	0.52	1.02	0.71	0.50	1.00	12,732	0.93	0.76	1.13	0.91	0.74	1.11
Smoking Status														
Never smoker														
Exsmoker														
Current smoker														
Missing														
Index of Multiple Deprivation Score														
4/5 (least deprived)	382				0.66	0.27	1.62	669				0.75	0.56	0.99
3	1,142				0.79	0.48	1.29	2,309				0.81	0.64	1.04
2	3,395				1.01	0.77	1.33	6,437				0.88	0.79	0.98
1 (most deprived)	3,891				1			9,473				1		

Table continues on next page

[a] For each age group, the results from two models are shown. The first model "+Age, Sex, Ethnicity, and Practice" controlled for age (within age group), sex, ethnicity, and practice (random-effects model). The second model "+Age, Sex, Practice, Ethnicity, and IMD"controlled for age (within age group), sex, practice, ethnicity, Index of Multiple Deprivation, and — for the age groups older than 15 years — smoking. Note that the practice variable is fitted as a random effect in both models. OR indicates odds ratio, L95 indicates lower 95 percent confidence limit, and U95 indicates upper 95 percent confidence limit.

[b] Note that the two practices that had no patients with asthma in this age group were not included in the analysis to enable comparison with fixed-effects models.

[c] See Table 6 for ranges of NO_x concentrations (μg/m³) in each decile. Deciles 1 to 4 are not included; no Lambeth patients were exposed to these low concentrations because Lambeth is an inner city area (see Table 8).

[d] P value for test for NO_x trend indicates positive trend unless indicated.

[e] Subgroups for ages 1–4 yr are 1 = 1 yr, 2 = 2 yr, 3 = 3 yr, 4 = 4 yr; for ages 5–14 yr, 1 = 5–6 yr, 2 = 7–8 yr, 3 = 9–10 yr, 4 = 11–12 yr, 5 = 13–14 yr; for ages 15–44 yr, 1 = 15–19 yr, 2 = 20–24 yr, 3 = 25–29 yr, 4 = 30–34 yr, 5 = 35–39 yr, 6 = 40–44 yr; for ages 45–64 yr, 1 = 45–49 yr, 2 = 50–54 yr, 3 = 55–59 yr, 4 = 60–64 yr; and for ages ≥ 65 yr, 1 = 65–69 yr, 2 = 70–74 yr, 3 = 75–79 yr, 4 = 80–84 yr, 5 = ≥ 85 yr.

[f] Ethnicity codes are: W = White, M = Mixed, AB = Asian or Asian British, BB = Black or Black British, C = Chinese or Other Chinese or Other ethnic group, NA = No ethnicity code recorded or ethnic origin not stated.

Table 10 (*continued*). Summary of Regression Analyses for Asthma Ever from the Lambeth Practices[a]

	Ages 15–44 yr (N = 111,569)							Ages 45–64 yr (N = 36,688)						
	+ Age, Sex, Ethnicity, and Practice				+ Age, Sex, Ethnicity, Practice, Smoking, and IMD			+ Age, Sex, Ethnicity, and Practice				+ Age, Sex, Ethnicity, Practice, Smoking, and IMD		
	n	OR	L95	U95	OR	L95	U95	n	OR	L95	U95	OR	L95	U95
NO_x Decile[c]														
5	764	1.32	0.98	1.80	1.26	0.97	1.64	303	0.78	0.64	0.95	0.84	0.69	1.03
6	7,870	1.22	1.05	1.42	1.22	1.05	1.42	3,711	1.00	0.83	1.21	1.05	0.86	1.29
7	20,811	1.07	0.94	1.21	1.07	0.96	1.20	7,649	1.01	0.86	1.18	1.02	0.88	1.18
8	44,647	1			1			13,751	1			1		
9	24,071	0.98	0.91	1.06	0.98	0.90	1.06	7,602	1.03	0.89	1.19	1.01	0.87	1.17
10	13,406	0.88	0.76	1.03	0.90	0.76	1.07	3,672	1.01	0.87	1.17	1.00	0.87	1.15
Test for trend[d]		P = 0.014 (neg)			P = 0.034 (neg)				P = 0.835			P = 0.707 (neg)		
Sex														
Male	56,587	1			1			20,557	1			1		
Female	54,982	1.00	0.96	1.05	0.92	0.87	0.97	16,131	1.84	1.64	2.07	1.71	1.52	1.92
Age Subgroup[e]														
1	9,194	1			1			13,525	1			1		
2	11,391	0.72	0.64	0.80	0.50	0.44	0.56	9,786	0.94	0.86	1.03	0.95	0.87	1.04
3	23,816	0.51	0.45	0.57	0.31	0.27	0.36	7,391	0.97	0.86	1.09	0.97	0.86	1.10
4	26,042	0.46	0.41	0.52	0.27	0.24	0.31	5,986	1.02	0.92	1.13	1.01	0.90	1.13
5	22,366	0.45	0.40	0.50	0.26	0.23	0.29							
6	18,760	0.46	0.41	0.51	0.27	0.23	0.31							
Ethnicity[f]														
W	40,320	1			1			11,635	1			1		
M	2,941	1.07	0.91	1.25	1.08	0.92	1.27	574	0.90	0.67	1.21	0.89	0.67	1.20
AB	2,529	0.86	0.72	1.03	0.89	0.74	1.08	786	1.16	0.91	1.48	1.27	1.00	1.62
BB	13,834	0.76	0.68	0.85	0.79	0.70	0.88	4,851	0.83	0.72	0.95	0.86	0.76	0.97
C	3,300	0.46	0.38	0.55	0.49	0.41	0.59	851	0.75	0.60	0.94	0.79	0.63	0.98
NA	48,645	0.73	0.65	0.83	0.87	0.78	0.98	17,991	0.62	0.54	0.72	0.77	0.69	0.87
Smoking Status														
Never smoker	50,078				1			14,717				1		
Exsmoker	13,162				1.57	1.38	1.80	6,109				1.73	1.48	2.01
Current smoker	28,361				1.14	0.99	1.31	9,888				1.36	1.23	1.50
Missing	19,968				0.29	0.25	0.35	5,974				0.21	0.15	0.28
Index of Multiple Deprivation Score														
4/5 (least deprived)	3,990				0.98	0.87	1.10	1,662				0.81	0.64	1.02
3	12,147				1.01	0.88	1.16	4,844				0.76	0.64	0.91
2	48,352				1.04	0.96	1.13	14,690				0.93	0.82	1.04
1 (most deprived)	47,080				1			15,492				1		

Table continues on next page

[a] For each age group, the results from two models are shown. The first model "+Age, Sex, Ethnicity, and Practice" controlled for age (within age group), sex, ethnicity, and practice (random-effects model). The second model "+Age, Sex, Practice, Ethnicity, and IMD"controlled for age (within age group), sex, practice, ethnicity, Index of Multiple Deprivation, and — for the age groups older than 15 years — smoking. Note that the practice variable is fitted as a random effect in both models. OR indicates odds ratio, L95 indicates lower 95 percent confidence limit, and U95 indicates upper 95 percent confidence limit.

[b] Note that the two practices that had no patients with asthma in this age group were not included in the analysis to enable comparison with fixed-effects models.

[c] See Table 6 for ranges of NO_x concentrations (μg/m³) in each decile. Deciles 1 to 4 are not included; no Lambeth patients were exposed to these low concentrations because Lambeth is an inner city area (see Table 8).

[d] P value for test for NO_x trend indicates positive trend unless indicated.

[e] Subgroups for ages 1–4 yr are 1 = 1 yr, 2 = 2 yr, 3 = 3 yr, 4 = 4 yr; for ages 5–14 yr, 1 = 5–6 yr, 2 = 7–8 yr, 3 = 9–10 yr, 4 = 11–12 yr, 5 = 13–14 yr; for ages 15–44 yr, 1 = 15–19 yr, 2 = 20–24 yr, 3 = 25–29 yr, 4 = 30–34 yr, 5 = 35–39 yr, 6 = 40–44 yr; for ages 45–64 yr, 1 = 45–49 yr, 2 = 50–54 yr, 3 = 55–59 yr, 4 = 60–64 yr; and for ages ≥ 65 yr, 1 = 65–69 yr, 2 = 70–74 yr, 3 = 75–79 yr, 4 = 80–84 yr, 5 = ≥ 85 yr.

[f] Ethnicity codes are: W = White, M = Mixed, AB = Asian or Asian British, BB = Black or Black British, C = Chinese or Other Chinese or Other ethnic group, NA = No ethnicity code recorded or ethnic origin not stated.

Table 10 (*continued*). Summary of Regression Analyses for Asthma Ever from the Lambeth Practices[a]

	Ages ≥ 65 yr (N = 15,803)						
	+ Age, Sex, Ethnicity, and Practice				+ Age, Sex, Ethnicity, Practice, Smoking, and IMD		
	n	OR	L95	U95	OR	L95	U95
NO_x Decile[c]							
5	133	0.86	0.61	1.21	0.93	0.63	1.36
6	1,812	1.04	0.81	1.33	1.03	0.70	1.50
7	3,279	0.92	0.76	1.11	0.90	0.73	1.10
8	5,772	1			1		
9	3,385	0.97	0.85	1.10	0.96	0.84	1.10
10	1,422	0.91	0.76	1.09	0.91	0.75	1.09
Test for trend[d]			P = 0.941			P = 0.916	
Sex							
Male	7,384	1			1		
Female	8,419	1.53	1.34	1.75	1.66	1.45	1.89
Age Subgroup[e]							
1	4,899	1			1		
2	3,732	1.12	0.96	1.31	1.08	0.92	1.26
3	3,119	1.01	0.83	1.24	0.99	0.81	1.21
4	2,139	0.85	0.66	1.09	0.83	0.64	1.06
5	1,914	0.78	0.65	0.94	0.81	0.68	0.98
6							
Ethnicity[f]							
W	7,151	1			1		
M	186	1.46	1.05	2.04	1.57	1.14	2.17
AB	451	1.11	0.82	1.51	1.22	0.90	1.65
BB	2,473	0.88	0.77	1.01	0.97	0.83	1.13
C	254	0.75	0.43	1.31	0.83	0.48	1.45
NA	5,288	0.62	0.50	0.77	0.82	0.69	0.97
Smoking Status							
Never smoker	6,696				1		
Exsmoker	4,954				1.90	1.63	2.21
Current smoker	2,662				1.45	1.17	1.80
Missing	1,491				0.11	0.06	0.19
Index of Multiple Deprivation Score							
4/5 (least deprived)	810				0.65	0.44	0.94
3	2,362				0.93	0.79	1.08
2	6,187				0.97	0.87	1.08
1 (most deprived)	6,444				1		

[a] For each age group, the results from two models are shown. The first model "+Age, Sex, Ethnicity, and Practice" controlled for age (within age group), sex, ethnicity, and practice (random-effects model). The second model "+Age, Sex, Practice, Ethnicity, and IMD"controlled for age (within age group), sex, practice, ethnicity, Index of Multiple Deprivation, and — for the age groups older than 15 years — smoking. Note that the practice variable is fitted as a random effect in both models. OR indicates odds ratio, L95 indicates lower 95 percent confidence limit, and U95 indicates upper 95 percent confidence limit.

[b] Note that the two practices that had no patients with asthma in this age group were not included in the analysis to enable comparison with fixed-effects models.

[c] See Table 6 for ranges of NO_x concentrations ($\mu g/m^3$) in each decile. Deciles 1 to 4 are not included; no Lambeth patients were exposed to these low concentrations because Lambeth is an inner city area (see Table 8).

[d] P value for test for NO_x trend indicates positive trend unless indicated.

[e] Subgroups for ages 1–4 yr are 1 = 1 yr, 2 = 2 yr, 3 = 3 yr, 4 = 4 yr; for ages 5–14 yr, 1 = 5–6 yr, 2 = 7–8 yr, 3 = 9–10 yr, 4 = 11–12 yr, 5 = 13–14 yr; for ages 15–44 yr, 1 = 15–19 yr, 2 = 20–24 yr, 3 = 25–29 yr, 4 = 30–34 yr, 5 = 35–39 yr, 6 = 40–44 yr; for ages 45–64 yr, 1 = 45–49 yr, 2 = 50–54 yr, 3 = 55–59 yr, 4 = 60–64 yr; and for ages ≥ 65 yr, 1 = 65–69 yr, 2 = 70–74 yr, 3 = 75–79 yr, 4 = 80–84 yr, 5 = ≥ 85 yr.

[f] Ethnicity codes are: W = White, M = Mixed, AB = Asian or Asian British, BB = Black or Black British, C = Chinese or Other Chinese or Other ethnic group, NA = No ethnicity code recorded or ethnic origin not stated.

Table 11. Summary of All the Regression Analyses for Age Groups and DIN and Lambeth Practices[a]

	0–4 yr		5–14 yr		15–44 yr		45–64 yr		≥ 65 yr	
	DIN	Lambeth	DIN	Lambeth	DIN	Lambeth	DIN	Lambeth	DIN	Lambeth
Asthma	0.73	0.079 (neg)	0.15 (neg)	0.063 (neg)	0.003 (neg)	0.034 (neg)	0.02 (neg)	0.707 (neg)	0.62	0.916
Ischemic heart disease	—	—	—	—	—	—	0.03 (neg)	0.466	0.34	0.276
Chronic obstructive pulmonary disease	—	—	—	—	—	—	—	—	0.24 (neg)	—
Heart failure	—	—	—	—	—	—	—	—	0.07 (neg)	—
Atrial fibrillation	—	—	—	—	—	—	—	—	0.55	—
Hay fever	—	—	0.07 (neg)	—	0.05 (neg)	—	0.41 (neg)	—	0.002 (neg)	—
Wheeze	0.09 (neg)	—	0.003 (neg)	—	0.41 (neg)	—	0.02 (neg)	—	0.47 (neg)	—
Respiratory tract infection	0.01 (neg)	—	0.05 (neg)	—	0.75 (neg)	—	0.02 (neg)	—	0.26	—
Asthma drugs	0.59	—	0.005 (neg)	—	0.05 (neg)	—	0.88	—	0.88 (neg)	—
Asthma drugs (Asthma ever)	—	—	0.18 (neg)	—	0.31 (neg)	—	0.56	—	0.88 (neg)	—
Loop diuretics	—	—	—	—	—	—	—	—	0.92	—
Nitrates	—	—	—	—	—	—	—	—	0.56	—

[a] *P* value for test for NO_x trend indicates positive trend unless indicated as negative (neg). — indicates that no analysis was done because there were no data on that outcome because of very low numbers.

