



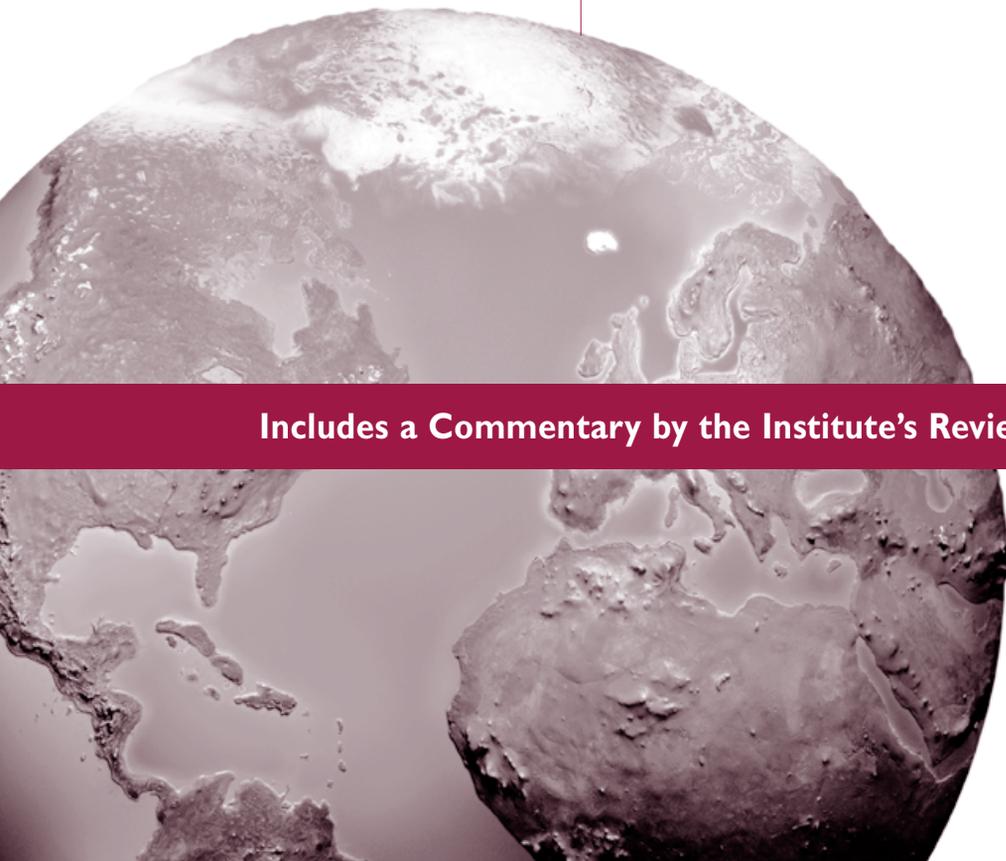
## RESEARCH REPORT

HEALTH  
EFFECTS  
INSTITUTE

Number 190  
January 2017

### **The Effects of Policy-Driven Air Quality Improvements on Children's Respiratory Health**

Frank Gilliland, Edward Avol, Rob McConnell, Kiros Berhane,  
W. James Gauderman, Fred W. Lurmann, Robert Urman,  
Roger Chang, Edward B. Rappaport, and Stephen Howland

A grayscale image of the Earth as seen from space, showing the continents and oceans. The image is partially obscured by a dark red horizontal bar at the bottom.

Includes a Commentary by the Institute's Review Committee



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with a Commentary by the HEI Review Committee



Research Report 190

Health Effects Institute

Boston, Massachusetts

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Publishing history: This document was posted at [www.healtheffects.org](http://www.healtheffects.org) in January 2017.

Citation for document:

Gilliland F, Avol E, McConnell R, Berhane K, Gauderman WJ, Lurmann FW, et al. 2017. The Effects of Policy-Driven Air Quality Improvements on Children's Respiratory Health. Research Report 190. Boston, MA:Health Effects Institute.

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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 balanced funding from the U.S. Environmental Protection Agency and 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 330 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 more than 260 comprehensive reports published by HEI, as well as in more than 1000 articles in the peer-reviewed literature.

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 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 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 Review Committee are widely disseminated through HEI's Web site ([www.healtheffects.org](http://www.healtheffects.org)), printed reports, newsletters and other publications, annual conferences, and presentations to legislative bodies and public agencies.



# ABOUT THIS REPORT

Research Report 190, *The Effects of Policy-Driven Air Quality Improvements on Children's Respiratory Health*, presents a research project funded by the Health Effects Institute and conducted by Dr. Frank Gilliland of the University of Southern California, Los Angeles, and his colleagues. The 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 Review Committee's comments on the study.

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

**The Commentary**, prepared by members of the Review Committee with the assistance of HEI staff, 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 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 Commentary reflects the information provided in the final version of the report.



# PREFACE

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## HEI's Accountability 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 *accountability research*, *outcomes 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 accountability research, Communication 11, *Assessing Health Impact of Air Quality Regulations: Concepts and Methods for Accountability Research* (HEI

Accountability Working Group 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 accountability 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 Accountability Research program, which is discussed below.

Between 2002 and 2004, HEI issued four requests for applications (RFAs), under which eight studies were funded (see Table). A ninth study was funded later, under Request for Preliminary Applications (RFP) 05-3, "Health Effects of Air Pollution." Following this first wave of research, HEI held further workshops to discuss lessons learned, identify key remaining questions, and plan a second wave of research. These efforts led to the publication of Communication 14 (van Erp and Cohen 2009) and Communication 15 (HEI 2010b), and the issuance of RFA 11-1, "Health Outcomes Research — Assessing the Health Outcomes of Air Quality Actions." The first wave of research primarily consisted of studies evaluating relatively short-term, local-scale, and sometimes temporary interventions; RFA 11-1 solicited additional studies with a focus on longer-term, regional- and national-scale regulations, including programs targeted at improving air quality surrounding major ports, as well as further methods development.

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

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## BACKGROUND

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The first step in assessing the effectiveness of air quality regulations is to measure emissions of the targeted

## Preface

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### HEI's Accountability Research Program

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RFA / Investigator (Institution)	Intervention	Study or Report Title
<b>First-Wave Studies<sup>a</sup></b>		
<b>RFA 02-1</b>		
Douglas Dockery (Harvard T.H. Chan School of Public Health, Boston, MA)	Coal ban in Irish cities	Effect of Air Pollution Control on Mortality and Hospital Admissions in Ireland (Research Report 176; 2013)
Annette Peters (Helmholtz Zentrum München–German Research Center for Environment and Health, Neuherberg, Germany)	Switch from brown coal to natural gas for home heating and power plants, changes in motor vehicle fleet after reunification of Germany	The Influence of Improved Air Quality on Mortality Risks in Erfurt, Germany (Research Report 137; 2009)
<b>RFA 04-1</b>		
Frank Kelly (King's College London, U.K.)	Measures to reduce traffic congestion in the inner city of London	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 (Research Report 155; 2011)
<b>RFA 04-4</b>		
Frank Kelly (King's College London, U.K.)	Measures to exclude most polluting vehicles from entering greater London	The London Low Emission Zone Baseline Study (Research Report 163; 2011)
Richard Morgenstern (Resources for the Future, Washington, DC)	Measures to reduce sulfur emissions from power plants east of the Mississippi River	Accountability Analysis of Title IV Phase 2 of the 1990 Clean Air Act Amendments (Research Report 168; 2012)
Curtis Noonan (University of Montana, Missoula, MT)	Wood stove change-out program	Assessing the Impact of a Wood Stove Replacement Program on Air Quality and Children's Health (Research Report 162; 2011)
Jennifer Peel (Colorado State University, Fort Collins, CO)	Measures to reduce traffic congestion during the Atlanta Olympics	Impact of Improved Air Quality During the 1996 Summer Olympic Games in Atlanta on Multiple Cardiovascular and Respiratory Outcomes (Research Report 148; 2010)
Chit-Ming Wong (University of Hong Kong)	Measures to reduce sulfur content in fuel for motor vehicles and power plants	Impact of the 1990 Hong Kong Legislation for Restriction on Sulfur Content in Fuel (Research Report 170; 2012)
<b>RFA 05-3</b>		
Junfeng (Jim) Zhang (University of Medicine and Dentistry of New Jersey, Piscataway, NJ)	Measures to improve air quality during the Beijing Olympics	Cardiorespiratory Biomarker Responses in Healthy Young Adults to Drastic Air Quality Changes Surrounding the 2008 Beijing Olympics (Research Report 174; 2013)

*Table continues next page*

<sup>a</sup> Abbreviations: RFA, Request for Applications; RFA, Request for Preliminary Applications

## Preface

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### HEI's Accountability Research Program *(continued)*

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RFA / Investigator (Institution)	Intervention	Study or Report Title
<b>Second-Wave Studies<sup>a</sup></b>		
<b>RFA 11-1</b>		
Frank Gilliland (University of Southern California)	California and federal programs to improve air quality, including control of emissions from diesel engines and other sources targeted at freight transport and ports, as well as stationary sources	The Effects of Policy-Driven Air Quality Improvements on Children's Respiratory Health (Current report)
Ying-Ying Meng (University of California—Los Angeles)	2006 California Emissions Reduction Plan for Ports and Goods Movement to control emissions from road, rail, and marine transportation, focusing on the ports of Los Angeles and Long Beach	Improvements in Air Quality and Health Outcomes Among California Medicaid Enrollees Due To Goods Movements (Study ongoing)
Armistead Russell (Georgia Institute of Technology)	Programs to control emissions from major stationary sources and mobile sources in the Southeast United States	Impacts of Emission Changes on Air Quality and Acute Health Effects in the Southeast, 1993–2012 (Report in review)
Corwin Zigler (Harvard T.H. Chan School of Public Health)	National regulations to improve air quality focusing on State Implementation Plans for particulate matter	Causal Inference Methods for Estimating Long-Term Health Effects of Air Quality Regulations (Research Report 187; 2016)

<sup>a</sup> Abbreviations: RFA, Request for Applications; RFPA, Request for Preliminary Applications

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 accountability 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 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 have been 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.