Table 12. Summary of Sensitivity Analyses for Both DIN and Lambeth Practices to Examine the Effect of Different Practice Adjustments on the Results for Two Outcomes[a]

Outcome (Ever)/ Adjustment[b]	Practice Adjustment	0–4 yr		5–14 yr		15–44 yr		45–64 yr		≥ 65 yr	
		DIN	Lambeth	DIN	Lambeth	DIN	Lambeth	DIN	Lambeth	DIN	Lambeth
Asthma											
Age, sex, and ethnicity	None	0.13	0.264 (neg)	0.38	0.346 (neg)	< 0.001 (neg)	< 0.001 (neg)	0.13 (neg)	0.735	0.05	0.909
Age, sex, and ethnicity	Fixed effect	0.23	0.391 (neg)	0.62 (neg)	0.133 (neg)	0.006 (neg)	< 0.001 (neg)	0.55 (neg)	0.631 (neg)	0.67	0.499 (neg)
Age, sex, ethnicity, smoking, and IMD	Fixed effect	0.33	0.294 (neg)	0.43 (neg)	0.065 (neg)	0.003 (neg)	< 0.001 (neg)	0.04 (neg)	0.284 (neg)	0.003 (neg)	0.513 (neg)
Age, sex, and ethnicity	Random effect	0.27	0.108 (neg)	0.72 (neg)	0.358 (neg)	< 0.001 (neg)	0.014 (neg)	0.15 (neg)	0.835	0.15 (neg)	0.941
Age, sex, ethnicity, smoking, and IMD	Random effect	0.73	0.079 (neg)	0.15 (neg)	0.063 (neg)	0.009 (neg)	0.034 (neg)	0.62	0.707 (neg)	0.62	0.916
Ischemic Heart Disease											
Age, sex, and ethnicity	None	_	_	_	_	_	_	0.001 (neg)	0.238	0.001 (neg)	0.989 (neg)
Age, sex, and ethnicity	Fixed effect	_	_	_	_	_	_	0.12 (neg)	0.833	0.82 (neg)	0.533 (neg)
Age, sex, ethnicity, smoking, and IMD	Fixed effect	_	_	_	_	_	_	0.08 (neg)	0.648 (neg)	0.46	0.624 (neg)
Age, sex, and ethnicity	Random effect	_	_	_	_	_	_	0.10 (neg)	0.273	0.97	0.988 (neg)
Age, sex, ethnicity, smoking, and IMD	Random effect	_	_	_	_	_	_	0.03 (neg)	0.466	0.34	0.276

[a] *P* value for test for NO_x trend indicates positive trend unless indicated as negative (neg).

[b] Only Lambeth data were adjusted for ethnicity. Smoking status was included only for ages ≥ 15 yr.

DISCUSSION

The aim of this part of the study was to develop a method for using primary-care databases to evaluate the health effects of regulatory interventions, in particular the proposed LEZ scheme. The objectives described earlier will be discussed in turn below. The study was not primarily concerned with testing hypotheses about exposure to traffic pollution and health outcomes; however, in the course of the feasibility study, various cross-sectional associations were explored, and the results of these will be discussed briefly.

Objective 1

The first objective was to establish the feasibility of describing exposures at a fine geographic resolution and to link them to clinical records. Modeling was undertaken at a 20 × 20–m grid resolution and used successfully to estimate mean annual concentrations of PM_{10} and NO_x for the London postcodes that could be digitized (the great majority). We anticipated no problems in expanding this method to evaluate changes in modeled exposures across the time period of the implementation of the LEZ using electronic primary-care databases that contain postcodes. We did however encounter a number of postcodes that had no horizontal spatial characteristics (i.e., vertical streets). It is very likely that the latter correspond to single tower blocks. In the full evaluation of the LEZ, we will explore alternative methods of assigning exposure to these postcodes. One possibility is to assign the modeled exposure for the 20 × 20–m unit that encompasses the grid point of the postcode, together with a buffer of perhaps 20 to 40 m around it.

The use of primary-care databases for epidemiologic research is widely accepted in the U.K. However, because a postcode refers to a small number of dwellings, it was necessary to obtain additional ethics approval to link exposures to clinical records by way of postcodes using a multi-stage procedure that ensured that investigators would not have access to the postcode data. This approval was obtained independently for each of the two data sets used in the study. Future work with research databases such as the General Practice Research Database will require more stringent conditions than were required for this pilot study using DIN and Lambeth DataNet. Such studies now require approval by the National Information Governance Board for Health and Social Care (NIGB). The NIGB considers requests for disclosure and temporary access to identifiable patient information without individual patient consent. The use of primary-care data now requires complex anonymization procedures that involve several independent parties. The NIGB must give approval to each individual study. The NIGB has not yet considered a proposal to link pollution at postcode level, so the feasibility of using such data has not been demonstrated.

Unexpectedly, we found that some postcodes had unique pollution signatures so there was a least a theoretical possibility of identifying a clinical record for one of these postcodes if an investigator were in possession of both the anonymized record and the postcode–pollution file. This would be unacceptable to administrators of the research databases and might be unacceptable to ethics committees. Owing to time constraints, and in order to observe the spirit of the ethics approval, we therefore restricted our analysis to a single pollutant (NO_x), categorized in 1000ths to reduce the possibility of a postcode having a unique air pollution value. These coarser values were linked to the clinical record; we would have preferred to link the actual pollution values in the main analysis. Various solutions that alone or in combination provide the necessary protection of individuals have been discussed with the data providers. One is that the postcode–pollution file should be constructed by a third party in another organization that is independent of the statistical analysis and deals directly with the data provider, who will in turn produce the linked, anonymized clinical record files. Another possibility is to manipulate the postcode–pollution file using various categorizations to reduce the number of unique postcodes. These could then be censored or merged with adjacent categories.

At the outset, we anticipated that in the final evaluation we would need to visit collaborating practices and carry out the linkage and downloading of data individually using trained staff. We have demonstrated in the Lambeth practices that this approach is feasible, but over time it has become increasingly unnecessary and inefficient. A better option is to carry out the process online as was done with the 13 DIN practices in this feasibility study. Although the 13 DIN practices had an insufficient number of patients for the final evaluation, there are now other organizations that have more patients and the capacity for online linkage. One of these, QResearch, has 60 practices with 500,000 patients and had agreed, in principle, to collaborate with our team (*www.qresearch.org*). Disappointingly, QResearch informed us that under its rules of governance, research is not allowed if there is a theoretical possibility of identifying a patient, however remote this might be. Another organization, the General Practice Research Database (*http://gprd.com*), has records for a similar number of practices with 450,000 patients. It provides access for research in what is expected to be a more straightforward manner because it operates under rules of governance that do not exclude the kind of research we are proposing. It is important to protect the

confidentiality of the practices, but we shall not need this information, because we shall be assigning exposures by means of postcodes. We shall still need to know which patients belong to the same practices in order to implement a multilevel model, but this should not be a problem, because a variable in the patient record could be used to indicate it.

Objective 2

The aim of this part of the study was to evaluate the analytic aspects of using these data for evaluative purposes. This fell into four parts: (1) examining, at the level of individual practices, the distribution of exposures in patients and the relationships between exposures and important potential confounders (i.e., smoking and socioeconomic status); (2) identifying suitable outcome variables; (3) designing an appropriate analytic strategy and sensitivity analyses; and (4) performing a cross-sectional analysis of the associations between air pollution and health outcomes. It must be emphasized that many of these cross-sectional analyses, especially those using "ever" outcomes, are relevant to the future spatial-temporal evaluation insofar as these outcome variables would, in the longitudinal study, serve as denominators for measuring the incidence of exacerbations during defined periods before and after the intervention. They have also been included to show that the data can be obtained, categorized, linked with pollution, and analyzed.

NO_x was the main focus of investigation because it is a more specific indicator than PM_{10} of mobile source pollution. We were also constrained to using only one of three pollutants modeled for privacy reasons, as explained earlier. A wide range of NO_x exposures among patients was found within and between practices. Among the 160,000 postcodes representing the whole of London, there was about a twofold range of exposures between the second and ninth deciles. This broad range suggested that there was sufficient heterogeneity of exposure for cross-sectional analysis. In cross-sectional analyses such as these, potential confounding by smoking is important, because smoking is often a strong risk factor for the health outcomes of interest and relates to socioeconomic status, which in turn is often related to place of residence. Basic qualitative smoking status data were reasonably well recorded in both the DIN and Lambeth data sets. No important associations were found between smoking and exposure to NO_x, within practices or when the practices were combined. Smoking was therefore an unlikely confounding factor in this study.

Small-scale spatial studies such as ours often attempt to control for confounders related to socioeconomic status, such as smoking and poverty-related risk factors, by including a marker of socioeconomic status at the ecologic level. Three of these markers were investigated: Index of Multiple Deprivation scores, ACORN categories, and ethnicity. The one that was available for both data sets, and which would be available to a final evaluation was the Index of Multiple Deprivation score, which comprises census variables and is available at the super output area level (400 households with 1500 residents). There is a wealth of information relating Index of Multiple Deprivation scores to various health outcomes in London. We found a strong relationship between greater deprivation and higher NO_x exposure. Clearly Index of Multiple Deprivation scores will need to be included as a confounder in any future analysis.

The ACORN categorization, which was available in the DIN data set, showed some association with NO_x exposure but no consistent pattern across practices, probably because many prosperous areas in the center of London are more highly polluted. Although the use of ACORN gave some insight into the social distribution of exposures in London, it will not be recommended for the final evaluation because it is not as conducive to numerical ranking as the Index of Multiple Deprivation. Furthermore, it is not generally available in the primary-care databases that are likely to be used.

We had an unexpected opportunity in Lambeth to investigate the potential for confounding by ethnic status. These data are not routinely available but were added to the Lambeth database as part of a special project concerned with ethnicity. The ethnicity variables were therefore not available for the full analysis of the intervention but did provide insight into possible influences of ethnicity and cross-sectional associations in a relatively more polluted borough. The associations between ethnicity and asthma ever and ischemic heart disease ever were in line with current epidemiologic evidence, which provided some internal validity to the data set. Some evidence was found for a positive association between white ethnicity and exposure to NO_x, but no other obvious patterns were observed. There were some associations between ethnicity and asthma ever in several age groups and between ethnicity and ischemic heart disease ever, but these were not substantially attenuated by controlling for Index of Multiple Deprivation. From this it seems that there is some potential for ethnicity to be a confounder in cross-sectional air pollution–health outcome associations.

The outcome variables were chosen to indicate chronic cardiorespiratory diseases and their exacerbations and acute respiratory infections. The linked nature of the records based on registered patients and the hierarchical method of classification presented problems not found in

purpose-designed prevalence or cohort studies. The indicators of chronic disease were records of an ever diagnosis of conditions such as asthma and ischemic heart disease. Diagnoses such as these will be on a patient's medical record even if they were made at a prior practice or before the current practice was computerized. In the record, it is possible to identify the date of first mention of the diagnosis. We did not have information on changes of address for patients in the practice, so we could not measure the amount of time spent at the current address. Exacerbations of chronic diseases or the incidence of acute diseases (such as respiratory infections) were indicated by consultations or prescriptions in the chosen year or years of the study. It was possible to investigate exacerbations by identifying events in a subgroup with an ever diagnosis. This was done for asthma prescriptions in 2005 for those with asthma ever through the end of 2004. Although this investigation was potentially important, because asthma drugs are given widely for wheezing in children and chronic obstructive pulmonary disease in adults, we gained no new insights over and above the analysis that used all asthma drug prescriptions in 2005 irrespective of diagnosis.

Generally, the relationships with sex, age, Index of Multiple Deprivation, and ethnicity were those that would have been predicted from epidemiologic data based on purpose-designed prevalence studies. This provides evidence of validity in terms of external criteria. Our prior hypotheses relating to associations with NO_x exposure were that there would be a modest increased risk in prevalence and acute exacerbations of respiratory (and possibly heart) diseases with increasing exposure. In this cross-sectional analysis we found that associations between the chosen outcomes and NO_x were either not significant or significantly negative and that this general conclusion was robust to various sensitivity analyses. These results did not support the associations reported in a number of cities between prevalence of respiratory symptoms and proximity to traffic emissions (see Introduction). It does not follow from this that traffic emissions are not harmful. In Tokyo, for example, it was found that the prevalence of persistent wheezing and breathlessness was not related to proximity to roads or associated gradients in ambient NO_x. There was however an adverse effect on chronic phlegm, chronic cough, and lung function, which suggested that some respiratory outcomes might be more sensitive to traffic emissions than others (Nakai et al. 1999). Another explanation for the lack of positive cross-sectional associations in the current study is that underlying adverse associations were masked by error in exposure characterization. However, other published studies, referred to earlier, have observed positive associations under similar or less precise exposure protocols.

The most significant findings in our cross-sectional analyses were negative associations in both data sets between NO_x and asthma ever and prescriptions of asthma drugs in school-age children and young adults. This is unlikely to have been due to chance. Confounding by smoking seems unlikely, because there was no strong relationship between smoking and NO_x and because it was controlled for in the analysis. Confounding by socioeconomic status not accounted for by the Index of Multiple Deprivation was unlikely, because in the U.K. there is little correlation between social class and asthma prevalence. We noted however that there was a correlation between Index of Multiple Deprivation and use of asthma drugs that was stronger than for asthma ever itself. This might reflect social variations in severity of asthma or in the use of medical services for asthma; however, we did control for Index of Multiple Deprivation in the analysis. One reason for a null association could be that the exposure assessment was too imprecise, possibly for reasons relating to the model used or to a lack of correlation between ambient concentrations of pollution at the address and the personal exposures of the subjects. Exposure studies have generally found that there is a reasonable association between ambient concentrations of fine particles and personal exposure to outdoor fine particles (Brauer et al. 2002a). However, indoor sources might dominate overall personal exposure, especially where there is secondhand smoke or indoor cooking sources of fine particles. However, indoor sources would not explain why significant negative associations were observed, unless these were chance findings or the result of uncontrolled negative confounding.

These are intriguing findings, and we shall investigate them further on their own account. Many of the outcomes used in our cross-sectional analyses were of the "ever diagnosed" type. Such outcomes are insensitive to any influence of air quality on frequency of symptoms or on severity but might be important indicators of incidence. The implication is that our intended longitudinal controlled comparison should focus on such measures of frequency and severity. Because such a study will be a controlled before-and-after comparison, it should not be susceptible to any of the uncontrolled negative confounding that might have underlain the significant negative associations in our cross-sectional analyses. It should be emphasized that we do not believe the results of the longitudinal study can be predicted from our cross-sectional results. It should also be emphasized that this was not a study of the effects of traffic on health but of the effects of a traffic emissions control scheme on health, and the results should be evaluated in this light.

Objective 3

The third objective was to investigate the power of primary-care databases in evaluating changes in health outcomes associated with interventions such as the LEZ. A definitive evaluation of the LEZ would not be a cross-sectional analysis but a temporal-spatial analysis that would compare periods before and after the intervention, using medical records of groups of patients who have or have not experienced the change in exposure. Three things would be required to test the hypothesis that the LEZ scheme has a beneficial effect on health: (1) an estimate of changes in exposure; (2) an estimate, with appropriate precision, of a change in health outcomes; and (3) control for confounding factors. In this case, confounders would be factors that change over time in a manner associated with the changes in air pollution and are related to the health outcomes.

Classifying Patients by Amount of Change in Exposure

In a temporal-spatial evaluation of the health effects of the LEZ, patients would be classified by amount of exposure change at the postcode level. Models of the predicted changes in exposure indicate — unsurprisingly — that the greatest change in exposure to traffic pollution will be experienced by populations living close to busy roads (Figure 22). We thus hypothesize that any health changes would be greatest in people living close to roads most affected by the implementation of the LEZ. We would not know, for privacy reasons, the locations of the general practices providing the data. However, if the patients in the practices were living at addresses distributed evenly throughout London, it seems clear that the majority of patients would not be living near the affected roads.

In the current study, by comparing the differences between modeled annual concentrations of NO_x in the 2010 base case (i.e., the no LEZ scenario) and the preferred scenario for implementing the LEZ best case (i.e., Scenario 6), we estimated that approximately one quarter of the population would be exposed to more than a 3% reduction in NO_x (Figure 26). By linking the postcode to these modeled differences, subjects were sorted according to the distribution of predicted NO_x reduction; it was assumed that this sorting would follow the distribution shown in Figure 26. Essentially, we were using the scenario models for NO_x to categorize the population according to the likely degree of exposure to the intervention. Having done this, there are several analytic strategies that might be employed in a final evaluation of the LEZ. The first would be to dichotomize the subjects according to the predicted NO_x reduction into those with the greatest reduction and those with the least reduction. The second would be to use the entire distribution in the analysis. The latter strategy would have the advantage of maximizing the power of the analysis. A third strategy — if permitted under privacy arrangements — would be to assign a distance from the road to the centroids of the subjects' postcodes. This step would enable analysis by distance from the center of the road, stratified by traffic intensity data. By the end of the study period such an analysis could be informed by actual data on traffic intensity and on evidence of compliance with the LEZ. However, because the NO_x predictions take into account proximity to roads and other factors such as traffic nature and flow, we feel that the first and second strategies are preferable.

Statistical Approach

Our analysis examined changes in the occurrence of various health outcomes associated with the introduction of the LEZ in cohorts stratified by the change in annual exposure to a range of pollutants predicted by the model. We might for example be interested in the impact of the introduction of the LEZ on prescriptions for asthma drugs. The two periods being compared might be the two years before and after implementation of the LEZ. The cohorts would be patients who are registered with general practices during both periods. One advantage of limiting our analysis in this way is that we would not need to be concerned about population movements, because the same subjects would be included in both time periods and because the percentage of patients lost to the study between the two time periods is estimated to be small (~13%).

However, the main justification for our approach is based on two arguments. The first argument addresses the issue of modeling the odds of having a health event over the two-year period either before or after the introduction of the LEZ. The probability of having that health event for

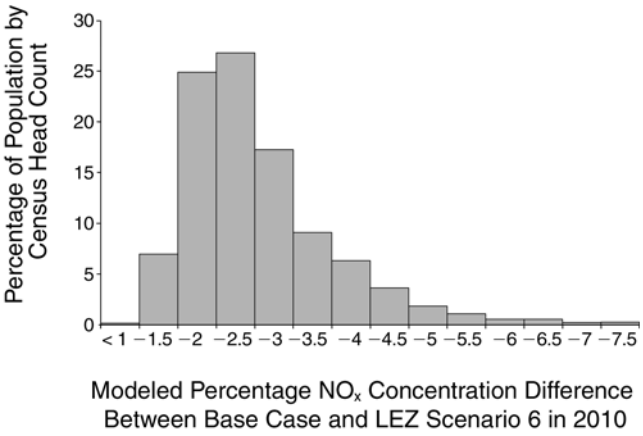

Figure 26. Percentage distribution of population by differences in modeled NO_x concentrations between the base case and LEZ Scenario 6 in 2010.

an individual is a function of many individual characteristics, such as age, sex, or social class, and some environmental characteristics, such as weather or air pollution. The individual characteristics are largely fixed; the environmental characteristics can be time dependent. Although it is possible to think of modeling the probability of an event as a function of all these variables, it is important to remember that many of the determinants of individual susceptibility are unknown or unmeasured. For patients with measurements both before and after the introduction of the LEZ, it makes sense to model the difference in rates of health events in the two periods. This removes the need to consider either individual characteristics or, indeed any environmental characteristics, that remain fixed.

The second argument for our approach is that any time-dependent factor, such as weather or flu epidemics, that are the same across London, are also controlled for by the design, because the effect of the time-dependent factor will be similar for all patients whether their exposure to air pollutants was reduced by the introduction of the LEZ or not. The only factors we have to consider are those that affect the two exposure groups differently (or, more generally, according to the extent of the difference in exposure before and after the introduction of the LEZ). One such factor is the particular practice with which the patient is registered, because the way in which each practice records data may change over time. Although, for privacy reasons we will not know which practices are collaborating in the study, we will know which patients are in the same practice.

In our cross-sectional analysis of this report, we explored three different approaches to controlling for potential practice effects: no adjustment for practice, adjustment using practice as a fixed effect, and adjustment using practice as a random effect. These three analyses represent a spectrum of degrees of control for otherwise uncontrolled risk factors that might have varied between practices. In general, inclusion of a practice as a fixed-effect gives the most stringent control but with potential loss of precision. Making no adjustment for practice maximizes precision but leaves potential for confounding bias and spuriously narrow confidence intervals. Inclusion of practice as a random effect provides an intermediate trade-off between these polarities. In our final evaluation, we will include practice as a random effect but also conduct sensitivity analyses. Factors such as age, sex, and Index of Multiple Deprivation (based on postcode) will be considered as potential effect modifiers rather than as confounders. More formally, for each subject in the cohort (n = 350,000) we will have the time-fixed variables practice i, Index of Multiple Deprivation z, and unknown covariates u; and the time-varying variables outcome Y_t (number of visits for, e.g., asthma) and pollution x_t, where $t = b$ (before 2006) or a (after 2006). For model motivation we assume $Y_t \sim$ Poisson, with

$$E(Y_b) = \exp(\alpha_i + \beta x_b + \gamma z + \delta u)$$

(that is, practice, Index of Multiple Deprivation, and unknown covariate effects), and

$$E(Y_a) = \exp(\alpha_i + \alpha_i' + \beta x_a + \gamma z + \gamma' z + \delta u)$$

(that is, as before plus change depending on practice and Index of Multiple Deprivation), conditional on

$$Y = Y_a + Y_b,\ Y_b \sim \text{Bin}(\pi, Y) \text{ with}$$

$$\begin{aligned}\text{logit}(\pi) &= (\alpha_i + \beta x_b + \gamma z + \delta u) \\ &\quad - (\alpha_i + \alpha_i' + \beta x_a + \gamma z + \gamma' z + \delta u) \\ &= \beta(x_b - x_a) - \alpha_i' - \gamma' z\,.\end{aligned}$$

The model to be used for estimation is thus a logistic regression model of the proportion of visits for each patient occurring before the introduction of the LEZ — as an indicator of the change in the rate of visits after versus before. The parameter of interest in this model (β) can be interpreted as the change in the visit frequency per unit of pollution. In the final model, the determinants of visit frequency related to practice, Index of Multiple Deprivation, or unmeasured covariates (u) cancel out, provided they do not determine the change of visit frequency over time beyond that explicable by practice and Index of Multiple Deprivation, for which change is allowed in the model (through α_i' and $\gamma' z$). The change associated with a practice (i.e., the parameters α_i') will be handled in three ways ($\alpha_i = 0$ for all i, α_i is random, and α_i is entered as fixed effects) to obtain a spectrum of results of increasing stringency of control for confounding at the cost of the possible loss of precision (because variation of pollution change is expected to be lower within practices than between practices).

Power of Analyses to Detect Differences

The power calculations in Table 13 are now based on a simplification of the model presented above. Two dichotomous exposure classifications (10% and 25%, with greatest exposure reduction in NO_x versus the remaining subjects 90% and 75%, respectively) are considered. Taking the 10% versus 90% example, we will compare the proportion of visits occurring before the introduction of the LEZ (Y_b/Y, see above). This simplifies the problem to comparing two proportions (i.e., the proportion of visits by the 10% of patients with the greatest reduction in exposure compared with the proportion of visits in the remaining 90% of patients). We assume that $Y_b/Y = 0.5$ in the remaining 90%, though the exact value is not critical.

Table 13. Illustrative Power Calculations for Baseline Rate and Percentage Decreases in Rate of Health Metrics and for Two Categories of Subgroups Experiencing a Decline in Exposure[a]

Baseline Rate of Health Metric (%)	Decline in Rate of Health Metric (%)	Power (%) to Detect Difference at $P = 0.05$	
		10% Exposed Group	25% Exposed Group
1			
	5	9	14
	7.5	15	28
	10	24	47
	15	50	83
5			
	5	30	54
	7.5	58	88
	10	83	99
	15	99	100
7.5			
	5	43	72
	7.5	76	97
	10	95	100
	15	100	100
10			
	5	54	83
	7.5	87	99
	10	98	100
	15	100	100
15			
	5	70	95
	7.5	97	100
	10	100	100
	15	100	100
20			
	5	82	99
	7.5	99	100
	10	100	100
	15	100	100

[a] Sample size is assumed to be 350,000 subjects. Health metric indicates the occurrence of any health outcome including prescriptions. Exposed Group indicates two subgroups: the 10% who experience a reduction in NO_x versus the 90% who do not and the 25% who experience a reduction in NO_x versus the 75% who do not. Note: The final analysis will model the exposure as a continuous variable.

This allows estimation of power. For example, for a baseline rate of 1% and a 5% decrease in the rate in the group experiencing exposure reduction after introduction of the LEZ compared with the group experiencing no reduction, the expected proportion of visits before the LEZ is 1/1.95 = 0.513 (not shown in table). The usual formulas show that the power for detecting this difference between proportions (0.513 versus 0.5) for a total population of 350,000 with measurements both before and after the introduction of the LEZ is 9%. For a baseline rate of 10%, the power is 54%. For example, in Table 13, the power estimates are 14% and 84% for a 5% change for baseline rates of 1% and 10%, respectively, in the "25% exposed" category (i.e., 25% exposed and 75% not exposed). Table 13 shows the trade-off between the three parameters: degree of change, baseline rate, and the cut-off for the dichotomous variables (percentages of exposed and non-exposed). Overall, these calculations suggest that we have sufficient power to detect 5% changes in the rate of events with a baseline rate of 10% (e.g., asthma prescriptions or acute respiratory infections) but less power to detect changes in the rate of events that are less common (e.g., asthma incidence).

These calculations might be expected to underestimate power, because they do not exploit the pairing of the before and after periods of observation by subject. However, because the pairing effectively removes important differences in the probability of events between subjects, and our model for power calculation also ignores these, it is likely to be a reasonably accurate estimate in this respect. The calculation will tend to underestimate power, because we will model change in exposure as a continuous variable, but this will be balanced by any depletion in power arising from the need to control for determinants of change other than pollution, such as practice effects. The baseline rates shown in Table 13 will be higher because they reflect two years of observation rather than one.

The power calculation is based on the assumption that data for 350,000 patients would be gathered before and after the introduction of the LEZ. The General Practice Research Database contains data for 450,000 subjects. It is anticipated that the linkage of air pollution data to patient data will be achieved for 90% of practices and that 87% of subjects will be followed for the time period (hence $450{,}000 \times 0.90 \times 0.87 = 352{,}350$). In fact, the power calculation is not particularly sensitive to the exact sample size in the range of 320,000 to 380,000.

Spatial autocorrelation could potentially reduce power. We believe, however, that this will not be a major issue for our study. It is undoubtedly true that disease outcomes are autocorrelated. However, changes in disease rates or events within subjects are markedly less likely to be autocorrelated,

as individual susceptibility is effectively removed. In fact, the two main reasons that changes in disease rates might be spatially autocorrelated are that there are changes in practice recording procedures and/or in the effects of family characteristics. Because the General Practice Research Database has an indicator for both practice and family (i.e., living at the same address), it will be possible to allow for both in our analyses.