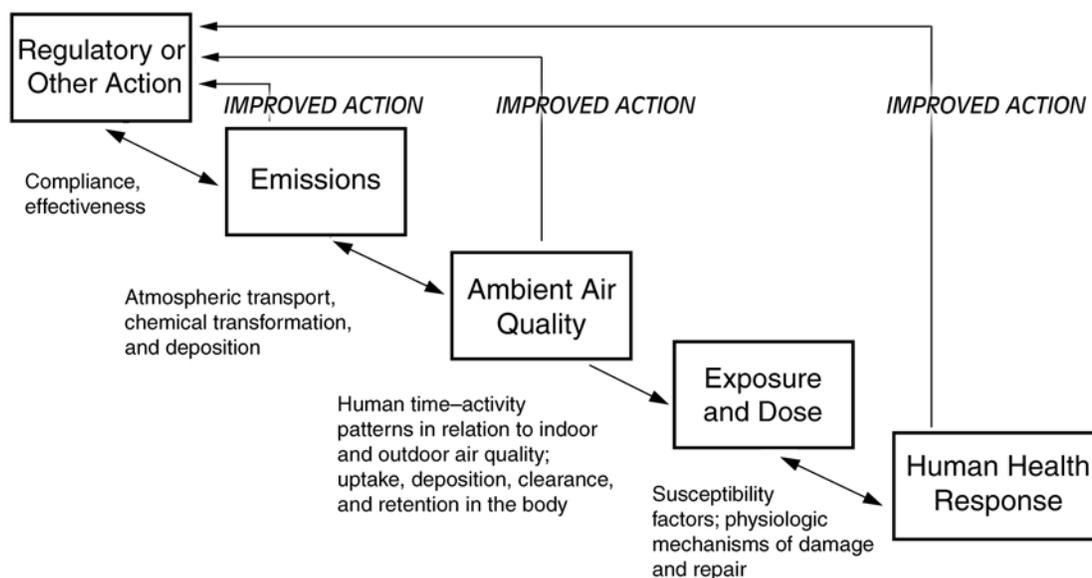
These inherent challenges are well documented in Communication 11 (HEI Accountability Working Group 2003), which was intended to advance the concept of accountability research and to foster the development of methods and studies throughout the

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 ACCOUNTABILITY 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 "accountability evaluation cycle" (see 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



**Accountability 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 accountability 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 accountability 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.

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### HEI'S ACCOUNTABILITY RESEARCH PROGRAM

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The first wave of HEI's Accountability Research program included nine studies (see Table). These studies involved the measurement of indicators along the entire accountability evaluation cycle, from regulatory or

other interventions to human health outcomes. Many 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 number of modern diesel-powered vehicles in eastern Germany. HEI also supported research, including the development of methods, in an especially challenging area, namely, assessment of the effects of regulations implemented incrementally over extended periods of time, such as those examined in the study by Morgenstern and colleagues (2012) that resulted 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.

Subsequently, HEI funded four studies as part of the second wave of HEI's Accountability program (see Table). Two studies evaluated regulatory and other actions at the national or regional level implemented over multiple years; a third study is evaluating 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 a fourth study has developed methods to support such accountability research. Gilliland and colleagues, as described in their Investigators' Report, evaluated respiratory symptoms and lung function growth in children in Southern California from 1993–2012. They used data from three cohorts of the Children's Health Study, attempting to relate changes in health outcomes to major air quality regulations during that time period (Berhane et al. 2016; Gauderman et al. 2015; Lurmann et al. 2015). Russell and colleagues are assessing the effect of major stationary source and mobile source control programs on emissions and air quality in the Southeast United States, using detailed emissions and air pollution measurements and modeling combined with time-series

analyses of cardiovascular and respiratory emergency department visits and hospital admissions. Meng and colleagues are evaluating the effects on air quality and health associated with the California Air Resources Board's Emission Reduction Plan for Ports and Goods Movement. They are examining the changes in criteria and hazardous air pollutants and characterizing health outcomes among Medicaid beneficiaries in the region surrounding the ports of Long Beach and Los Angeles. Phase 1, which focused on evaluating changes in air quality, has been completed (Su et al. 2016); Phase 2, to evaluate effects on health outcomes, is currently ongoing. Zigler and colleagues developed and applied statistical methods to evaluate long-term regulatory actions, focusing on the Clean Air Act and the role of attainment status of counties for PM<sub>10</sub>, O<sub>3</sub>, CO, and SO<sub>2</sub> concentrations. In particular, they focused on methods targeted on the question of whether air quality and health outcomes are causally related (Zigler and Domini 2014; Zigler et al. 2016).

Studies on health outcomes funded by HEI to date are summarized in the Table on pages x-xi. The first-wave studies are described in more detail in an interim evaluation of the HEI Accountability Research program (van Erp and Cohen 2009; van Erp et al. 2012).

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### FUTURE DIRECTIONS

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The second stage of accountability research was largely conceived during HEI's Strategic Plan for 2010 through 2015 (HEI 2010a). During the current Strategic Plan for 2015 through 2020 (HEI 2015), HEI will continue to look closely at opportunities for unique new contributions to accountability research. We envision that future studies will again focus on large-scale, complex regulations to improve air quality and will continue to develop and implement statistical methods to tackle these complicated questions.

In addition, HEI 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 were made available at the Johns Hopkins

Bloomberg School of Public Health Web site for several years after completion of the NMMAPS study but the site is no longer active); and

2. Data from the National Particle Component Toxicity (NPACT) initiative on concentrations of components of particulate matter with an aerodynamic diameter  $\leq 2.5 \mu\text{m}$  (PM<sub>2.5</sub>) collected at or near the 54 sites in the EPA's PM<sub>2.5</sub> Chemical Speciation Trends Network (STN) (data were made available at the Atmospheric and Environmental Research Web site until the end of 2016 but the site is no longer active).

While these databases were active, the data on pollution and health from a large number of U.S. cities, as documented by the NMMAPS team, constituted a valuable resource that allowed other researchers to undertake additional analyses, possibly including further accountability studies. The STN Web site provided scientists an opportunity to investigate specific questions about concentrations of PM<sub>2.5</sub> components and their association with adverse health effects in regions covered by the STN network and to address questions related to accountability research when interventions in these regions were 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 recommendations of this workshop 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. As part of

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the Strategic Plan 2015–2020, HEI plans to discuss the future of accountability research during the next two years.

In the interim, 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 190

### The Effects of Policy-Driven Air Quality Improvements on Children's Respiratory Health

#### INTRODUCTION

The report by Dr. Frank Gilliland and colleagues, *The Effects of Policy-Driven Air Quality Improvements on Children's Respiratory Health*, is the latest in a series of studies funded as part of HEI's accountability research program. Launched in 2001, the program has supported a number of studies aimed at evaluating whether regulatory and other actions taken to improve air quality have resulted in the intended improvements in air quality, population exposures, and health outcomes. Gilliland and colleagues' study addressed a

critical issue: assessment of the effects of regulatory actions taken at both a national and a regional level that have been implemented over multiple years.

The investigators built on their earlier work in the Children's Health Study (CHS), which has for more than 20 years been evaluating associations between levels of several major outdoor pollutants and the respiratory health of children who live in Southern California. The CHS has shown that long-term exposure of children to elevated levels of outdoor air pollution has adverse effects on the development of their lung function and that exposure to

#### What This Study Adds

- Gilliland and colleagues addressed a key public health issue: Do regulations enacted to decrease emissions of major outdoor air pollutants result in long-term decreases in levels of the targeted pollutants and in improvements in the health of the exposed population?
- A major strength of the study was that it used data on PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, O<sub>3</sub> levels, and lung function and respiratory symptoms collected over 20 years as a part of the Children's Health Study, covering three cohorts living in Southern Californian communities; these communities had different air pollution characteristics allowing for cross-cohort comparisons.
- Nearly 20 major policy actions were implemented in Southern California from 1993 to 2012 to reduce pollution from transportation and other sources. Emissions and ambient levels of pollutants decreased during that period, but the large number of regulations made it difficult to link any specific action to an improvement in air quality.
- Decreases in long-term community-level averages of pollutants — particularly NO<sub>2</sub> and PM<sub>2.5</sub> — were associated with increased growth of children's lung function across the cohorts. Decreases in levels of NO<sub>2</sub>, PM<sub>2.5</sub>, PM<sub>10</sub>, and O<sub>3</sub> were associated with decreased prevalence of respiratory symptoms (bronchitis, cough, and phlegm), particularly in children with asthma.
- The Review Committee agreed with the major findings of this study, which were that emissions and pollutant levels decreased and the children's health status improved. There was, however, variability in the relationship between pollution decreases and changes in lung function and respiratory symptom measures among the communities, suggesting that unexplored between- and within-community factors could be important. The Committee also pointed to other areas where future research may be fruitful.
- These findings are important in indicating the potential for notable health benefits from the decreasing levels of major outdoor pollutants resulting from public policy measures.

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Dr. Frank Gilliland at the University of Southern California, Los Angeles, and colleagues. Research Report 190 contains both the detailed Investigators' Report and a Commentary on the study prepared by the Institute's Review Committee.

outdoor pollution in Southern California was associated with increased symptoms of airway disease in children.

Over the course of the CHS, the United States Environmental Protection Agency and regional agencies (including the California Air Resources Board) put in place many different regulations intended to curb emissions and reduce pollutant levels, and the levels of many outdoor pollutants have decreased in Southern California over the time period. Thus, the first goal of the current study was to identify the major air quality regulations for mobile, stationary, and area source emissions, enforced both nationally and in California over the 20 years between 1993 and 2012, and link them to improvements in air quality in Southern California communities. The second goal was to explore associations between the decreases in long-term levels of major outdoor pollutants and improvements in children's respiratory health over the same time period.

The focus of the respiratory health aspects of the current study were lung growth and symptoms of respiratory conditions: the investigators assessed how the observed decreases in pollutant levels affected the development of lungs in children during their teenage years, a crucial period for lung development. After the teenage years, there is little growth in lung size or capacity, and lung size at age 18 is a predictor of respiratory and cardiovascular morbidity and mortality in later life. The investigators also asked how the long-term changes in pollutant levels affected symptoms of respiratory conditions in children between ages 9 and 18. Outdoor pollutants affect children with asthma more than children without asthma, and the incidence of asthma has grown over the last several decades.

### APPROACH

#### Study Participants and Health Data

The goal of the study was to evaluate changes in outdoor pollutant levels and in participants' lung function and respiratory symptoms in communities that had data for children of the same ages across three cohorts recruited at different times over the course of the CHS (1992–1993 for Cohort C, 1995–1996 for Cohort D, and 2002–2003 for Cohort E). Participants were drawn from five CHS communities for lung-function analysis and eight CHS communities for the respiratory symptoms analysis —

the same five communities in the lung-function analysis plus three others. Continuous pollution measurements had been collected in these eight communities over the 20 years of the CHS.