Controlling for Confounding Factors

In the proposed temporal-spatial study of changes in health in relation to changes in air pollution, confounding factors are risk factors that show changes over time correlated with changes in air pollution associated with the intervention. Risk factors that vary spatially are a major problem in cross-sectional studies. However, if they do not vary temporally, they would not act as confounders in a temporal-spatial "change versus change" study, because they would not cause changes in health. To a large extent, socioeconomic status falls into this category. Similarly, risk factors that vary temporally but not spatially (e.g., population-wide changes in health-related habits) would not cause confounding unless they are associated with interactions. Nevertheless, we will control for socioeconomic status and smoking as appropriate. Socioeconomic status is recorded in two different ways at different levels of aggregation. Smoking data are reasonably complete, because the National Health Service Quality of Care Framework has created incentives to record smoking according to a coding scheme and was in operation during the time of the evaluation. Ethnicity is not recorded in the large databases, but we know from our feasibility study that it is not consistently linked with exposure to traffic pollution. (In fact, the tracking of ethnicity is on the rise in many general-practice databases across London, with the result that some control for individual-level ethnicity might well be possible.) As in the case of socioeconomic status and smoking, ethnicity is unlikely to change spatially over the four years of observation, meaning it will not constitute an uncontrolled confounding factor.

One can, however, envisage temporal-spatial confounding factors. For example, the U.K. has recently instituted a ban on smoking in public places. It is possible that this will cause different health changes (through changes in passive and active smoking) in different segments of the population. In particular, it might benefit low socioeconomic status groups more than higher socioeconomic status groups. To the extent that such variations in health changes were associated with measured factors (e.g., socioeconomic status), it would be possible to control for confounding by them by allowing for associated health changes and socioeconomic status–time interactions in the analysis (Janes et al. 2007).

It has been seen in the cross-sectional analysis that there were some anomalous findings, especially with respect to young adults with asthma. As noted above, from the point of view of the longitudinal (i.e., change versus change) analysis, the reasons for these anomalous findings are not important, provided that whatever is responsible for them is constant over time.

Objective 4

The fourth objective was to develop a strategy for recruiting suitable practices and procuring the necessary data for evaluating the LEZ in an efficient and acceptable manner. To this end, we are negotiating with the General Practice Research Database, which has about 450,000 patients and can link data anonymously online. We had originally considered weighting the practices according to the proximity of their populations to roads that the model predicts would be associated with the greatest reduction in exposure after the introduction of the LEZ. Under the anonymity restrictions of the database organizations, such weighting was not possible. But in the end it was not necessary, because, as demonstrated in the baseline study, we can directly classify patients at the postcode level by the modeled differences in exposure predicted as a result of the LEZ. Inclusion of an anonymous practice identifier in the clinical data set will ensure that we know which patients are in the same practice so that multilevel models can be implemented.

SUMMARY AND CONCLUSIONS

The work described in this report aimed to develop the methodology for evaluating the health impact of the LEZ using computerized primary-care records. These are used by the majority of practices in the U.K. and comprise linked clinical information on prescriptions and consultations together with smoking and area-level socioeconomic status data. Using an existing research database with data on practices throughout London and another with data on practices in an inner London Borough, we showed that it is operationally and ethically feasible to link patient records with modeled air pollution exposure data (at a 20×20–m grid resolution) by way of postcodes. The main administrative issue that remains to be resolved concerns the theoretical possibility that knowledge of the pollution signatures of the postcodes might enable identification of the postcode of an individual clinical record and that this might contravene the governance of the research databases required for the main evaluation.

Using these data sets we have shown that respiratory and cardiac outcomes of interest can be defined and expressed as incidence or prevalence. The health data include not

only diagnosis and prescriptions but codes for undifferentiated symptoms such as cough. This is a valuable dimension of health outcome measurement and will be included in our future full evaluation of the LEZ. Nearly all London residents are registered with general practices, and the health care provided by the practices is free, with the consequence that, compared with some other health care systems, access to health care across various age and social groups is equitable. The primary-care data show age, sex, socioeconomic, and ethnic patterns consistent with patterns seen in epidemiology based on population surveys.

Our cross-sectional analyses found that exposure to NO_x was positively associated with greater socioeconomic deprivation but not with smoking or with ethnicity. We found no cross-sectional positive association between exposure to NO_x and any of the health outcomes selected, and some associations were significantly negative. These findings emerged from analyses designed to demonstrate the feasibility of obtaining, linking, and analyzing the data, not from analyses intended to study the effect of traffic pollution on health. The implications of these findings for a full evaluation of the LEZ in a temporal-spatial study design will only be clarified by doing the study.

We estimated, for the whole of London, the frequency distribution of modeled predicted change in exposure to NO_x resulting from the LEZ. If this is also representative of the distribution in NO_x changes in practices ultimately included in future study, it will be possible to evaluate the health impact of the LEZ using a temporal-spatial analysis with change in exposure analyzed as either a categorical or continuous variable.

One primary-care research organization, General Practice Research Database, has agreed in principle to collaborate in a future evaluation of the LEZ. It comprises about 60 practices with 450,000 patients and has the capacity to carry out online linkage of pollution data with clinical records by way of postcodes. Simple power calculations based on a sample of 350,000 patients who have lived at the same address for 4 years suggests that we would have the power to show a 5% decrease in common health outcomes, such as drug treatment for asthma or consultations for respiratory infections. The power of the final study would be increased by analyzing the pollution data as a continuous rather than dichotomous variable.

Evaluations of the health outcomes of traffic interventions like the LEZ are challenging, because both the change in exposure and the likely proportional effect on health outcomes are small and because it is important to have an appropriately controlled design. Field surveys are not feasible on the scale required and would generally be limited to cross-sectional designs. The power of studies using routine data on mortality and hospital admissions is low. Primary-care databases therefore provide the most efficient way of evaluating, using a controlled design, impacts on relevant health outcomes over time in large populations. On the basis of the work described, we believe that the use of electronic primary-care records to evaluate the health impact of the LEZ is feasible.

FINAL DISCUSSION AND CONCLUSIONS

The LEZ, which was introduced across Greater London on February 4, 2008, is one of a number of measures designed to address widespread public concern about poor air quality and the associated risk to human health. This particular environmental intervention, which created a 2644-km^2 zone in which only vehicles meeting modern Euro emissions standards had free access, restricted the entry of the oldest and most polluting vehicles (specifically, diesel-engine heavy-goods vehicles, buses and coaches, larger vans, and minibuses). The zone is an area in which more than 8 million people live and work and includes areas with the highest exceedences of air pollution in Greater London, namely central London, Heathrow, and areas near the main arterial and ring road networks.

If the LEZ initiative reduces emissions from targeted vehicles and, in turn, the concentrations of pollutants present in the atmosphere as has been predicted from modeling, one would expect reduced public exposures to traffic-related pollutants and, hopefully, a range of health benefits for London residents. It is our ultimate aim to conduct research to investigate the validity of this expectation. The present study was undertaken before the implementation of the LEZ scheme in order to accumulate robust baseline data on air quality and PM oxidative activity and metal content in Greater London and to develop a method for using primary-care databases to evaluate potential health effects. The key achievements and insights derived from assembling the baseline environmental and health data and from developing the methodology for assessing health impacts are summarized in the following sections.

MODEL PREDICTIONS OF THE EFFECTS OF THE LEZ

Our study began with a detailed emissions modeling exercise in which the agreed LEZ scenario and year-on-year vehicle stock changes (as newly purchased vehicles replaced older ones) were used to predict air pollution in London for the years 2005, 2008, and 2010. The exercise was based on 2002 meteorologic data and average air pollution concentrations across postcode areas in London established by linking postcode areas and average air pollution-modeled for grids across London. Details of general practices

were linked, by way of a database, to the national postcode data set, in order to represent the location of each general practice as an average location within each postcode area. Results from modeling output-difference plots estimated the areas in London that would be expected to show the greatest change in atmospheric concentrations and population exposures after the implementation of the LEZ. Specifically, the areas predicted to experience the greatest changes in NO_2 (i.e., at least 3 $\mu g/m^3$) and PM_{10} (i.e., 0.75 $\mu g/m^3$) concentrations for 2010 in response to the LEZ were immediately adjacent to certain sections of major trunk routes throughout Greater London and a number of major roads in Central London. The data generated were then used to identify the best placement of an LEZ monitoring network for pollutant analysis as well as a strategy for evaluating the health impact of these changes using primary-care records.

LEZ IMPACTS ON MONITORING NETWORK

The results from the emissions modeling exercise for NO_2 and PM_{10} summarized in this report suggested that the clearest indication of pollution change in response to the implementation of the LEZ was likely to be recorded at roadside sites close to trunk routes and major intersections. Based on these results, we identified existing monitoring sites that were likely to be of key importance in carrying out an accountability study and locations where additional analyzers should be placed.

Seven key locations were identified and formed the basis of the LEZ pollution impacts monitoring network needed to carry out a study of the impact of the LEZ on air quality and health. Other existing monitoring sites in the LAQN were used to support the network. Two of these sites already had monitors with a full complement of instrumentation. At four of the key sites existing monitoring equipment was upgraded. At a fifth location, where no monitoring site existed, one was established. Capital and revenue funding for the upgrades and new site was provided by Transport for London in early 2006, and monitoring equipment was installed between May and September 2006. With the upgrades and new installation in place and operational, fully ratified pollutant data (for PM_{10}, $PM_{2.5}$, NO_x, and O_3 at all sites and for particle number, BS, CO, and SO_2 at selected sites) could be collected to produce a robust baseline LEZ data set. In addition, vehicle profiling, available in unprecedented detail at each of the seven key monitoring sites (through automated and manual traffic counters as well as plate-recognition cameras), made it possible to identify associations between vehicle emissions and ambient pollutant concentrations.

ANALYSIS OF PM OXIDATIVE PROPERTIES

To maximize our ability to observe the anticipated decreases in the oxidative potential of ambient PM_{10} and $PM_{2.5}$ in association with changes in traffic densities and vehicle mix after the introduction of the LEZ, we established a detailed pre-implementation measurement campaign. This entailed an assessment of the intrinsic oxidizing properties of PM collected from the monitoring sites chosen for the study of the LEZ, with a focus on the contribution of traffic-derived components. By using a synthetic RTLF model (Mudway et al. 2004) we obtained an integrative activity of the redox-active components of PM. The use of a simplified AA-only model, with or without metal chelators, enabled us to distinguish the relative contributions of metals and organic radicals to the oxidative activity.

With this pre-implementation measurement campaign, we extended work conducted as part of a secondary objective of the HEI study of the London Congestion Charging Scheme (Kelly et al. 2011a, b) (which was a more limited spatial mapping exercise restricted to 16 sites that focused solely on TEOM PM_{10} samples) by measuring PM oxidative activity at 41 sites, including the 7 roadside locations identified as key monitoring sites for assessing the impact of the introduction of the LEZ. Of the of 41 PM_{10} sites, 11 were urban background sites and 30 were roadside sites. In addition, $PM_{2.5}$ was collected and analyzed from 9 of these sites (1 urban background site and 8 roadside sites). As a result, we established the first data set that describes in detail the oxidative potential and metal content of PM_{10} and $PM_{2.5}$ in a major city's airshed. Furthermore, of the 41 sites examined, 4 (2 urban background and 2 roadside) were located outside the Greater London area, which permitted characterization of the PM oxidative potential specific to PM collected in London.

Particulate matter samples collected in London showed considerable oxidative activity, equivalent to, and in many cases greater than, that seen for our positive control particle (residual oil fly ash). Marked variations were found for both PM_{10} and $PM_{2.5}$ between the sites studied, with evidence that particles from the roadside locations had greater oxidative potential than those from the background sites, thus confirming and extending the preliminary observations from the CCS study (Kelly et al. 2011a, b). In samples from the nine urban background or roadside sites that monitored both PM_{10} and $PM_{2.5}$, we observed little evidence to suggest that the oxidative activity of $PM_{2.5}$ was enhanced compared with that of the PM_{10} samples collected from the same sites. Rather, overall PM_{10} oxidative potentials were enhanced compared with $PM_{2.5}$ oxidative potentials. Although the relationship varied on a site-by-site basis, it

indicates that $PM_{2.5–10}$, the coarse PM fraction, probably contained components with considerable oxidative activity.

To investigate whether metals or organic radicals were the dominant components in the oxidative potential of PM, we examined the ability of all of the PM samples collected in the LEZ baseline study to deplete AA, with or without an excess of the transition-metal chelator DTPA, to derive total, metal-dependent, and metal-independent oxidative potentials. Using this simplified model we observed that a significant proportion (60% to 70%) of the total oxidative activity could be attributed to metals, although this value varied between samples. It was notable that, although there were differences from site to site for total, metal-dependent, and metal-independent oxidative potentials, the differences were less pronounced with the metal-independent values, suggesting that much of the variation in PM oxidative potential in London reflects local differences in metal emissions. The contribution of metals to the measured oxidative potential was also investigated using a larger panel of chelators (including DTPA and DFO). These studies confirmed that much of the oxidation of AA observed in this model could be attributed to metals, although the fact that coincubation with the antioxidant enzymes Cu,Zn–SOD/CAT inhibited AA depletion indicated the involvement of the superoxide ion in proportion to the depletion observed.

We examined a panel of metals, chosen to reflect known traffic sources related to emissions from exhaust and other sources (tire, brake, and carriage wear) (de Miguel et al. 1997; Onianwa 2001; Weckwerth 2001; Manoli et al. 2002; Harrison et al. 2003; Laschober et al. 2004; Zechmeister et al. 2005). In aqueous extracts, which are considered to be a better correlate of metal availability in vivo than the total pool (Kelly et al. 2011b), we observed marked site-dependent contrasts in all of the soluble metal concentrations in PM_{10} and in the concentrations of Al, As, Cu, Fe, Mn, Pb, V, and Zn in $PM_{2.5}$. In line with our analysis of the impact of the CCS, we found that concentrations of Ba, Cu, and Mo were higher in PM_{10} from roadside locations and that concentrations of water-soluble Al, As, Cd, Fe, Ni, Pb, V, and Zn were higher in PM_{10} from urban background locations. However, a similar pattern was not apparent in the $PM_{2.5}$ samples, in which no contrast was found between the roadside and urban background sites. This discrepancy strongly supports the contention that the higher concentrations of Ba, Cu, and Mo in PM_{10} reflects contributions from the $PM_{2.5–10}$ fraction. Both Ba and Cu have been used as markers of brake wear (Sternbeck et al. 2002; Boulter 2006), and the majority of the mass of brake wear particles have been found to be associated with coarse PM (Berdowski et al. 1997), which leads us to speculate that the elevated concentrations of Ba, Cu, and Mo associated with the $PM_{2.5–10}$ fraction at the roadside sites might reflect emissions from brakes or other mechanical wear processes. In contrast to the results for water-soluble Fe, when we used the chromogenic chelator BPS to assess the size of the bioavailable Fe pool, our results indicated that the amount of BPS Fe was greater in PM_{10} roadside samples than in urban background samples, in accord with our previous findings (Kelly et al. 2011b). In contrast, no difference in BPS Fe concentrations was observed between roadside and urban background sites in the $PM_{2.5}$ samples examined. The source of the insoluble Fe in $PM_{2.5–10}$ at roadside sites is not clear at this time, but Fe silicates associated with road-surface erosion or wear of brake linings (Hildemann et al. 1991) might be potential sources.

Finally, by comparing sites in Greater London with the four sites (two urban background sites and two roadside sites) outside the city, we observed clear evidence of increased OP^{AA}/μg and OP^{GSH}/μg at the background sites in London compared with sites outside of London, a difference that was magnified when the oxidative potentials were expressed per m^3. Similarly OP^{GSH}/μg, OP^{AA}/m^3, and OP^{GSH}/m^3 were found to be elevated at roadside sites within the city. Although this preliminary examination provided suggestive evidence for the presence at roadside of a PM component with increased oxidative activity, a more detailed study will be required to fully assess its magnitude and the contribution of regional particulate oxidative potential to the London airshed.

DEVELOPMENT OF METHODS TO EVALUATE THE HEALTH IMPACT OF THE LEZ

The final component of this baseline study has established that it is feasible, in ethical and operational terms, to link air pollution data to the U.K.'s extensive electronic primary-care records in order to evaluate, using data on medical consultations and prescriptions, the health effects (including the incidence and exacerbations of chronic and acute disease) of regulatory interventions, specifically of the LEZ. This evaluation made use of data from primary-care records from a pilot set of general practices (obtained opportunistically from two existing studies) and classified patients according to exposure to traffic pollution and to predicted changes resulting from the implementation of the LEZ. The pilot set comprised 13 practices distributed across London with 100,000 patients and 29 practices in the London Borough of Lambeth with 200,000 patients.

Each data set comprised individual linked primary-care records and mean annual PM_{10} and NO_x concentration estimates (based on exposure modeling at a 20×20–m grid resolution). The linkage between the primary-care data and the assigned air pollution values were achieved

by way of postcodes, using a multistage procedure that ensured that the investigators would not have access to location data. Because the postcodes referred to a small number of dwellings (approximately 15), ethics approval was required and was obtained for both data sets.

To examine the potential for using these data for evaluative purposes, we examined, at the practice level, the distribution of NO_x exposures (representing the best indicator of traffic exposure) at the postcode level in patients and the relationships between exposure and two important potential confounders, namely smoking and socioeconomic status. A wide range of NO_x exposures was found in London as well as within and between practices. For the 160,000 postcodes representing the whole of London, there was about a twofold range of exposures between the second and ninth deciles, suggesting that there was enough heterogeneity of exposure for cross-sectional analysis. We found no important associations between smoking and exposure to NO_x either within practice or overall, making smoking an unlikely confounding factor. Index of Multiple Deprivation data (which include census variables and are available at the super output area level [i.e., 400 households with 1500 residents]) were available for both data sets and were therefore used to indicate confounders related to socioeconomic status; the data would also be available for use in a final evaluation that includes other practices. A strong relationship was found between greater deprivation and NO_x exposure, and clearly Index of Multiple Deprivation is a potential confounder in any cross-sectional analysis. Ethnicity is not routinely available in primary-care records but was available for the records from the practices in Lambeth. Analysis of the Lambeth records suggested that there was some potential for ethnicity to be a confounder in associations between air pollution and health outcomes. Although these socioeconomic confounders are relevant to cross-sectional analyses of pollution and health, they are less relevant for the planned controlled longitudinal evaluation of the LEZ except insofar as there might be interaction effects.

The outcome variables (asthma, chronic obstructive pulmonary disease, wheeze, hay fever, upper and lower respiratory tract infections, ischemic heart disease, heart failure, and atrial fibrillation) were chosen to indicate the prevalence and incidence of chronic cardiorespiratory diseases and their exacerbations. In general, the associations between these outcomes and age, sex, smoking, socioeconomic status, and ethnicity were the same as those predicted from epidemiologic studies. In our cross-sectional analyses, which controlled for age, smoking, and socioeconomic status (as well as ethnicity, in the case of the Lambeth practices), we found no evidence of an adverse effect of NO_x concentrations, modeled at the postcode level, on the outcome variables. Some associations were significantly negative — analysis of both data sets showed negative associations with asthma ever and prescriptions for asthma drugs in school-age children and young adults. Although these cross-sectional results were unexpected and puzzling, it should be emphasized that the final evaluation will be longitudinal, not cross-sectional. From the viewpoint of the LEZ evaluation, the important result of our analyses was that sufficient numbers of relevant outcomes can be defined and analyzed using these complex data sets.

The following observations from our baseline study can be applied to future studies of the effects of the LEZ on the health of those who live or work in London:

- In developing a strategy for recruiting suitable practices and procuring the necessary data, we originally anticipated a need to visit collaborating practices and carry out the linkage and downloading of data individually using trained staff. Although the feasibility of this approach was demonstrated in the Lambeth practices, a better and far more efficient option is to carry out the whole process online, as was achieved for the 13 DIN practices. One primary-care research organization, General Practice Research Database, has agreed in principle to collaborate with us in a future evaluation of the LEZ.
- We anticipate no problems in expanding the methodology needed to evaluate changes in modeled exposures across the time period of the implementation of the LEZ.
- Similarly, we anticipate no problems in gaining the relevant ethical approvals for linking air pollution and primary-care data by way of postcodes. In the current study, we unexpectedly found that some postcodes had unique pollution signatures, thus presenting a theoretical possibility of identifying the postcode. Because of time constraints, and in order to observe the spirit of the ethics approval, we restricted the current analysis to a single pollutant described in percentile terms. However, because these pollution variables were derived from an in-house model, they are unlikely to be replicable by outsiders and, even if this were possible, would be meaningless without access to the pollution-linked clinical data. We therefore anticipate (although this would need to be confirmed) that ethics committees will probably agree that there is no serious danger to confidentiality and that researchers should not be restricted to aggregated pollution variables.
- Classifying patients according to the amount of change in exposure will be done at the postcode level.

By comparing the 2010 base case with the preferred LEZ scenario, we estimate that approximately one quarter of the population will experience a greater than 3% reduction in NO_x concentrations. Simple power calculations suggest that we have the power to show a 5% decrease in common outcomes, such as drug treatment for asthma or consultations for respiratory infections, and a 10% decrease in less common outcomes, such as the incidence of new asthma.

CONCLUSIONS

The work undertaken in this LEZ baseline study has opened up a number of opportunities for analyzing the impacts of the LEZ in London as well as the benefits of other policies affecting exposure of the population to vehicle emissions. London resembles many U.S. cities in terms of its population demographics, health status, and ambient PM concentrations. The results presented in this report, the implementation of the LEZ, and the final research to evaluate the LEZ's impact on air quality and health are therefore of relevance to U.S. and international public health and might provide a model for the implementation and analysis of other such schemes that will undoubtedly follow.

The following points summarize the attributes the current study will bring to future assessments of the LEZ's effect on air quality and health.

- The ability to plan and put in place an extensive impacts monitoring network, including adequate roadside sites, provides an invaluable foundation for assessing the effects of the LEZ on air quality and, consequently, health.
- A full archive of PM samples that includes a comprehensive range of metrics from the sites outlined in this report has been collected up to the current date, and provision was made to continue collection up to and throughout the implementation period. We are therefore at this time ideally situated (1) to investigate the impacts of the introduction of this large traffic management scheme on PM composition and toxicity and (2) to further our understanding of the relative importance of particulate sources, including tire and brake wear. In addition, increased availability of data on roadside O_3 concentrations will increase our appreciation of the behavior of primary NO_2 emissions, an issue that is little understood but of great concern to researchers and policy makers.
- Finally, we estimated, for the whole of London, the frequency distribution of modeled predicted changes in exposure to NO_x resulting from the LEZ. Assuming that this distribution will also be representative of the distribution of changes in NO_x in the study practices that have agreed to collaborate with us, it will be possible to evaluate the health impact of the LEZ by means of a temporal-spatial analysis of individual clinical records with exposure change analyzed as either a categorical or continuous variable.

IMPLICATIONS OF FINDINGS

London's LEZ presents a unique opportunity to estimate the impact of reduced vehicle emissions on air quality and health. The present study has accumulated robust baseline data on air quality, PM oxidative activity, and metal content and has developed methods for using primary-care databases to evaluate impacts on health. With these data and methods in place, there is now an opportunity to evaluate the impact of the LEZ. Furthermore, the impacts monitoring network now in place provides an excellent opportunity to assess both the impact on air quality overall and, specifically, to further our understanding of the link between PM composition and toxicity.

Importantly, this baseline study has established that it is feasible, in ethical and operational terms, to link air pollution data to the U.K.'s extensive electronic primary-care records in order to evaluate, through data on consultations and prescriptions, the health effects (including the incidence and exacerbations of chronic and acute disease) of regulatory interventions in the context of the London LEZ.

Finally, the work undertaken in this baseline study has opened up a number of opportunities for analyzing, not only the impacts of the LEZ in London, but also the benefits of other policies affecting exposure of the population to vehicle emissions. London resembles many U.S. cities in terms of its population demographics, health status, and ambient PM concentrations. The results presented in this report, the implementation of the LEZ, and the final accountability research to establish the LEZ's impact on air quality and health are therefore of relevance to U.S. and international public health and might provide a model for the implementation and analysis of the effects of other such schemes that will undoubtedly follow.

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ABOUT THE AUTHORS

Frank Kelly obtained his Ph.D. in 1982 and holds the chair in Environmental Health at King's College London where he is also the head of the ERG and deputy director of the MRC-HPA Centre for Environment & Health. He has considerable experience in managing and coordinating interdisciplinary research in multi-center settings, including the HEI-funded CCS study and the Low Emission Zone baseline study. He contributes to the activities of a number of expert groups including U.K. government and WHO panels.

Ben Armstrong is an applied medical statistician at the London School of Hygiene and Tropical Medicine, and has a long-standing interest in the application of statistics to environmental health. He is a member of the Committee on the Medical Effects of Air Pollution (COMEAP) and the HEI Health Review Committee.

Richard Atkinson is a lecturer in statistics at St. George's, University of London, and has a special interest in the methods for quantifying the health impacts of outdoor air pollution. He is member of COMEAP sub-committee set up to re-evaluate the evidence for health effects of outdoor air pollution.

Ross Anderson is professor of epidemiology at the Centre for Epidemiology at St. George's, University of London. He has an international reputation as a leading researcher in the field of air pollution epidemiology, having a long track record of national and international research commitments. He is a member of the Expert Panel on Air Quality Standards (EPAQS) and the WHO Air Quality Expert Group. He was also a member of COMEAP. He was also a member of the U.S. National Academy of Science committee that reported on methods for estimating the health benefits of reducing ambient air pollution through regulations.

Ben Barratt has worked within the Air Quality Monitoring Team at the ERG, King's College London since 1994 and is currently deputy manager. His key skills lie in the establishing and managing regional air quality monitoring networks and interpreting monitoring results through software systems development, internet reporting methods and assessment intervention impacts.

Sean Beevers has more than 10 years of experience with air pollution measurement, and emissions and air pollution modeling at the ERG, King's College London. He has managed the emissions assessments for a number of large infrastructure projects in London and South East England as well as a number of key London developments including the London Atmospheric Emissions Inventory and the Congestion Charging Impacts Assessment.

Derek Cook is professor of epidemiology at the Centre for Epidemiology at St. George's, University of London. He has extensive experience using electronic general-practice databases and, of particular relevance for this study, the Doctors Independent Network Database and the General Practice Research Database.

David Green manages the 16 monitoring sites within the LAQN that are affiliated with the Automatic Urban and Rural Network at the ERG, King's College London. He managed the installation of the Marylebone Road site and is responsible for its operation. It is situated on the IRR (boundary of the CCZ) and gathers the most comprehensive set of air pollution data in the Automatic Urban and Rural Network. His research interests include methods for measuring airborne particles.

Dick Derwent is director of rdscientific. He has considerable experience working with large data sets, extensive understanding of air quality issues in London, and a background in atmospheric science. He is a member of EPAQS and the UK Air Quality Expert Group.

Ian Mudway leads the Lung Biology Group at King's College London and has 15 years of experience studying the

oxidative basis of air pollution, initially focusing on the oxidative gases O_3 and NO_2, but more recently addressing the toxicity of ambient and vehicle-derived particulates.

Paul Wilkinson is an environmental epidemiologist and public health physician at the London School of Hygiene & Tropical Medicine, with particular interest in environmental hazards to health, including climate change and outdoor air pollution. He is holder of a Public Health Career Scientist Award, which focuses on the methods of quantitative public health impact.

APPENDIX A. HEI Quality Assurance Statement

The conduct of this study was subjected to independent audits by Dr. Richard Kwok and Dr. James Flanagan of RTI International. Kwok and Flanagan are experts in quality assurance for air quality monitor studies and related epidemiologic studies. The audits included on-site reviews of study activities for conformance to the study protocol and standard operating procedures. The dates of the audits and the phases of the study examined are shown below.