The principal markers of lung function used in the lung-growth substudy were forced expiratory volume in the first second of exhalation (FEV<sub>1</sub>) and forced vital capacity (FVC). FEV<sub>1</sub> and FVC were measured annually for children between the ages of 10 and 18 in Cohorts C and D and every 2 years (at approximate ages 11, 13, and 15) in Cohort E. The investigators then calculated the 4-year growth in FEV<sub>1</sub> and FVC for the children in all three cohorts ( $N = 2,120$ ) between the ages of 11 and 15. Using data from the children for whom they had data at both ages 11 and 15 in all three cohorts ( $n = 1,585$ ), they also calculated the percentage of children in each cohort who had clinically important deficits in FEV<sub>1</sub> and FVC using three cutoffs (<90%, 85%, or 80% of expected function for that age), taking into account such factors as ethnicity, sex, height, and body mass index.

From responses to annual questionnaires, the investigators also collected information for the respiratory symptoms substudy about each child's asthma status and respiratory symptoms over the previous 12 months. Data were analyzed from all children from ages 9 to 18 years old ( $N = 4,602$ ) in the eight communities in all three cohorts. The questionnaires also provided other relevant information, including age, sex, race, ethnic background, insurance coverage, and education of parents; prior and current health conditions; and other potential sources of pollutant exposure in the home, such as environmental tobacco smoke and the presence of a dog or cat.

#### Exposure Assessment

Beginning in 1994 for the original 12 CHS communities, the investigators collected measurements at one central site in each community of levels of nitrogen dioxide (NO<sub>2</sub>), particulate matter (PM) equal to or less than 2.5 microns in aerodynamic diameter (PM<sub>2.5</sub>), PM equal to or less than 10 microns in aerodynamic diameter (PM<sub>10</sub>), and ozone (O<sub>3</sub>). The investigators calculated daily and monthly averages for each pollutant and calculated an annual average in each community from the monthly averages. For the lung-function substudy, the investigators calculated the mean air pollutant concentrations for each community over the relevant 4-year exposure period for each cohort. In the respiratory symptoms

substudy, the investigators used community-specific annual averages of PM<sub>10</sub>, PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub> to compute cohort-specific mean levels for the relevant period of follow-up (9 years in Cohorts C and D, 10 years for Cohort E). Because asthma symptoms were defined in the year before the children responded to the questionnaire, the investigators used a 1-year lagged annual average for each pollutant in the symptom substudy.

### Statistical Methods

The main goal of the lung-function substudy was to estimate the association of individual pollutants with the growth of lung function in children between the ages of 11 and 15, as measured by FEV<sub>1</sub> and FVC. Because lung-function growth is non-linear, the investigators used a linear spline model they had previously developed, with knots at ages 12, 14, and 16, to construct growth curves of lung function over the entire age range of the cohorts (approximately 9 to 19 in Cohorts C and D and 10 to 16 in Cohort E) in the five communities in which they had measured children's lung function. The model included adjustments for factors such as sex, race, ethnicity, height, and body mass index.

To determine whether the changes in the proportion of children with clinically important deficits in FEV<sub>1</sub> and FVC at age 15 were associated with long-term changes in air quality, Gilliland and colleagues used data from all three cohorts to develop linear prediction models for FEV<sub>1</sub> and FVC that included adjustments for factors that included age, sex, race and ethnicity, height, and body mass index. They then used a logistic regression model to test for temporal trends in the proportion of children with low lung function.

To estimate associations between cohort- and community-specific levels of individual pollutants and respiratory symptoms, the investigators used multilevel models they had developed previously. Data were analyzed from all children ( $N = 4,602$ ) from ages 9 to 18 years old in the eight communities in all three cohorts. Sensitivity analyses included owning a dog or cat and exposure to secondhand smoke in the home.

### Regulations and Emissions

Gilliland and colleagues identified nearly 20 major policies introduced at the national or California-wide level at various times between 1985 and 2012 that they predicted would have major impacts on air

pollution. The investigators then used information from the California Air Resources Board and the South Coast Air Quality Management District, agencies responsible for air pollution regulations affecting Southern California, to make "backcasted" estimates of air pollutant emissions in multiple categories for oxides of nitrogen (NO<sub>x</sub>), PM<sub>2.5</sub>, PM<sub>10</sub>, oxides of sulfur (SO<sub>x</sub>), and reactive organic gases (ROG). They made estimates for 1993 and 2011 in various parts of Southern California (the Southern California Basin around Los Angeles as well as Santa Barbara and San Diego counties).

### KEY RESULTS

Total emissions of NO<sub>x</sub>, ROG, PM<sub>2.5</sub>, PM<sub>10</sub>, and SO<sub>x</sub> and emissions in nearly all major categories (stationary, area-wide, on-road and other mobile sources) decreased in Southern California between 1993 and 2012. The largest decrease was in NO<sub>x</sub> and ROG emissions from on-road motor vehicles.

Annual levels of individual pollutants, particularly NO<sub>2</sub> and PM<sub>2.5</sub>, generally decreased over the course of the study, with the lowest multiyear average levels recorded in Cohort E, the most recently recruited cohort. However, the investigators noted that the large number of air quality policies put in place by national and state agencies made it difficult to link any specific action to any specific improvements in air quality.

The two principal health findings of the study were that, first, decreases in multiyear average levels of outdoor pollutants — particularly NO<sub>2</sub> and PM<sub>2.5</sub> — were associated with cross-cohort improvements in the growth of children's lung function; in Cohort E, with the lowest overall levels of outdoor pollutants fewer children had clinical deficits in FEV<sub>1</sub> and FVC at age 15 than did children in the other two cohorts. Second, decreases in the levels of outdoor pollutants (NO<sub>2</sub>, PM<sub>2.5</sub>, PM<sub>10</sub>, and O<sub>3</sub>) were associated with cross-cohort decreases in the prevalence of symptoms of respiratory conditions in children at ages 10 and 15, particularly in children with asthma. The association between the reduction in levels of NO<sub>2</sub> and PM<sub>2.5</sub> and the decrease in respiratory symptoms in children with asthma at both ages 10 and 15 was greater in boys and among children with family dog ownership.

### CONCLUSIONS

The HEI Review Committee considered that Gilliland and colleagues conducted an important study

to evaluate the outcomes of long-term regulatory actions. The study assessed how air pollution regulations introduced during the study period affected emissions and ambient levels of air pollutants in Southern California and whether changes in pollutant levels were, in turn, associated with improvements in children's respiratory health.

A major strength of the study was that it brought together extensive pollutant monitoring data and health effects information collected over 20 years in this unique and well-studied dataset from participants in the CHS. The investigators used data from a large number of children who lived in several communities in Southern California that differed in sources and levels of major pollutants (NO<sub>2</sub>, PM, and O<sub>3</sub>). They also collected detailed information about the children's health and relevant covariates in the cohort population.

The investigators found that emissions of pollutants and precursors decreased over the 20-year time frame of the study, as did most ambient pollutant levels, and particularly in communities with initially high levels of NO<sub>2</sub> and PM<sub>2.5</sub>. Gilliland and colleagues noted that the large number of pollution control policy measures taken, with a focus on reducing motor vehicle and other emissions, made it difficult to link any specific action closely to a specific improvement in air quality. The Committee agreed that the regulations likely did contribute to those reductions, although it also noted the absence of analyses for other factors that might have contributed to changes in pollutant emissions.

The major health findings of the study were that decreases in long-term community-level averages of pollutants (particularly NO<sub>2</sub> and PM<sub>2.5</sub>) across cohorts were associated with increased growth of children's lung function. In addition, in the cohort with the lowest overall levels of outdoor pollutants (Cohort E) there were fewer children with clinically relevant deficits in FEV<sub>1</sub> and FVC at age 15 than in the other two cohorts. Furthermore, decreases in levels of NO<sub>2</sub>, PM<sub>2.5</sub>, PM<sub>10</sub>, and O<sub>3</sub> were also associated with decreases in the prevalence of bronchitic symptoms across the cohorts, particularly in children with asthma.

The Committee agreed with these health findings. However, it noted that the changes in lung function and respiratory symptoms were not uniform with regard to decreases in pollutant levels across the communities. There was, however, variability in the relationship between pollution decreases and changes in lung-function and respiratory symptom measures among the communities. This variability in lung-function and respiratory-symptoms results across communities suggested that unexplored between-community and within-community factors could be important. In addition, for all analyses, the reliance on multiyear averages from a single central monitor in each community likely reduced the ability to understand how exposure varied within a community and how to assess the impact of regulations and emissions reductions.

In summary, the Committee concurred with the investigators that decreases in levels of major outdoor pollutants were associated with improvements in children's health. However, the Committee noted that the analyses did not fully consider some differences between successive cohorts over time that might also have contributed to improvements in children's health making it more challenging to draw strong conclusions from the study unless alternative explanations for the health benefits can be ruled out.

Taken together, the findings of this important contribution to the accountability literature indicate that regulations directed toward reductions in emissions of mobile-source and other pollutants over the course of the study by national and California agencies were likely contributors to improvements in air quality that were linked to improvements in children's health, although the regulations themselves could not be definitively linked to the health improvements. Even so, the findings suggest the potential for important public health benefits resulting from levels of major outdoor pollutants that have been decreasing as a result of public policy measures.

## The Effects of Policy-Driven Air Quality Improvements on Children's Respiratory Health

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### ABSTRACT

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#### INTRODUCTION

Ambient air pollution causes substantial morbidity and mortality in the United States and worldwide. To reduce this burden of adverse health effects, a broad array of strategies to reduce ambient air pollution has been developed and applied over past decades to achieve substantial reductions in ambient air pollution levels. This has been especially true in California, where the improvement of air quality has been a major focus for more than 50 years. Direct links between regulatory policies, changes in ambient pollutant concentrations, and improvements in public health have not been extensively documented. Data from the Children's Health Study (CHS\*), a multiyear study of children's respiratory health development, offered a unique opportunity to evaluate the effects of long-term reductions in air pollution on children's health.

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This Investigators' Report is one part of Health Effects Institute Research Report 190, which also includes a Commentary by the Review Committee and an HEI Statement about the research project. Correspondence concerning the Investigators' Report may be addressed to Dr. Frank Gilliland, 2001 N. Soto Street, MC 9237, Los Angeles, CA 90089; e-mail: [gillilan@usc.edu](mailto:gillilan@usc.edu).

Although this document was produced with partial funding by the United States Environmental Protection Agency under Assistance Award CR-83467701 to the Health Effects Institute, it has not been subjected to the Agency's peer and administrative review and therefore may not necessarily reflect the views of the Agency, and no official endorsement by it should be inferred. The contents of this document also have not been reviewed by private party institutions, including those that support the Health Effects Institute; therefore, it may not reflect the views or policies of these parties, and no endorsement by them should be inferred.

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

#### METHODS

We assessed whether changes in ambient air quality and emissions were reflected in three important indices of children's respiratory health: lung-function growth, lung-function level, and bronchitic symptoms. To make the best use of available data, these analyses were performed across the longest chronological period and largest CHS population available for the respective lung-function or bronchitic symptoms data sets. During field study operations over the course of the CHS, children's health status was documented annually by testing lung-function performance and the completion of standardized questionnaires covering a broad range of respiratory symptoms. Air quality data for the periods of interest were obtained from community monitoring stations, which operated in collaboration with regional air monitoring networks over the 20-year study time frame. Over the 20-year sampling period, common protocols were applied to collect data across the three cohorts of children. Each cohort's data set was assessed to investigate the relationship between temporal changes in lung-function development, prevalence of bronchitic symptoms, and ambient air pollution concentrations during a similar, vulnerable adolescent growth period (age 11 to 15 years). Analyses were performed separately for particulate matter  $\leq 10 \mu\text{m}$  in aerodynamic diameter ( $\text{PM}_{10}$ ), particulate matter  $\leq 2.5 \mu\text{m}$  in aerodynamic diameter ( $\text{PM}_{2.5}$ ), ozone ( $\text{O}_3$ ), and nitrogen dioxide ( $\text{NO}_2$ ). Emissions data and regulatory policies were collected from the staff of state and regional regulatory agencies, modeling estimates, and archived reports.

#### RESULTS

Emissions in the regions of California studied during the 20-year period decreased by 54% for oxides of nitrogen ( $\text{NO}_x$ ), 65% for reactive organic gases (ROG), 21% for

PM<sub>2.5</sub>, and 15% for PM<sub>10</sub>. These reductions occurred despite a concurrent 22% increase in population and a 38% increase in motor vehicle miles driven during that time frame (State of California 2007; 2015a,b). Air quality improved over the same time frame, with reductions in NO<sub>2</sub> and PM<sub>2.5</sub> in virtually all of the CHS communities. Annual average NO<sub>2</sub> decreased by about 53% (from ~41 to 19 ppb) in the highest NO<sub>2</sub>-reporting community (Upland) and by about 28% (from ~10 to 7 ppb) in one of the lowest NO<sub>2</sub>-reporting communities (Santa Maria). Reductions in annual average PM<sub>2.5</sub> concentrations ranged from 54% (~33 to 15 µg/m<sup>3</sup>) in the community with the highest concentration (Mira Loma) to 13% (~9 to 8 µg/m<sup>3</sup>) in a community with one of the lowest concentrations (Santa Maria). Improvements in PM<sub>10</sub> and O<sub>3</sub> (measured during eight daytime hours, 10 AM to 6 PM) were most evident in the CHS communities that initially had the highest levels of PM and O<sub>3</sub>. Trends in annual average NO<sub>2</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> ambient air concentrations in the communities with higher-pollution levels were generally consistent with observed trends in NO<sub>x</sub>, ROG, PM<sub>2.5</sub>, and PM<sub>10</sub> emissions.

Significant improvements in lung-function growth in progressive cohorts were observed as air quality improved over the study period. Improvements in four-year growth of both forced expiratory volume in the first second of exhalation (FEV<sub>1</sub>) and forced vital capacity (FVC) were associated with declining levels of NO<sub>2</sub> ( $P < 0.0001$ ), PM<sub>2.5</sub> ( $P < 0.01$ ), and PM<sub>10</sub> ( $P < 0.001$ ). These associations persisted after adjustment for important potential confounders. Further, significant improvements in lung-function growth were observed in both boys and girls and among asthmatic and non-asthmatic children. Within-community decreases in O<sub>3</sub> exposure were not significantly associated with lung-function growth. The proportion of children with clinically low FEV<sub>1</sub> (defined as <80% predicted) at age 15 declined significantly, from 7.9% to 3.6% across the study periods, respectively, as the air quality improved ( $P < 0.005$ ). We found little evidence to suggest that improvements in lung-function development were attributable to temporal confounding.

Reductions in outdoor levels of NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> across the cohort years of participation were associated with significant reductions in the prevalence of bronchitic symptoms regardless of asthma status, but observed improvements were larger in children with asthma. Among asthmatic children, the reductions in prevalence of bronchitic symptoms at age 10 were 21% ( $P < 0.01$ ) for NO<sub>2</sub>, 34% ( $P < 0.01$ ) for O<sub>3</sub>, 39% ( $P < 0.01$ ) for PM<sub>10</sub>, and 32% ( $P < 0.01$ ) for PM<sub>2.5</sub> for reductions of 4.9 ppb, 3.6 ppb, 5.8 µg/m<sup>3</sup>, and 6.8 µg/m<sup>3</sup>, respectively. Similar reductions in prevalence of bronchitic symptoms were observed at age 15 among these same asthmatic children. As in the

lung-function analyses, we found little evidence that temporal confounding accounted for the observed associations of symptoms reduction with air quality improvement.

The large number and breadth of regulatory activities, as well as the prolonged phase-in periods of several policy approaches to reduce emissions, precluded the close temporal linkage of specific policies with specific changes in health status. However, the combination of policies addressing motor vehicle emissions — from on-board diagnostics to emission controls, from low-sulfur fuels to vehicle smog-check recertification, and from re-formulated gasoline to the various strategies contained within the San Pedro Bay Ports Clean Air Plan (especially the Clean Truck Program) — all contributed to an impressive and substantial reduction in emissions. These reductions collectively improved local and regional air quality, and improvements in local and regional air quality were associated with improvements in respiratory health.

## CONCLUSIONS

This study provides evidence that multiyear improvements in air quality and emissions, primarily driven through a broad array of science-based regulatory policy initiatives, have resulted in improved public health outcomes. Our study demonstrates that improvements in air quality, brought about by science-based regulatory actions, are associated with improved respiratory health in children. These respiratory health metrics include reductions in respiratory symptoms and improvements in lung-function development in a population widely accepted to be at risk and highly vulnerable to the effects of air pollution. Our research findings underscore the importance of sustained air regulatory efforts as an effective means of achieving improved respiratory health in communities and regions affected by airborne pollution.

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## INTRODUCTION

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Recent decades have witnessed marked improvements in outdoor air quality levels for several ambient air pollutants of human health concern. This has especially been true in Southern California, where air pollution has been historically persistent and pervasive. Exposure to elevated levels of ambient air pollutants has been associated with an increasingly wide spectrum of adverse health effects across the life course. The effects of chronic exposure to elevated pollution levels on children's respiratory health are of special concern because childhood respiratory diseases are common, and adverse effects during vulnerable periods of growth and development are likely to have lifelong health consequences.

The Children's Health Study began in the early 1990s and is a multiyear investigation of longitudinal respiratory growth and development of children enrolled in public schools in multiple communities of Southern California (Peters et al. 1999a,b). For more than two decades, study investigators have quantified and documented adverse health effects associated with growing up in communities with poor air quality. CHS investigators have annually assessed the respiratory health of thousands of Southern California schoolchildren and examined the effects of concurrently monitored ambient air pollutants. Published findings from the CHS (Avol 2001; Gauderman et al. 2000, 2002, 2004; McConnell et al. 1999, 2003) have been used at all levels of policy making to support regulations designed to protect public health by improving air quality.

Development of lung function in children offers a sensitive indicator for assessing the effects of exposure reductions during the period of childhood growth and development. Other investigators have suggested that improved air quality over a short time period could result in lung-function benefits for children aged 11–14 years (Frye et al. 2003), and thus has the potential to impact long-term respiratory health. Normal lung-function development during childhood is a prerequisite for optimal respiratory health across the life course. The normal trajectory of lung function over a lifetime typically shows rapid growth until the late teens or early twenties. In the mid-twenties (among nonsmokers without respiratory symptoms), lung function reaches a maximum plateau and then begins a slow but steady annual decline. If lung-function growth is substantively impaired, reduced growth rates can lead to lungs that fail to reach their developmental potential, resulting in respiratory symptoms earlier in life than otherwise might be expected. Reduced lung-function growth rates may also be followed by a period of accelerated decline, leading to early onset of chronic respiratory diseases (Lange et al. 2015).

We have previously reported that long-term exposures to elevated levels of air pollution have adverse effects on children's lung-function development (Gauderman et al. 2000, 2002, 2004). The effects of air pollution on postnatal growth, as observed in the CHS, indicate that lung-function growth is diminished in children growing up in communities with high levels of fine PM ( $PM_{2.5}$ ) and  $NO_2$ . Children in communities with high levels of larger-diameter PM ( $PM_{10}$ ) and related pollutants had an average 10% deficit in regional airflows and fivefold increase in the proportion with clinically relevant deficits (less than 80% predicted) compared with children residing in less-polluted areas (Gauderman et al. 2004). The largest effects of  $PM_{2.5}$ ,  $PM_{10}$ , and  $NO_2$  have been documented for measures of small airway function (Gauderman et al. 2004, 2007).

The impact of transportation change on childhood asthma events has been previously reported (Friedman et al. 2001). In past studies, we have also reported the substantial impact of ambient pollution on bronchitic symptoms in vulnerable children with asthma (McConnell et al. 1999, 2003, 2006b). Chronic productive cough and bronchitis are considered a complex of nonspecific symptoms among children, especially those suffering from asthma. This symptom complex was shown to be sensitive to ambient PM effects more than 20 years ago in the Harvard Six-Cities study (Dockery et al. 1989) and was replicated across multiple CHS cohorts (McConnell et al. 1999, 2003). The observed associations occurred in CHS children with asthma, but we also observed ~40% prevalence of annual bronchitic symptoms in the higher-PM CHS communities. The prevalence was approximately double that observed in lower-pollution communities and tenfold higher than that observed among children without asthma. We have developed novel statistical methods to examine the temporal variation in symptoms and additional susceptibility characteristics, which provided additional evidence for a highly plausible role of air pollution (McConnell et al. 2003, 2006b). These methods provided a framework for accounting for relevant yearly variation in pollution and symptoms in order to identify the effects of long-term reductions in air pollution levels. Although there has been relatively little research into the pathogenesis of chronic productive cough associated with air pollution in children with asthma, recent research by CHS investigators has shown that bronchitic symptoms have large consequences in burden-of-asthma exacerbation (Künzli et al. 2008; Perez et al. 2009).