QUALITY ASSURANCE AUDITS

December 6–8, 2006

In phase 1, the auditors conducted an on-site audit at King's College London to verify the integrity of the reported data. The audit reviewed the following study components: progress reports, personnel and staff, adequacy of equipment and facilities, internal quality assurance procedures, air quality sampling methodology, and data processing procedures. Several data points for each parameter were traced through the entire data processing sequence to verify that the described procedures had been followed and to verify the integrity of the database. The audit also included spot checks of the monitoring stations' original data record against the project database for any data transcription errors. No errors were noted.

April 3–4, 2008

In phase 2, the auditor conducted on-site audits at St. George's Hospital, London and King's College London. The auditors assessed the investigators' responses to the phase 1 audit and extended the review to the health data being compiled by investigators at St. George's Hospital.

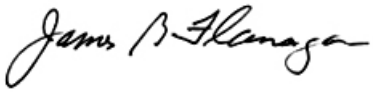
July–August, 2009

In phase 3, the auditors reviewed the draft final report to ensure data issues noted earlier were addressed. No further issues were noted.

Written reports of the Quality Assurance oversight inspections were provided to the HEI project manager, who transmitted the findings to the Principal Investigator. These quality assurance oversight audits demonstrated that the study was conducted by a well-coordinated, experienced team according to the study protocol and standard operating procedures. Interviews with study personnel revealed a consistently high concern for data quality. The report appears to be an accurate representation of the study.

Richard K. Kwok, Ph.D.

Epidemiologist, Quality Assurance Officer



James Flanagan, Ph.D.

Chemist, Quality Assurance Officer

APPENDICES AVAILABLE ON THE WEB

Appendices B, C, D, and E contain supplemental material not included in the printed report. They are available on the HEI Web site *http://pubs.healtheffects.org*.

Appendix B. Spatial Analysis of Modeled Air Pollution Data

Appendix C. Assessing the Oxidative Properties of Ambient PM_{10} and $PM_{2.5}$ Across Greater London

Appendix D. Emission Modeling, Read Codes, and Regression Analysis — Use in the Development of Methods for Using Primary Care Databases in Evaluating Health Impacts

Appendix E. LAQN Sites Used in This Study

OTHER PUBLICATIONS RESULTING FROM THIS RESEARCH

van Erp A, Kelly F, Demerjian K, Pope C, Cohen A. 2011. Progress in research to assess the effectiveness of air quality interventions towards improving public health. Air Qual Atmos Health *DOI 10.1007/s11869-010-0127-y.*

Tonne C, Beevers S, Kelly FJ, Jarup L, Wilkinson P, Armstrong B. 2010. An approach for estimating the health effects of changes over time in air pollution: An illustration using cardio-respiratory hospital admissions in London. Occup Environ Med 67:422–427.

Kelly FJ, Kelly J, HEI London Consortium. 2009. London air quality: A real world experiment in progress. Biomarkers 14:5–11.

ABBREVIATIONS AND OTHER TERMS

AA	ascorbate
ACORN	A Classification of Residential Neighborhoods
BPS Fe	bathophenanthroline disulfonate–mobilized Fe
BS	black smoke
CCS	Congestion Charging Scheme
CO	carbon monoxide
CPC	condensation particle counter
DFO	desferroximine
DIN	Doctors' Independent Network
DTPA	diethylenetriamine pentaacetic acid
EDTA	ethylenediaminetetraacetic acid
ERG	Environmental Research Group
GSH	glutathione
LAEI	London Atmospheric Emissions Inventory
LAQN	London Air Quality Network
LEZ	Low Emission Zone
NIGB	National Information Governance Board for Health and Social Care
NO_2	nitrogen dioxide
NO_x	nitrogen oxides
O_3	ozone
$O^{-\bullet}$	superoxide radical
OP	oxidative potential
PM	particulate matter
$PM_{2.5}$	particles with an aerodynamic diameter of 2.5 μm or smaller
PM_{10}	particles with an aerodynamic diameter of 10 μm or smaller
RFA	Request for Applications
RTLF	respiratory tract lining fluid
SCR	selective catalytic reduction
SO_2	sulfur dioxide
SOD/CAT	superoxide dismutase and catalase
TEOM	tapered element oscillating microbalance
WHO	World Health Organization

ELEMENTS

Al	aluminum
As	arsenic
Ba	barium
Cd	cadmium
Cu	copper
Fe	iron
Mo	molybdenum
Pb	lead
V	vanadium
Zn	zinc

Research Report 163, *The London Low Emission Zone Baseline Study,* F. Kelly et al.

INTRODUCTION

For several years, HEI has supported research designed to evaluate the extent to which air quality regulations succeed in protecting public health (see the Preface of this report for a summary of HEI's health outcomes research program). Given the substantial improvements in air quality that have been observed in the United States and Western Europe, attributable in part to increasingly stringent — and often costly — air quality regulations, it is prudent to ask whether the regulations have actually yielded demonstrable improvements in public health or have generated information that can inform future efforts to do so.

The baseline study of the London Low Emission Zone (LEZ*) originated as a response to the fourth Request for Applications (RFA) issued as part of HEI's health outcomes (formerly accountability) research program. RFA 04-4, Measuring the Health Impacts of Actions Taken to Improve Air Quality (HEI 2004b), was issued to request proposals for studies (1) to assess the health impacts of mandatory and incentive-based regulations at local to national levels to improve air quality and (2) to develop methods required for, and specifically suited to, conducting such research. Although the RFA was primarily intended to estimate the impact of actions taken in the United States, proposals for studies of actions taken in other countries were considered if the studies were relevant to current U.S. conditions (e.g., studies of interventions at comparable ambient concentrations to reduce emissions from sources commonly found in North America). The RFA primarily sought studies of intentional interventions rather than natural experiments, such as the copper smelter closure in Utah (Pope 1989; Pope et al. 2007).

In response to the RFA, Professor Frank Kelly of King's College London and a multidisciplinary team of investigators from St. George's, University of London, and the London School of Hygiene and Tropical Medicine submitted in 2005 an application entitled "The London Low Emission Zone: Assessing its impact on air quality and health." The creation of the London LEZ was one of a series of strategies proposed in 2002 by the Mayor of London to improve air quality in the city. By progressively restricting the oldest and most polluting vehicles from a large part of Greater London, the Mayor hoped to reduce air pollution from road traffic, a major contributor to emissions of nitrogen oxides (NO_x) and particulate matter (PM) with an aerodynamic diameter ≤ 10 μm (PM_{10}).

Kelly and his co-investigators proposed to study impacts of the LEZ on both air quality and public health. They planned to build upon Kelly's earlier investigation of the impacts of a smaller traffic reduction initiative, the London Congestion Charging Scheme (CCS) (Kelly et al. 2011), that was conducted under a previous HEI RFA (HEI 2004a). For the LEZ study, the investigators proposed to assess the projected impacts of the LEZ implementation on air quality across Greater London, to assess the oxidative potential of London's particulate matter (PM) and its relationship to reduction-oxidation ("redox")–active metals, and to assess the feasibility of using the United Kingdom's computerized primary-care data for evaluating the impact of the LEZ on health outcomes.

In its review of the application, the HEI Research Committee expressed concerns about whether changes in pollutant concentrations and corresponding changes in health outcomes attributable to the LEZ would be measurable in the proposed timeframe. The Committee asked Professor Kelly for a revised proposal that focused (1) on collecting and evaluating pertinent baseline air quality data before the implementation of the LEZ and (2) on identifying potential data gaps and challenges to obtaining critical health data and related time-varying confounding factors from the primary-care database. Professor Kelly submitted a revised application that responded to these concerns, and the Committee recommended the approximately 2-year baseline study for funding.

This Critique is intended to aid the sponsors of HEI and the public by highlighting both the strengths and limitations of the study and by placing the Investigators' Report into scientific and regulatory perspective.

Professor Frank Kelly's 2-year study, "The London Low Emission Zone Baseline Study," began in December 2005. Total expenditures were $710,000. The draft Investigators' Report from Kelly and colleagues was received for review in December 2007. A revised report, received in September 2008, was revised a second time in April 2009 and accepted for publication in July 2009. During the review process, the HEI Health Review Committee and the investigators had the opportunity to exchange comments and to clarify issues in both the Investigators' Report and the Review Committee's Critique.

This document has not been reviewed by public or private party institutions, including those that support the Health Effects Institute; therefore, it may not reflect the views of these parties, and no endorsements by them should be inferred.

* A list of abbreviations and other terms appears at the end of the Investigators' Report.

SCIENTIFIC BACKGROUND

In research designed to evaluate the impact of interventions to improve air quality on the health of a population, the most direct evaluations consider how rates of illness or death compare before and after the intervention is put in place. Such evaluations are challenging in any case, but especially if the changes in air pollution caused by the intervention are small or gradual; concurrent changes in social, economic, and other factors can also affect health outcomes making those associated with air pollution more difficult to identify (HEI 2010).

Some successful long-term health outcomes studies have been done; one by Pope and colleagues (2009), for example, indicated improvements in life expectancy from reduction in fine-particle concentrations in the United States over the past several decades. However, some of the most convincing health outcomes studies conducted to date have been those that evaluated a discrete or step change in pollution. Examples include time-series pollution studies of daily mortality before and after a regulatory order forcing the removal of sulfur from fuel in Hong Kong (Hedley et al. 2002) and the shutdown of a copper smelter during a strike in Utah (Pope et al. 2007). Because major actions to reduce traffic congestion can be implemented in relatively short periods of time, recent actions of this kind have attracted increasing interest as opportunities to study the health impacts of changes in air quality that might accompany changes in traffic levels. One of the first of these was a study by Friedman and colleagues (2001) of the impact on air quality of traffic-reduction measures taken during the 1996 Atlanta Olympics; this work was recently expanded in an HEI-funded study (Peel et al. 2010). A study by Kelly and colleagues (2011) of the London CCS, which laid the groundwork for the present study, was one of the largest studies of the impact on air quality of a traffic reduction program in a major city.

However, the studies of the Atlanta Olympics and the CCS have both demonstrated showed that interventions whose primary goal is not air quality improvements pose additional challenges to health outcomes research. The London LEZ, whose purpose was to improve air quality by restricting more highly polluting vehicles from a larger area of London than was targeted by the CCS, was therefore an intriguing research opportunity.

In addition, countries around the world are increasingly considering low emissions zones, sometimes referred to as environmental zones, as a means to improve air quality in urban areas or around motorways. Beginning in 1996, Sweden implemented environmental zones in the Stockholm, Gothenburg, and Malmö city centers; the program was extended to Lund in 2002 (*www.dieselnet.com/standards/se/zones.php*). These programs applied only to heavy freight vehicles (> 3.5 metric tons) that did not meet then-current European emissions standards. The city of Tokyo has had a low emission zone since October 2003. A website launched in 2008 to track the development of low emission zones across Europe indicated that, as of this writing, 10 countries (Austria, the Czech Republic, Denmark, Hungary, Italy, Sweden, the Netherlands, Norway, Germany, and the United Kingdom) have or are planning low emission zones of varying sizes and designs in many of their cities (*www.lowemissionzones.eu*).

The London LEZ is the largest of these types of zones, covering approximately 2644 km^2 of the Greater London area (roughly the area inside the M25 motorway, a major highway encircling the city). The LEZ was part of a broader strategy developed by the Mayor of London to help the city meet national and European Union air quality objectives for 2010; the LEZ works by restricting entry of the most highly polluting vehicles to the zone. The LEZ was planned to be implemented in phases, beginning in February 2008, gradually requiring first diesel trucks, buses, and finally large vans and minibuses to meet increasingly stringent European emissions standards (see Table 1 in the Investigators' Report). Passenger cars were not included. The LEZ was designed to operate 24 hours a day, 365 days a year; it is enforced by the use of automatic number-plate-recognition cameras to identify vehicles and the issuance of heavy fines for noncompliant vehicles.

Modeling studies conducted by investigators at the Environmental Research Group at King's College London on behalf of the city's transportation authority, Transport for London, had predicted that modest reductions in total emissions of PM_{10} (from both exhaust and tire and brake wear), NO_x, and nitrogen dioxide (NO_2) would result from implementation of the LEZ. The investigators projected that the LEZ would reduce PM_{10} emissions by 2.6% (64 metric tons) in 2008 and by 6.6% by 2012 compared with baseline levels. Similarly, the LEZ was projected to reduce NO_x emissions by 3.8% (1288 metric tons) in 2008 and by 7.3% by 2012. The investigators did not report projected emissions reductions for NO_2 but estimated that the area of Greater London in which NO_2 would exceed the European Union annual mean air quality objectives would be reduced by about 15% by 2012.

A particular challenge to studying the impact of traffic-related interventions on public health is the availability of health data at spatial and temporal scales that are relevant to the changes expected in air pollutant concentrations. Britain's primary-care system offered a potential solution and an alternative to reliance on mortality and hospital

admissions statistics. Approximately 98% of the population is registered with a general practice that collects electronically primary-care data on a wide range of chronic and acute morbidity categories or prescription drug usage that might not be captured by hospital admissions or mortality data but might be relevant to air pollution exposure. In London, the potential exists for linking these records to other important variables, such as socioeconomic status, at a small spatial scale (e.g., the postcode level, which involves as few as 15 households).

On the basis of the projected changes in air pollutants in London and the opportunity to link these changes to health data using electronic primary-care data, Professor Kelly and his team undertook the London LEZ baseline study.

SUMMARY OF STUDY DESIGN

SPECIFIC AIMS

1. The overall objective of the study was to collect relevant baseline air quality and health data across Greater London for the period prior to the implementation of the LEZ (i.e., before February 4, 2008) that could later support research on the LEZ's impact on both air quality and health outcomes. The investigators had four specific aims: To use model predictions to identify the areas in Greater London that might show the greatest change in ambient pollution concentrations and potential for population exposure ("hot spots") under the presumed scenario for implementation of the LEZ.
2. To design a comprehensive monitoring network within Greater London for assessing air pollution concentrations prior to implementation of the LEZ.
3. To establish a robust PM toxicologic dataset and produce a spatiotemporal map of the oxidative potential of the ambient PM in London; and
4. To develop procedures and methods for the use of electronic primary-care records to evaluate the health effects of the LEZ.

To meet the first three specific aims, Professor Kelly and his colleagues relied heavily on methods they had developed in their earlier study of the impact of the London CCS on air quality. These included air quality modeling techniques, the design of an air monitoring network, and the use of the respiratory-tract-lining-fluid (RTLF) assay to assess the oxidative potential of PM extracts; they were presented and discussed in detail in the report on the CCS (Kelly et al. 2011) and are summarized briefly in the current report. The investigators' assessment of the feasibility of using Britain's primary-care records to evaluate the impact of the LEZ on various health outcomes (Specific Aim 4) was unique to this study.

MODEL PREDICTIONS OF THE LEZ'S EFFECTS ON AMBIENT AIR QUALITY (SPECIFIC AIM 1)

Professor Kelly and his team conducted detailed emissions and air pollution modeling to compare the projected impacts of LEZ implementation on the mix of vehicles entering the zone, emissions, and air pollutant concentrations with a base case scenario in which the LEZ was assumed not to have been implemented. Results for both scenarios were projected for 2010. The investigators used the King's College London Emissions Toolkit (a linked set of emissions databases and models) to simulate vehicular emissions of NO_x, NO_2, PM_{10} from exhaust, and PM_{10} from tire and brake wear throughout the Greater London road network. Nonvehicular emissions (from industrial processes, large boiler plants, domestic and commercial fuel combustion, agriculture, and air, rail, and ship transport) were estimated using the 2002 and 2003 London Atmospheric Emissions Inventory.

The investigators then used the King's College London Air Pollution Toolkit (a set of databases, algorithms, and dispersion models for streets and urban areas) to model the dispersion of emissions spatially across London. They predicted annual mean concentrations of each pollutant at an output resolution of 20 m^2. Data on meteorologic conditions for 2002 were used for both the LEZ and baseline scenarios projected through 2010.

DESIGN OF A COMPREHENSIVE AIR MONITORING NETWORK FOR THE LEZ (SPECIFIC AIM 2)

From the output of the models, the investigators created "difference" plots in order to identify the greatest projected changes in NO_2 concentrations (3 $\mu g/m^3$ or more) and in PM_{10} concentrations (0.75 $\mu g/m^3$ or more) for 2010 resulting from the implementation of the LEZ. These maps were then overlaid with maps of existing air monitoring sites and of major roadways to identify the best placement of a monitoring network with which to monitor anticipated LEZ-related changes in pollutant concentrations.

EVALUATION OF PM_{10} AND $PM_{2.5}$ OXIDATIVE POTENTIAL ACROSS GREATER LONDON (SPECIFIC AIM 3)

The investigators examined the oxidative potential of PM extracts from archived PM_{10} and PM with an aerodynamic diameter $\leq$ 2.5 µm ($PM_{2.5}$) filter samples from sites in the monitoring network developed under Specific Aim 2.

The basic method the investigators used to characterize oxidative potential is based on an assay developed by Zielinski and colleagues (1999), further explored by Mudway and colleagues (2004, 2005), and described in detail in the investigators' earlier study of the London CCS (Kelly et al. 2011). The assay measures the ability of extracts from PM filter to deplete antioxidants in a synthetic RTLF within a fixed time period. The RTLF is made up of equimolar concentrations of ascorbate, urate, and reduced glutathione, three common antioxidant compounds found in fluids on the surface of the lung; no lung tissue or cells are present. The reduction in concentration of each antioxidant after addition of each filter extract was hypothesized to represent the raw oxidative activity of the extract. The investigators derived expressions for the oxidative potential (OP) of the extracts, expressed as the percentage loss of oxidative activity per μg of PM_{10} or $PM_{2.5}$ or per m^3 air compared with a particle-free control solution and scaled from 0 to 2. The metrics were derived only for the two antioxidants in the assay where variability in activity was observed (i.e., ascorbate [OP^{AA}/μg and OP^{AA}/m^3] and glutathione [OP^{GSH}/μg and OP^{GSH}/m^3]; urate showed no variability). Positive (residual oil fly ash), negative (carbon black), and particle-free controls were run in parallel with each batch of samples.

As in the previous study of the CCS, additional analyses of the filter extracts were carried out in an attempt to identify the relative contributions of metal or nonmetal components of PM to the oxidative potential observed. The investigators analyzed each filter extract for a panel of metals (aluminum, arsenic, barium, beryllium, cadmium, copper, iron, lead, manganese, molybdenum, nickel, vanadium, and zinc) previously associated with exhaust (e.g., diesel fuel and lubricating oil) or nonexhaust (e.g., brake wear and carriage and tire wear) sources. Metal concentrations were determined using inductively coupled plasma mass spectrometry. The investigators conducted a number of other experiments with the RTLF assay to explore factors that might explain the observed oxidative potentials. The experiments included (1) the use of the chromogenic chelator bathophenanthroline disulfonate (BPS) to better represent the total iron content that might be extractable from the PM in living systems and thus be more bioavailable than the aqueous iron concentrations determined by the extraction process in the RTLF assay, and (2) the use of a simplified version of the RTLF assay involving ascorbate only, to which a range of free-radical scavengers and metal chelators (e.g., diethylenetriamine pentaacetic acid) was added, to provide an indication of the relative contributions of free radicals, metals, and nonmetals to the overall oxidative potential.

Spatial differences in oxidative potential and metal concentrations across monitor locations were evaluated using several statistical approaches (i.e., analysis of variance and Student *t* tests), given differences in the underlying distributions of the data from the two analyses.

DEVELOPMENT OF METHODS TO EVALUATE THE IMPACT OF THE LEZ ON MORBIDITY (SPECIFIC AIM 4)

Professor Kelly and his colleagues undertook several steps to assess the feasibility of using electronic primary-care records to study the effects of the LEZ on health outcomes. They explored methods for classifying patients according to predicted exposure to air pollutants based on traffic density around their home address in ways that would maintain the confidentiality of individual patient data. They conducted exploratory cross-sectional analyses of health outcomes data and predicted exposure estimates and investigated ways to include data on potential confounding factors such as socioeconomic status and smoking. On the basis of the cross-sectional analyses and other data, they assessed the power of future longitudinal studies to detect changes in health outcomes associated with implementation of the LEZ.

In order to pilot-test their methods, health outcomes data were obtained from two databases of electronic medical records, (1) the Doctors' Independent Network (DIN) database, consisting of data on routine clinical activity for 100,000 patients in 13 practices distributed across London that had relatively complete recordkeeping between 2000 and 2005 and the majority of whose patients were registered with an address in London that fell inside the area bounded by the M25 motorway, and (2) the Lambeth primary-care database, consisting of data on 200,000 patients in 29 practices in the inner London Borough of Lambeth, one of the most densely populated boroughs within inner London. In both databases, data permitting the identification of individual patients had been removed.

The investigators collected data on medical conditions using standard medical diagnostic classifications used by both databases (see Tables D.1 to D.4 in Appendix D of the Investigators' Report) and on the numbers of prescriptions for various medications. The conditions considered were asthma, chronic obstructive pulmonary disease, wheeze, hay fever, respiratory tract infections, ischemic heart disease, heart failure, and atrial fibrillation.

The datasets were linked to socioeconomic status indicators using several methods. The DIN database included socioeconomic indicators linked to postcode using the ACORN (A Classification of Residential Neighborhoods) system of classification (*www.caci.co.uk/ACORN/whatis.asp*) and to the English Index of Multiple Deprivation (Index of Multiple Deprivation 2004), a measure of socioeconomic status for small geographic areas (i.e., including about 400 households). The Lambeth database also contained questionnaire data on ethnicity, religion, and language.

Using the modeling methods described earlier, the investigators predicted pre-LEZ (2005) concentrations of NO_x, NO_2, and PM_{10} throughout London at a resolution of 20 × 20 m. Concentrations of NO_x, NO_2, and PM_{10} were assigned to 176,965 postcodes using the average of all 20 × 20–m grids whose centroids were contained within the postcode. Postcodes were rank ordered according to the estimated NO_x concentrations, and each postcode was assigned a value of 0 to 999 corresponding to its percentile of the NO_x cumulative concentration distribution. The percentiles were then linked to patients' clinical records but without the postcode information, to ensure anonymity. The investigators used only the NO_x concentration percentiles because, they reported, the joint profiles for NO_x, NO_2, and PM_{10} could have allowed identification of postcodes, and NO_x was in any case highly correlated with the other pollutants.

The investigators used logistic regression to examine cross-sectional associations between the projected 2005 NO_x concentrations and disease outcomes and prescriptions in the 42 practices. The regression analyses explored the impact of potential clustering among practices using random and fixed effects in the investigators' models. Data were analyzed by age groups and were adjusted for sex, smoking, and measures of socioeconomic status. In the Lambeth dataset, ethnicity was also evaluated.

Using a simplified version of the logistic regression model, the investigators estimated the power of their study to detect small changes (1% or 5% decreases) in the pre-LEZ rate of visits to practices for various diagnoses across the predicted exposure categories. They compared visit rates in postcodes having the highest projected decreases in NO_x concentrations (i.e., the top 10% or 25% of postcodes with the greatest decreases in NO_x) with those having small or no decreases (i.e., the bottom 90% or bottom 75%, respectively). They used these results to estimate the potential power that a future longitudinal study might have to detect such rate changes given similar changes in air pollutant concentrations.

SUMMARY OF RESULTS

AIR QUALITY MODELING (SPECIFIC AIM 1) AND MONITORING NETWORK DESIGN (SPECIFIC AIM 2)

The investigators' analysis of the modeled predictions of the LEZ's impact on pollutant concentrations suggested that the greatest changes were likely to be found adjacent to major roads (i.e., "roadside") in central London and throughout Greater London (see Figure 4 [for NO_2] and Figure 5 [for PM_{10}] in the Investigators' Report). More detailed plots were developed for each of five major sectors of Greater London, juxtaposing modeled changes in pollutant concentrations with existing monitoring capability in order to identify strategic locations for monitoring sites with which to characterize baseline air quality in London and to study future impacts of the LEZ.

On the basis of these analyses, the investigators first identified seven key locations that should form the core of the monitoring network (see Table 2 in the Investigators' Report). Two of these locations already had monitoring sites with a full complement of the necessary instrumentation. Transport for London agreed to upgrade existing monitoring at four of the remaining locations and to establish a new monitoring site at the fifth where no monitoring had existed. Equipment installation took place between May and September 2006. With the upgrades and new installation in place and operational, the monitoring sites were equipped to collect baseline data on PM_{10}, $PM_{2.5}$, NO_x, and ozone (O_3) concentrations at all seven sites and particle number, black smoke (BS), carbon monoxide (CO), and sulfur dioxide (SO_2) concentrations at selected sites. In addition, Transport for London installed vehicle profiling systems (i.e., automatic traffic counters, automatic number-plate recognition cameras, and biannual manual traffic counts) adjacent to each of the sites to monitor changes in traffic type and density.

Next, the investigators completed their monitoring network by making use of other existing monitoring sites in the London Air Quality Network. In total, their network included 28 roadside locations (20 for PM_{10}, 8 for $PM_{2.5}$) and 9 urban background locations (8 for PM_{10}, 1 for $PM_{2.5}$) within London (see Table 4 in the Investigators' Report) and 4 locations (2 roadside, 2 urban background) outside London for PM_{10} only (see Table 5 of the Investigators' Report). PM_{10} and $PM_{2.5}$ monitors were co-located at 9 sites, including 5 of the key LEZ indicator sites.

From these monitoring sites, the investigators compiled a dataset of 456 PM_{10} filters and 96 $PM_{2.5}$ filters that were used to study the oxidative potential of PM.

OXIDATIVE POTENTIAL OF PM_{10} AND $PM_{2.5}$ (SPECIFIC AIM 3)

The investigators' basic findings regarding the spatial variations in oxidative potential of PM_{10} are summarized in the Critique Table. They reported significant variation or heterogeneity in all four measures of oxidative potential in PM_{10} among all the sites in their database. They reported that PM_{10} collected from roadside locations appeared to have greater oxidative potential on average than PM collected from urban background locations. The difference between roadside and urban background in oxidative potential of PM_{10} varied somewhat depending on whether the substrate was ascorbate or glutathione and whether oxidative potential was expressed per unit mass (μg) of PM or per m^3 of air. In this study, the investigators also compared the oxidative potential of PM_{10} at sites designated as inside metropolitan London with oxidative potential of PM_{10} from sites outside London and found increased PM oxidative potential inside London compared with outside London at both roadside and urban background sites.

In this study, the investigators had the opportunity to examine patterns in the oxidative potential of extracts from $PM_{2.5}$ filters from roadside and urban background sites; using co-located monitors, they were also able to compare the oxidative potential of $PM_{2.5}$ and PM_{10} more directly. As for PM_{10}, the investigators found that the oxidative potential of $PM_{2.5}$ from roadside monitors was higher than that of $PM_{2.5}$ from their one urban background monitor. They also reported that oxidative potential was greater in the PM_{10} samples than in $PM_{2.5}$ samples. They suggest that this result may be an indication that the coarse PM fraction ($PM_{2.5–10}$) contains components with greater oxidative activity than the fine PM fraction.

Their analysis of the aqueous metal and BPS-extractable iron content (BPS Fe) of filter extracts also showed that the concentrations of specific metals differed both between sites and between PM fractions. Barium, copper, and molybdenum concentrations were higher in PM_{10} samples in filters collected from roadside locations compared with those from urban background locations; this pattern was not found in $PM_{2.5}$ samples. Aluminum, iron, lead, vanadium, and zinc concentrations were elevated in both PM_{10} and $PM_{2.5}$ from urban background sites. BPS Fe concentrations were higher in roadside PM_{10} samples, but not in roadside $PM_{2.5}$ samples compared with urban background samples.