Studies investigating the chronic effects of changing PM levels on respiratory health have been limited, largely because the appropriate cohort resources have not been available. There are a few epidemiologic studies of air pollution and health effects that have taken advantage of real-world experiments in which regulatory actions led to large reductions in ambient air pollution levels. A common feature of these studies of intervention programs is that a ban on a particular air pollution source, over a short time scale, resulted in acute reductions in ambient pollution levels. In these studies, declines in various metrics of morbidity, such as asthma events, were found to be associated with the acute reduction in ambient pollution levels. In these studies, the observed magnitude of health changes varied, but decreases in asthmatic events ranged up to 42%, whereas declines in mortality were generally between 2% to 15% (Bayer-Oglesby et al. 2005; Clancy et al. 2002; Dockery et al. 2013; Hedley et al. 2002; Peel et al. 2010; Rich et al. 2012).

A large body of evidence linking negative human health outcomes with elevated concentrations of O<sub>3</sub>, NO<sub>2</sub>, carbon monoxide (CO), and PM has led to tightening of state and National Ambient Air Quality Standards (NAAQS) ([www.epa.gov/criteria-air-pollutants/naaqs-table](http://www.epa.gov/criteria-air-pollutants/naaqs-table)). As required under the Federal Clean Air Act (CAA) amendments of 1977, state implementation plans (SIPs) have been developed and updated to identify the emission control strategies needed to achieve NAAQS compliance. In regions with severe air pollution, increasingly stringent and broad emission control regulations and programs have been implemented to enable progress towards increasingly tighter NAAQS. California SIPs have included emission control programs covering virtually all controllable sources, including on-road mobile, stationary, off-road mobile, and areawide sources.

National emissions reductions programs have resulted in significant air quality improvements. The U.S. Environmental Protection Agency (EPA) estimates that since the enactment of the CAA in 1970, pollution levels have been decreased by almost two-thirds, and that today's cars emit a few percent of the smog-forming pollutants their predecessors did only decades ago (U.S. EPA 2016). Additionally, the EPA has estimated that clean air programs have prevented hundreds of thousands of premature deaths (U.S. EPA 2016). Most of the available evidence however has not linked specific regulatory policies to specific air pollution reductions or subsequent improvements in human health.

A primary objective of our current study was to assess relationships between emission reduction regulations, changes in air pollution concentrations, and children's respiratory health. In this investigation, we hypothesized that regulatory-driven improvements in ambient air quality for PM and NO<sub>2</sub> since 1993 have resulted in improved air quality in many Southern California communities. We further hypothesized that the improvements in local and regional air quality have resulted in substantial improvement in children's health. Moreover, we predicted that these improvements in children's health could be observed by comparing the respiratory health status of the current generation of schoolchildren to previous generations of children who had grown up in the same communities but in more polluted environments.

We examined data collected in the CHS over a 20-year period, from the 1990s to the present. We specifically assessed whether changes in ambient air quality and emissions were, in fact, reflected in changes in children's respiratory health indices. The respiratory health indices we utilized were lung-function level, lung-function growth, and prevalence of bronchitic symptoms.

In the CHS, children's health status was documented annually by school-based testing of lung-function performance and parental or student completion of standardized questionnaires covering a broad range of respiratory symptoms. Air quality data for the periods of interest were obtained from community monitoring stations. These monitoring locations were operated by or in collaboration with regional air monitoring agencies in the study's communities of interest over the 20-year time frame of the study. All of the data collected over the 20-year period of study were collected using common protocols. The results from three children's cohort study periods were compared. The study periods for lung function included 1994 to 1998 (identified for tracking purposes as CHS Cohort C), 1997 to 2001 (Cohort D), and 2007 to 2012 (Cohort E). Participant data for bronchitis symptoms were available from study participants in eight of the CHS communities for all three extended cohort time frames of interest. The corresponding periods for bronchitic symptoms included 1993 to 2001 (Cohort C), 1996 to 2004 (Cohort D), and 2003 to 2012 (Cohort E). Because of financial restrictions during various phases of field operations of the CHS, lung-function test data were available only for study participants from five of the eight CHS communities across the three cohort time periods. To optimize the analytical potential for each respective health outcome, we elected to include as much of the collected health and air monitoring data as possible for each analysis.

The age window for analytical comparison across the three study cohorts was 11 to 15 years for lung function. This age range represents a vulnerable adolescent growth window and was the widest possible window for which all cohorts could contribute useful information at the time of the analysis. Analyses were performed for each air pollutant of interest (PM<sub>10</sub>, PM<sub>2.5</sub>, O<sub>3</sub>, and NO<sub>2</sub>) and included subgroup analyses and careful assessment for temporal confounding. Information pertaining to emissions data and regulatory policies was obtained from the staff of state and regional regulatory agencies, modeling estimates, and archived reports.

This report summarizes the results from our assessment of emissions trends, the effects on air quality, and changes in children's respiratory health. We evaluated the public health effectiveness of air pollution regulatory policies by comparing the relative health impacts of policies incurred at the time of longitudinal respiratory health testing of three successive cohorts of California schoolchildren between 1993 and 2012. We assessed the effectiveness of regulatory policies with regard to air quality by comparing emission inventories and ambient air quality monitoring data for the respective regional areas and CHS communities over the same time period. The results from these parallel and complementary analyses provided important perspectives of the

connections between science-based regulatory policies meant to affect air quality and improvements in long-term respiratory health among children (Berhane et al. 2016; Gauderman et al. 2015; Lurmann et al. 2015).

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## SPECIFIC AIMS

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Our study addressed three specific aims:

**Aim 1:** To develop a list of critical air quality regulations in existence between 1993 and 2012 for mobile, stationary, and area source emissions in Southern California and link them to improvements in measured air quality.

**Aim 2:** To determine whether improvements in long-term PM<sub>10</sub>, PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub> ambient levels within CHS communities resulted in increased lung-function level and growth.

**Aim 3:** To determine whether improvements in long-term PM<sub>10</sub>, PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub> ambient levels within CHS communities resulted in decreased chronic bronchitic symptoms among children with and without asthma.

The data needed to address these aims were largely collected in the performance of a 20-year investigation of the respiratory growth and development of California public schoolchildren. As described in the following sections, health data were routinely collected in the course of the study. Continuously sampling air-monitoring networks were operated across the study region. Retrospectively, emissions data and policy information were collected to provide a firm and credible data foundation upon which to assess the objective of connecting policies and regulations to changes in emissions and air quality.

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## PART 1: AIR QUALITY POLICIES, AND AIR POLLUTION, EMISSIONS CHARACTERISTICS, AND TRENDS

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### DOCUMENTATION OF EMISSIONS CONTROL POLICIES AND TRENDS

Broad emissions control programs affecting stationary sources, area sources, on-road mobile sources, and other mobile sources were initiated in the 1970s and expanded and strengthened in subsequent decades. These programs were a combination of federal, state, and regional regulatory efforts.

Our emissions evaluation approach was consistent with tracking procedures used by the California Air Resources

Board (CARB) and the South Coast Air Quality Management District (SCAQMD), two key agencies responsible for air emission regulations and programs affecting Southern California communities. Planning and emissions inventory staff of both agencies were interviewed to confirm that although estimates of the emission reductions of individual rules and programs were made at the time of program inception, little effort has typically been made to track individual policy effects after passage of rules. Instead, trends in annual emissions inventories and air quality are relied upon to assess overall program effectiveness.

Despite the achievements made in improving air quality in Southern California, no one (to our knowledge) has presented an accountability analysis of the air pollution reduction policies for the decades-long efforts of pollution control. Accountability analyses are performed every five years or so, as part of air quality management plan (AQMP) emission inventory updates. Each AQMP update identifies the control measures implemented (and their estimated emission reductions) since the previous AQMP and provides new baseline emission estimates. However, because of the historical bias towards underestimation of actual emission rates (e.g., underestimation of motor vehicle emissions and omission of whole categories of area-source emissions), the AQMPs often used inconsistent baseline emissions data rates for the 1988 to 2007 time periods, and the differences in baseline emissions are not easily reconciled. To help address this shortcoming, the CARB provided “backcasted” emission inventories for the affected time periods.

For this study, we focused on policies responsible for changes in annual average NO<sub>2</sub> and PM<sub>2.5</sub> concentrations between 1993 and 2011. This approach was chosen because NO<sub>2</sub> and PM<sub>2.5</sub> are two NAAQS pollutants for which we have previously reported associations with children’s respiratory health (Gauderman et al. 2000, 2002, 2004; McConnell et al. 1999, 2003). Because both NO<sub>2</sub> and PM<sub>2.5</sub> are directly emitted and also chemically formed in the atmosphere, information on policies influencing NO<sub>x</sub>, PM<sub>2.5</sub>, oxides of sulfur (SO<sub>x</sub>), and ROG emissions was needed to properly implement the stated objective of pollutant-relevant regulatory review. This is because NO<sub>x</sub> emissions influence both NO<sub>2</sub> and PM<sub>2.5</sub> nitrate levels, SO<sub>x</sub> emissions affect PM<sub>2.5</sub> sulfate levels, and ROG and NO<sub>x</sub> emissions affect the rates of ROG, NO<sub>x</sub>, and SO<sub>x</sub> oxidation, which in turn influence levels of PM<sub>2.5</sub> organic aerosol, PM<sub>2.5</sub> nitrate, and PM<sub>2.5</sub> sulfate. Relationships between primary emissions and secondary constituents also may be nonlinear because of the nature of atmospheric chemical reactions. However, the nonlinearities are diminished for long averaging times and are less important for NO<sub>2</sub> and secondary PM<sub>2.5</sub> than for O<sub>3</sub> (Seinfeld and Pandis 1998).

A number of factors complicated determination of the accountability for ambient NO<sub>2</sub> and PM<sub>2.5</sub> concentrations changes for this region and time period. Emissions were likely influenced by a large number of control measures and programs. Many programs overlapped and evolved over time. Therefore, the magnitude and timing of the effects of many individual measures are not well known and were often difficult to quantify. As scientific knowledge of emissions has improved with time, estimates of historical baseline inventories have increased in magnitude and categories.

In recognition of these complexities, uncertainties, and limitations, we adopted a simplified approach with a focus on major control measures and programs that occurred during the study period of interest. Our approach was to identify major control measures and programs and then estimate emission reductions using backcasted emission inventory data. The geographic focus was on the South Coast Air Basin (SoCAB) — the airshed surrounding Los Angeles — which arguably underwent some of the most significant air quality changes in the country.

Emissions inventory trends data were acquired from the CARB's California Emissions Projection Analysis Model (CEPAM Nov. 2012 Version) and CARB's California on-road mobile source emissions model EMFAC2011 (Version 1.0). The CEPAM model and database contain "backcasted" emissions for criteria air pollutants from 2008 to 1988 and forecasted emissions from 2009 to 2020. CEPAM uses emissions data from CARB's 2009 Air Quality Almanac, which in turn includes 2008 emissions data and estimates (Cox et al. 2009). We chose to use the 2009 version because it also included pre-2000 emission estimates, which more current versions omit. However, on-road mobile source emissions in the 2009 Almanac were estimated from the EMFAC2007 (Version 2.3) model. Following recommendations from CARB staff, we updated the CEPAM on-road mobile emission estimates with estimates derived from the newer EMFAC2011 model for the study areas of interest. Differences between EMFAC2007 and EMFAC2011 emission estimates for SoCAB varied by year and pollutant, and generally were larger for particles than gases. Emissions from paved road dust were included as on-road mobile emissions in our tabulation. Though our focus was primarily on NO<sub>x</sub> and PM emissions changes, we included ROG and SO<sub>x</sub> emissions to help account for their contributions to secondary photochemical processes, including O<sub>3</sub>, organic aerosol, and sulfate aerosol formation.

Although our main focus for emission trends was in the SoCAB, the CHS also involves communities beyond the SoCAB region. To assess these geographically distant locations (Alpine in San Diego County; Atascadero in San Luis

Obispo County; and Santa Maria, Lompoc, and Santa Barbara in Santa Barbara County), we retrieved and evaluated the CEPAM and EMFAC2011 emission estimates for these areas as well.

Government emissions inventories are based on engineering models and representative data for all sources, except for the largest stationary sources that have continuous emissions monitoring data. Models, methods, and data have improved over time, but these inventories are still mostly informed estimates rather than objective data. NO<sub>x</sub> emissions are often deemed the most accurate portion of the inventory (Ban-Weiss et al. 2008). For this reason, we examined studies that independently evaluated the on-road mobile portion of the NO<sub>x</sub> inventory using data from tunnel studies and roadside remote sensing, and evaluated the overall NO<sub>x</sub> inventory using remote-sensing (satellite) data.

### AIR POLLUTION AND EMISSIONS CHARACTERISTICS AND TRENDS

#### CHS Air Quality Methods

For this evaluation, we focused on pollutants showing the strongest chronic health effects in previously published CHS health analyses and on selected NAAQS pollutants targeted by regulatory policies promulgated prior to and during the 1992 to 2012 time frame.

All air quality measurements were collected as part of previously funded CHS work (Peters et al. 1999a,b) and made available to this investigation. Ambient O<sub>3</sub>, NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> were systematically measured at centrally sited community air monitoring stations in most CHS communities beginning in 1993 (gases) and 1994 (PM) (see Figure 1 map). ROG and SO<sub>2</sub> were not measured routinely across the community network. O<sub>3</sub> and NO<sub>2</sub> were monitored hourly using ultraviolet photometers and chemiluminescent monitors, in conformance with Federal Reference Methods (FRM). PM data were collected using a variety of samplers and instruments, as shown in Table 1.

PM sampling approaches included integrated daily PM<sub>2.5</sub> and PM<sub>10</sub> FRM samplers, specially designed CHS PM<sub>2.5</sub> integrated two-week samplers (TWS), PM<sub>10</sub> tapered element oscillating microbalances (TEOMs, R&P Model 1400A), and PM<sub>2.5</sub> and PM<sub>10</sub> beta-attenuation mass monitors (BAMs, MetOne Model 1020). To minimize potential biases caused by changing PM instrumentation, non-FRM PM were periodically compared to collocated FRM data at numerous locations. All TWS, TEOM, and BAM PM data were adjusted to reflect a common FRM-equivalency using regression relationships derived from the comparisons. Original TWS and TEOM PM data were adjusted upward primarily to account for volatilization losses; BAM PM

data were adjusted downward primarily to account for excess aerosol water collection. Daily, monthly, and annual average concentrations were computed from quality-assured and algorithmically corrected data using a data acceptance criterion of at least 75% completeness. Concentrations for all hours of the day were averaged except for  $O_3$  for which we focused on the 10 AM–6 PM average because in the CHS communities it was highly correlated ( $r > 0.98$ ) with the NAAQS 8-hr daily maximum  $O_3$  concentrations. Annual averages were computed from monthly average data. To facilitate computation of annual

averages, missing monthly average data were imputed using the averaged concentration at the site during the same month in the prior and subsequent sampling year. This approach minimized biases that might otherwise have occurred in averages computed without the cleanest or most polluted months of the year.

Overall, the CHS ambient data are >95% complete for the expected sampling schedules and missingness is unlikely to produce biases impacting assessment of trends. Additional details regarding CHS air quality measurements have been previously described (Peters 2004).

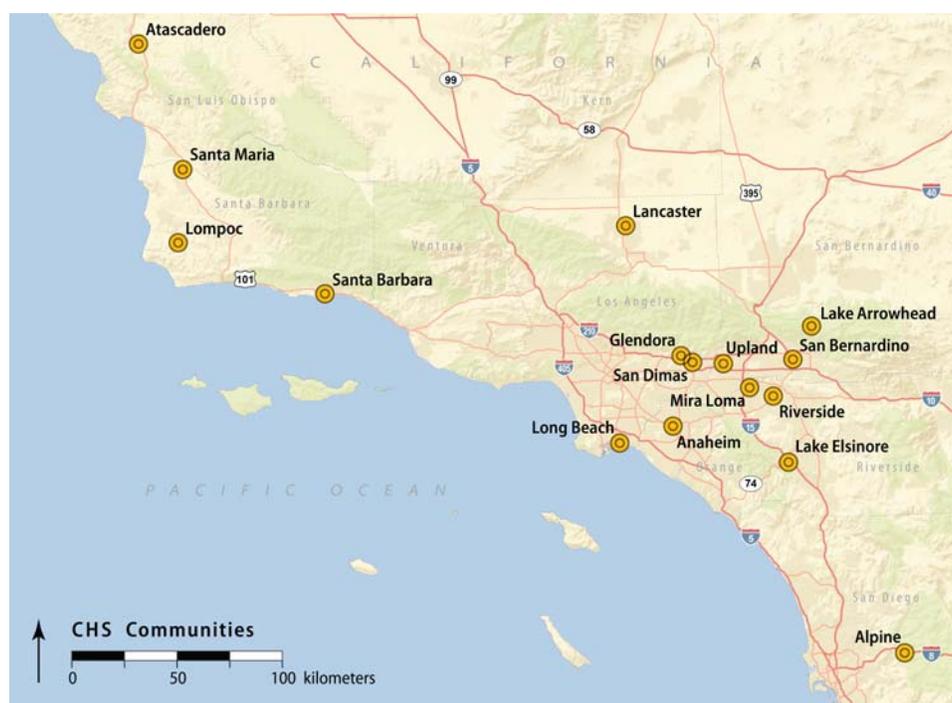


Figure 1. Map of CHS communities.

**Table 1.** PM Monitors and Samplers Used in the CHS

Time Period	PM <sub>2.5</sub>	PM <sub>10</sub>
1994–1997	CHS Two-week sampler	Tapered Element Oscillating Microbalance 1-in-6 day HiVol FRM sampler
1998–2004	CHS Two-week sampler Daily, 1-in-3, and 1-in-6 day FRM sampler	Tapered Element Oscillating Microbalance 1-in-6 day HiVol FRM sampler
2005–2007	Beta-Attenuation Mass Monitor Daily, 1-in-3, and 1-in-6 day FRM sampler	Tapered Element Oscillating Microbalance 1-in-6 day HiVol FRM sampler
2008–2011	Beta-Attenuation Mass Monitor Daily, 1-in-3, and 1-in-6 day FRM sampler	Beta-Attenuation Mass Monitor 1-in-6 day HiVol FRM sampler

**CHS Air Quality Results**

Annual average ambient pollutant concentrations across the 16 CHS communities are shown in Figure 2. Year-to-year variability was evident for all pollutants and most locations. Air quality improvements in outdoor NO<sub>2</sub> and PM<sub>2.5</sub> were observed in virtually all CHS communities. Annual average NO<sub>2</sub> reductions ranged from 53% (41 to 19 ppb) in Upland, the community with the highest-reported NO<sub>2</sub> levels, to 28% (10 to 7 ppb) in Santa Maria, one of the communities with the lowest-reported NO<sub>2</sub> levels. Changes in annual average PM<sub>2.5</sub> were slightly broader, from 54% (33 to 15 µg/m<sup>3</sup>) in Mira Loma, to 13% (9 to 8 µg/m<sup>3</sup>) in Santa Maria. Year-to-year variability in PM<sub>2.5</sub> in communities with lower

levels of pollution (e.g., Santa Maria) was large compared with changes in long-term concentration trends. Smaller improvements in daytime 8-hour (10 AM–6 PM) O<sub>3</sub> and PM<sub>10</sub> were evident in those CHS communities that were initially the most highly polluted. For example, from 1994 to 2011 the annual average 10 AM–6 PM O<sub>3</sub> decreased 27% (76.4 to 55.7 ppb) in Lake Arrowhead and 12% (64.3 to 56.7 ppb) in Riverside, the two CHS communities with the highest O<sub>3</sub> levels. PM<sub>10</sub> decreased 37% (67.4 to 42.2 µg/m<sup>3</sup>) in Mira Loma and 24% (42.4 to 32.4 µg/m<sup>3</sup>) in Riverside during the same period. PM<sub>10</sub> and O<sub>3</sub> concentrations in communities with moderate-to-lower outdoor levels were generally variable and lacked consistent trends over the 1994–2011 time period.