The aqueous metal and BPS Fe concentrations in PM_{10} were correlated with oxidative potential but primarily in relation to ascorbate depletion (OP^{AA}/μg or OP^{AA}/m^3), not glutathione depletion ($PM_{2.5}$ samples were not examined). From additional experiments with an ascorbate-only assay and the metal chelator, diethylenetriamine pentaacetic acid, the investigators concluded that most (about 60% to 70%) oxidative potential (expressed as OP^{AA}/μg) was metal-dependent or attributable to metals in both PM_{10} and $PM_{2.5}$ samples.

FEASIBILITY OF USING ELECTRONIC PRIMARY-CARE RECORDS IN EVALUATION OF HEALTH OUTCOMES ASSOCIATED WITH THE LEZ

The investigators were successful in demonstrating the feasibility of a process for obtaining medical data from health practices online for later linkage to exposure data at the postcode level. They piloted the process using health data from the 13 DIN practices across Greater London and the 29 practices in the inner London Borough of Lambeth.

Critique Table. Qualitative Overview of Oxidative Potential Findings for London LEZ

Analysis	PM_{10} Data	Ascorbate		Glutathione	
		OP^{AA}/μg	OP^{AA}/m^3	OP^{GSH}/μg	OP^{GSH}/m^3
Overall variability in oxidative potential (one-way ANOVA)	All sites	+	+	+	+
Roadside compared with urban background locations (*t* tests)	Individual site means, grouped by location	—	↑	↑	↑
Inside London compared with outside London (*t* test)	Roadside sites	↑	↑	—	↑
	Urban background sites	↑	↑	↑	↑

Notes: + = statistically significant variability across sites; ↑ = statistically significant increase (roadside versus urban background and inside versus outside London); and — = no statistically significant differences.

The investigators' modeling of baseline NO_x concentrations throughout London and Lambeth suggested a broad range of potential exposures across medical practices. Projected concentrations ranged from about 22 to 386 μg/m^3 across London postcodes, with a median of 54.2 μg/m^3. Highest concentrations were expected in central London and along roadways. They concluded that there was sufficient heterogeneity for their cross-sectional analyses of the associations of predicted NO_x concentrations with health outcomes.

Cross-Sectional Analysis of Baseline NO_x Concentrations and Health Outcomes

The cross-sectional analyses of the relationship between NO_x and selected indicators for asthma and other respiratory and cardiovascular diseases largely found no statistically significant associations. The one exception was the statistically significantly negative association between NO_x and ever having had a diagnosis of asthma and prescriptions of asthma drugs in school-age children and young adults. This result was robust to their efforts to control for smoking and for socioeconomic status. The authors considered the plausibility of a number of other explanations, including exposure measurement error, but could not rule out chance or some source of uncontrolled confounding.

Their evaluation of smoking, socioeconomic status, and ethnicity as potential confounders in their cross-sectional analysis suggested that smoking was not likely to be a concern. They found a strong relationship between NO_x exposures and some measures of lower socioeconomic status (as indicated by Index of Multiple Deprivation scores) and therefore their analyses controlled for this variable. They concluded that there was some potential for confounding by ethnicity that would need further evaluation.

Investigation of Study Power to Detect LEZ-Related Changes in Air Pollution

The investigators conducted simple power calculations using projected changes in NO_x concentrations associated with a possible scenario for implementation of the LEZ and an assumption that they would be able to link air pollution levels to 90% of practices in the General Practice Research Database, a much larger database encompassing about 60 practices and 350,000 patients. Patients were assumed to live at the same address for four years covering 2-year periods before and after the implementation of the LEZ. Their calculations suggested that they would have the power to detect a 5% decline in measures such as prescription drugs for asthma or consultations for respiratory infections in the percentage of the population experiencing the largest decreases in exposure.

HEI HEALTH REVIEW COMMITTEE'S TECHNICAL EVALUATION

The London LEZ program offered an unusual opportunity to investigate the potential impacts of a complex intervention specifically directed at improving air quality in the midst of a major European city. In its independent evaluation of the study, the HEI Review Committee thought the multidisciplinary investigative team had undertaken a careful, stepwise approach. The investigators built upon the data and methods developed in their earlier study of the CCS to characterize baseline exposure conditions prior to implementation of the LEZ and to evaluate the feasibility of using electronic primary-care data to examine impacts on health that might be associated with changes in air quality over time. However, their experience also underscores the many substantial challenges that must be anticipated and overcome to successfully demonstrate changes in air quality and health outcomes resulting from interventions of this kind.

AIR QUALITY MODELING

The Committee thought that the choice of emissions and air quality models was generally appropriate and in the case of the dispersion modeling, state of the art. Nevertheless, the Committee had lingering concerns over the role of meteorologic conditions in the dispersion modeling. The investigators took a standard approach to controlling for meteorologic conditions by assuming the same meteorologic conditions in 2002 for both their baseline and post-LEZ models. However, the Committee pointed out that 2002 was a particularly mild, wet year and that more typical meteorologic conditions could lead to somewhat different results both for the modeling and for the interpretation of the oxidative potential results.

The Committee commented that the report could have been more transparent about the level of uncertainty in the model predictions and its implications for both later phases of the study and for future studies of this kind. As the investigators acknowledged, their predicted changes in annual average pollutant concentrations after implementation of the LEZ were small. It is likely that the predicted mean differences in PM_{10}, NO_x, and NO_2 concentrations are well within the limited estimates of uncertainty and could be further obscured by other important sources of uncertainty, for example, larger regional weather patterns. Given experience with similar projected changes in the earlier CCS study, the Committee was concerned that an impact on air quality would also be difficult to detect in the monitoring data for the LEZ.

The Committee thought that the investigators had used the modeling results effectively to identify the number and location of sites necessary to monitor the actual impacts of the LEZ. These efforts were instrumental in obtaining additional support from Transport for London to establish additional sites and to augment existing sites with capabilities for monitoring for $PM_{2.5}$, particle number, and other particle components (elemental and organic carbon, nitrate, sulfate, and chloride). They suggested that future work consider other constituents that might be specific to mobile sources and thus more sensitive to LEZ-related changes, including PAHs (e.g., 1-nitropyrene), and compounds in lubricating oil (e.g., hopanes and steranes).

CHARACTERIZATION OF PM OXIDATIVE POTENTIAL

The Committee had already reviewed the investigators' in vitro RTLF assay for characterizing the oxidative potential of PM in their commentary on the investigators' report of the CCS (Kelly et al. 2011). As in that study, the Committee thought there was substantial conceptual appeal to finding a toxicologically relevant measure of the aggregate PM mixture given the challenges researchers face in predicting overall toxicity of PM on the basis of the properties of its individual components. The investigators' decision to focus on some measure of the ability of PM to trigger the oxidative stress pathway was logical, given increasing focus on the hypothesis that this pathway might play a role in the observed impacts of exposure to PM on human health.

Despite the assay's appeal, the Committee determined that several important details remained to be worked out in assay design and in the interpretation of its results. In particular, as the authors acknowledged, the RTLF assay likely provides an incomplete picture of the potential toxicity of London air pollution, focusing as it does on metals in archived filters. The roles of co-pollutant gases, organic compounds (oxy- and nitro-PAHs and quinones), and other reactive species present in the mixture, which have been the focus of other acellular assays (Li et al. 2002, 2003; Xia et al. 2004; Cho et al. 2005; Venkatachari and Hopke 2008; Biswas et al. 2009), were only partly addressed by the investigators' ascorbate-only experiments. Agreement between methods applied in the same cities has not been good (Künzli et al. 2006) and no standard methods for assaying oxidative potential have been agreed upon by the scientific community.

In any case — as the investigators acknowledge — in vitro methods are not able to reflect cell-associated mechanisms of oxidative stress (e.g., respiratory burst, metabolic redox cycling, and mitochondrial dysfunction). Further research has been recommended to explore the relationship between the ability of PM or its constituents to demonstrate oxidative activity in acellular models and their ability to trigger related activity in cellular and other biologically relevant assays (Ayres et al. 2008).

Finally, the Committee thought the investigators' conclusion that much of the oxidative potential appears in the coarse mode at roadside monitoring sites and is apparently related to tire and brake wear, was intriguing. It was somewhat surprising that the study did not find higher concentrations of zinc in samples from roadside sites because it is an element that has been used as an indicator of tire wear in previous studies. However, the Committee thought that the potential importance of tire and break wear raises a larger issue regarding the use of the oxidative potential metric to shed light on the potential health impact of broader changes in emissions that might be brought about by the LEZ. In particular, the LEZ was designed to target tailpipe emissions, and unless it were to affect overall traffic levels as well (something not determined by this baseline study), it could not be expected to affect oxidative potential related to tire and brake wear as characterized by the RTLF assay used in this study. The RTLF assay's value in explaining any health impacts associated with implementing the LEZ would therefore be limited. At the same time, the findings of a possible association between oxidative potential and tire and brake wear warrant further investigation if regulation of non-tailpipe emissions is to be considered in future traffic management schemes.

METHODS FOR USE OF ELECTRONIC PRIMARY-CARE RECORDS

The Committee thought that the investigators provided a clear description of the primary-care databases that they planned to use. They demonstrated the ability to link estimated exposures to postcodes and primary-care records while recognizing the methodologic and privacy issues involved in these types of analyses. However, the Committee thought that data access would remain a significant challenge for the use of electronic primary-care data in assessing the future impacts of the LEZ. At least one major data provider — governing records for nearly 500,000 patients — indicated reluctance to release any data if there were even a remote possibility of identifying individual patients. [Note: Since the completion of the research for this study, the General Practice Research Database is now governed by the National Information Governance Board, which requires stringent procedures to ensure anonymity of the medical records and should alleviate these concerns. (Personal communication from Frank J. Kelly to Katherine Walker 8-22-2011.)]

The Committee remained unconvinced that the issue of statistical power had been adequately addressed by the investigators. The investigators utilized the magnitude of effect estimates from longitudinal studies conducted elsewhere, coupled with projected changes in exposure from the LEZ, to argue that the statistical power of the study would be sufficient. Although this is a standard approach to estimating power, the Committee pointed out that the results of the cross-sectional study of the LEZ were largely null, despite being based on much greater variation in exposure than was predicted for the longitudinal study. Future health outcomes research proposals would benefit from a rigorous investigation of actual changes in air pollutant concentrations (as opposed to projected changes) and of the resulting impact on the statistical power of the study.

The Committee recognized that there were inevitable uncertainties associated with the assumed impacts of LEZ on changes in NO_x concentrations in this power calculation. The investigators' choice of NO_x concentration as the sole measure of exposure was a compromise solution to the problem that identification of specific postcodes was possible when NO_x and PM_{10} were used together to characterize exposure. At the time, they also thought that it would be a better overall indicator of changes in traffic-related exposures and thus suitable for ranking populations according to the reduction in exposure experienced as a result of the LEZ. Another source of uncertainty given the timing of this study was that the investigators' estimates of changes in concentrations necessarily reflected assumed, rather than actual, responses of vehicle operators to the LEZ scheme. Their findings from the earlier CCS study had shown, however, that NO_x changes in response to that intervention were unexpectedly small — the apparent net effect of decreases in NO related to exhaust emissions and increases in NO_2 concentrations related to increased use of diesel particle traps.

The final challenge facing future health outcome studies of the LEZ is one that the investigators could not have anticipated. Although the first two phases of the planned implementation of the LEZ went into effect in 2008 as scheduled, implementation of the third phase covering larger vans and minibuses, has since been postponed from 2010 to 2012 (*www.tfl.gov.uk/roadusers/lez/*). Consequently, the modeling assumptions used in the current LEZ study about the declines in air pollutant emissions associated with the third phase would no longer hold. The impact of the LEZ on air quality would therefore be spread gradually over an even longer timeframe, making impacts on health potentially more difficult to detect (HEI 2010).

SUMMARY AND CONCLUSIONS

Professor Kelly and his colleagues' baseline study of the planned LEZ in London was a timely investigation of an intervention that was specifically intended to improve air quality, an intervention that is increasingly being considered in various forms in cities throughout Europe and around the world. Because London is one of the largest cities to undertake such an initiative and to enforce it using traffic-control cameras and substantial fines for vehicles that do not comply, it was a potentially fruitful subject for research.

The investigators undertook a careful stepwise approach to their study, building on methods for air quality outcomes research they had first explored in their investigation of the London CCS. Whereas the London CCS study had encountered significant gaps in the quality of data and numbers of monitors located at key roadside sites after the scheme was underway, the LEZ study was able to anticipate such problems. The investigators were able to use their air quality modeling results to help identify gaps in the monitoring network and to convince Transport for London to install additional monitoring at critical sites in advance of the LEZ implementation. Furthermore, they extended the use of their modeling studies to help assess the feasibility of linking possible future LEZ-related changes in air quality to health outcomes obtained electronically from primary-care databases in London. They developed a process for linking air quality data to primary-care health outcome data but were unable to assure all of the major providers of electronic medical records of the confidentiality of the records, thus losing potential access to data from a large number of patients.

Given that the LEZ used essentially the same methodologies as the earlier CCS study, it was not surprising that the LEZ study found similar patterns in projected air pollution concentrations across London and in the oxidative potential and metal content of archived PM filter samples. However, some of the same reservations held by the Committee in the evaluation of the CCS study also remained. Despite the much larger area affected by the LEZ, the modeled changes in PM_{10} and NO_2 were generally small. Given that this was a baseline study preceding the implementation of the LEZ, the investigators could not confirm the modeled estimates by evaluating actual monitoring data. However, the Committee suspected that the small modeled differences would be as difficult to detect in monitoring results as they had been in the CCS study. The Committee continues to view the RTLF assay as an intriguing and potentially valuable effort to characterize spatial variability in the oxidative potential of urban PM, but considers it to be

largely exploratory. Its usefulness for this study was limited because it seems primarily to measure the oxidative potential of metals that have been associated with tire and brake wear, not of the tailpipe emissions that are the target of the LEZ.

Despite these challenges, the LEZ baseline study remains a creative effort to lay the necessary groundwork to study the spatial and temporal changes in air pollutant concentrations and in health outcomes in advance of a major regulatory intervention. It provides important lessons for future research into the health outcomes of actions to improve air quality.

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