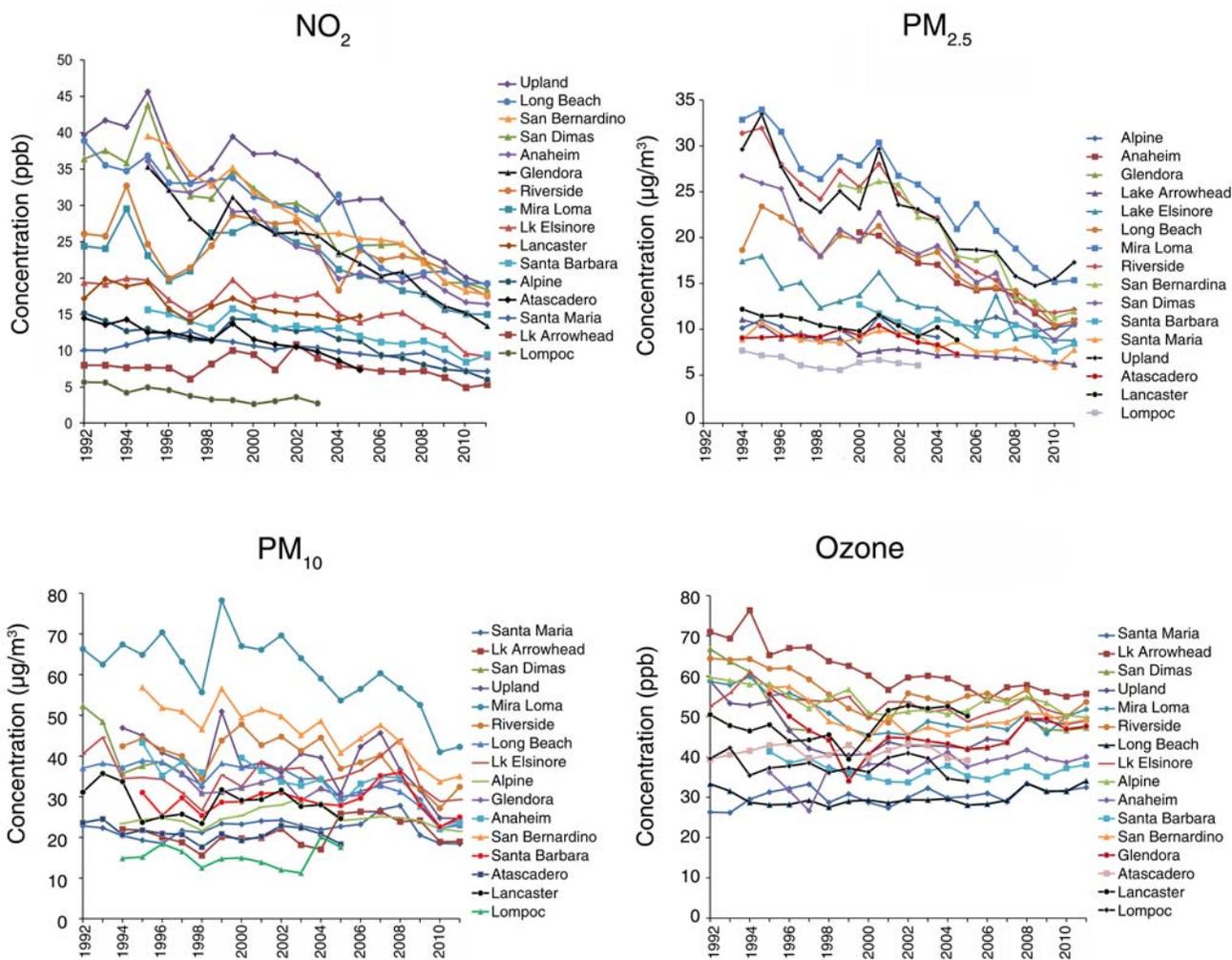


Figure 2. Air quality trends (1992–2011) in pollutant annual averages in the CHS communities. Concentrations for all hours of the day were averaged except for O<sub>3</sub> for which the average between 10 AM and 6 PM was calculated.

For purposes of clarity in later discussion, the air quality trends for the subset of communities utilized in the lung-function (Long Beach, San Dimas, Mira Loma, Upland, and Riverside,  $n = 5$ ) and in the bronchitic symptoms analyses (Long Beach, San Dimas, Mira Loma, Upland, Riverside, Alpine, Santa Maria, and Elsinore,  $n = 8$ ) are summarized in Figure 3 and Figure 4, respectively. The data presented are identical to that compositely presented in Figure 2.

### Emissions Trends Results

Estimated 1993 and 2012 emissions, emission reductions, and emission trends in the SoCAB are listed in Table 2 and Figure 5. On-road mobile sources were the dominant source of  $\text{NO}_x$ , ROG,  $\text{PM}_{2.5}$ , and  $\text{PM}_{10}$  emissions in Southern California in 1993. On-road mobile  $\text{NO}_x$  accounted for 883 of the 1425 tons per day (62%) of total  $\text{NO}_x$  emissions, and on-road mobile  $\text{PM}_{10}$  contributed 202 of the 344 tons per day (59%) of total  $\text{PM}_{10}$  emissions across the Los Angeles Basin. After on-road mobile sources, emission categories (in decreasing level of emissions per source category) included “other” mobile sources of  $\text{NO}_x$ , stationary sources of ROG and  $\text{SO}_x$ , and areawide sources of  $\text{PM}_{2.5}$  and  $\text{PM}_{10}$ . Estimates for 2012 show a dramatic reduction in total emissions of  $\text{NO}_x$ , ROG,  $\text{SO}_x$ ,  $\text{PM}_{2.5}$ , and  $\text{PM}_{10}$ . On-road mobile sources remained an important contributor

to total  $\text{NO}_x$ , ROG,  $\text{PM}_{2.5}$ , and  $\text{PM}_{10}$  emissions in 2012, but their relative contributions decreased substantially (e.g., from 62% to 50% of total  $\text{NO}_x$  emissions).

The 1993-to-2012 time frame was a period of strong economic growth in California, with statewide gross domestic product (GDP) growing at 2.7% per year, or a total of 66%, in constant dollars, over the 20-year period (U.S. EPA 2016). Despite vigorous economic growth, a 22% increase in population (State of California 2007, 2015a,b), and a 38% increase in motor vehicle activity in the SoCAB (Figure 6), total estimated emissions of  $\text{NO}_x$ , ROG,  $\text{SO}_x$ ,  $\text{PM}_{2.5}$ , and  $\text{PM}_{10}$  decreased by 54%, 65%, 40%, 21%, and 15%, respectively, during the study time period. The largest reductions were seen in the on-road motor vehicle emissions category, especially among  $\text{NO}_x$  and ROG motor vehicle emissions. Large percentage reductions were also reported for stationary source  $\text{NO}_x$  (64%) and ROG (69%) emissions. The estimates suggest that almost all categories of pollutant emissions were reduced during this period; only areawide and other mobile sources of  $\text{SO}_x$  emissions, areawide  $\text{PM}_{2.5}$  emissions, and areawide and stationary source  $\text{PM}_{10}$  emission estimates increased by small amounts (less than 7 tons per day). The inventory data indicate that the annual compounded rates of change of emissions during this period were  $-5.1\%$   $\text{NO}_x$ ,  $-8.1\%$  ROG,

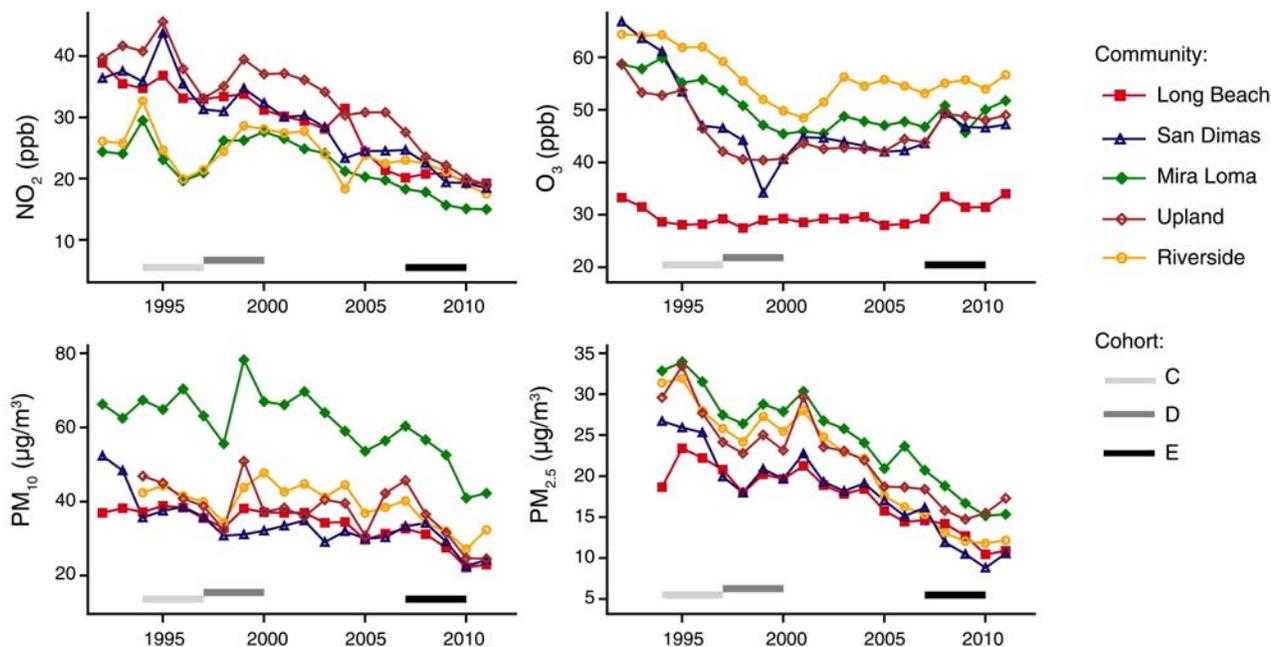


Figure 3. Levels of four air pollutants from 1994 to 2011 in five Southern California communities. Bands represent the relevant four-year averaging period for the analysis of lung-function growth in each of the three cohorts.

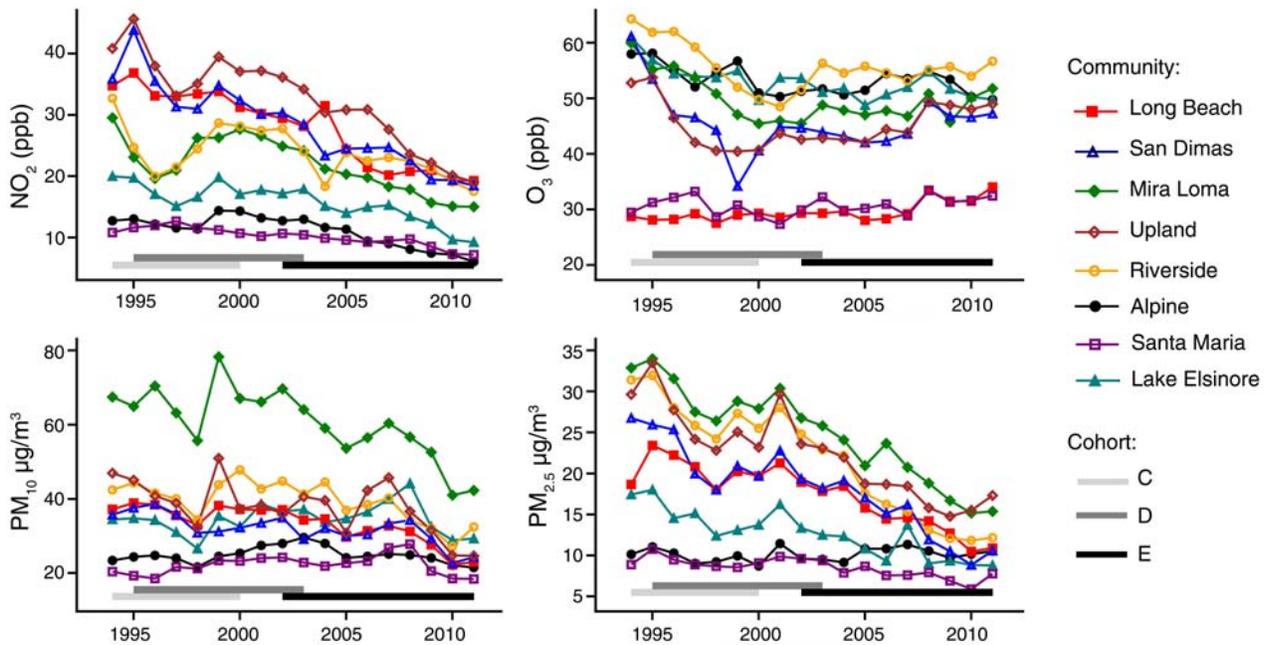


Figure 4. Levels of four air pollutants from 1994 to 2011 in eight Southern California communities. Bands represent the relevant nine- or ten-year averaging period for the analysis of bronchitic symptoms in each of the three cohorts.

Table 2. Estimated Emissions in the SoCAB (1993 and 2012)

Source Type	NO <sub>x</sub>	ROG	SO <sub>x</sub>	PM <sub>2.5</sub>	PM <sub>10</sub>
<b>1993 Emissions in Tons/Day</b>					
Stationary	151	355	26.8	19.1	24.8
Areawide	38	210	0.6	29.3	92.9
On-road motor vehicles	883	726	21.7	55.4	202.5
Other mobile sources	353	231	17.9	21.2	23.5
Total	1,425	1,522	67.0	125.0	343.8
<b>2012 Emissions in Tons/Day</b>					
Stationary	54.5	111.1	18.2	15.7	25.1
Areawide	22.7	146.2	0.9	35.4	99.3
On-road motor vehicles	327.9	144.1	2.1	33.1	152.0
Other mobile sources	245.6	133.3	19.3	14.9	16.9
Total	650.7	534.7	40.4	99.1	293.4
<b>1993–2012 Emissions Change in Tons/Day</b>					
Stationary	-97.0	-244.2	-8.6	-3.4	0.3
Areawide	-15.4	-63.4	0.2	6.0	6.4
On-road motor vehicles	-554.6	-582.2	-19.6	-22.3	-50.5
Other mobile sources	-107.0	-97.9	1.4	-6.4	-6.6
Total	-774.0	-987.7	-26.6	-25.9	-50.4
<b>1993–2012 Emissions Change in Percent</b>					
Stationary (%)	-64	-69	-32	-18	1
Areawide (%)	-40	-30	36	21	7
On-road motor vehicles (%)	-63	-80	-91	-40	-25
Other mobile sources (%)	-30	-42	8	-30	-28
Total (%)	-54	-65	-40	-21	-15

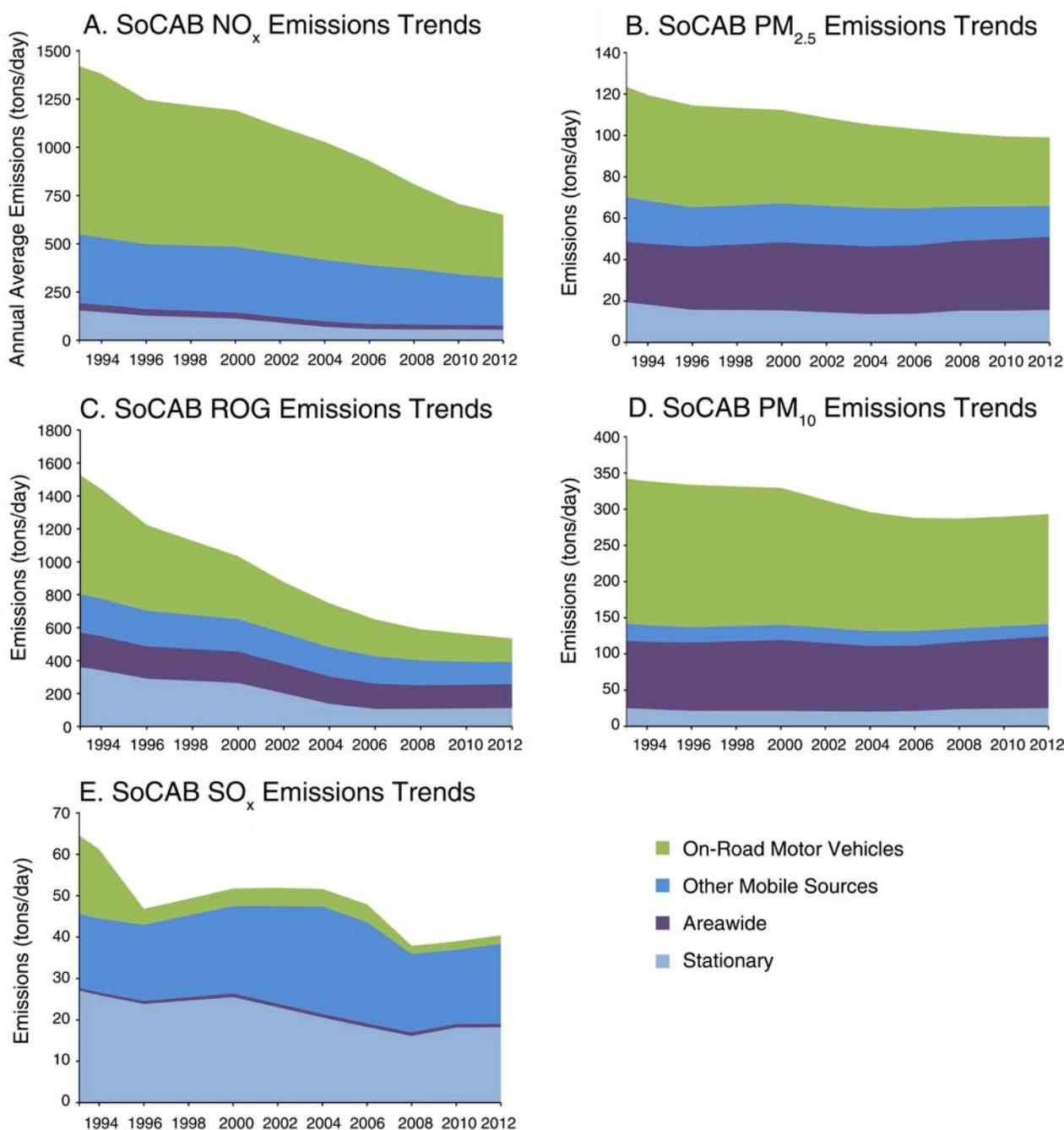


Figure 5. Estimated emissions in the South Coast Air Basin (SoCAB) from 1993 to 2012 for (A) NO<sub>x</sub>, (B) PM<sub>2.5</sub>, (C) ROG, (D) PM<sub>10</sub>, and (E) SO<sub>x</sub>.

−11.9% SO<sub>x</sub>, −2.6% PM<sub>2.5</sub>, and −1.5% PM<sub>10</sub> per year from on-road mobile sources, and −4.0% NO<sub>x</sub>, −5.4% ROG, −2.6% SO<sub>x</sub>, −1.2% PM<sub>2.5</sub>, and −0.85% PM<sub>10</sub> per year from all sources of emissions combined.

The CHS included six communities outside the SoCAB region (Figure 1). The southernmost CHS community,

Alpine, is in San Diego County (240 km from Los Angeles) whereas the northernmost community, Atascadero, is in San Luis Obispo County (340 km from Los Angeles). Lancaster (~115 km from Los Angeles) is located in the high-desert region of northern Los Angeles County and Lompoc (245 km away), Santa Maria (260 km away), and Santa Barbara

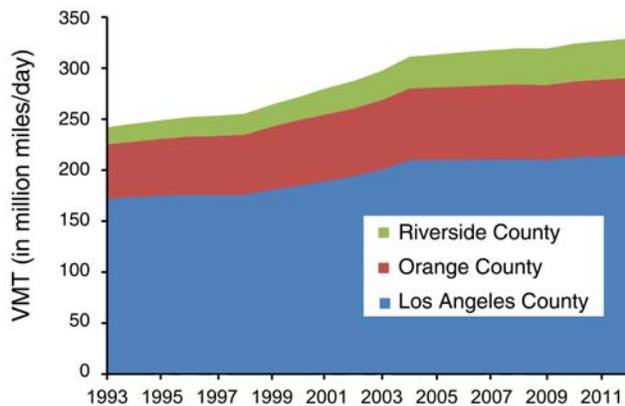


Figure 6. Vehicle miles traveled per day in the South Coast Air Basin (SoCAB) from 1993 to 2012. (From CARB’s EMFAC2011 database and model.)

(160 km away) are all in Santa Barbara County, northwest of Los Angeles. We retrieved the CEPAM and EMFAC2011 emission estimates for these areas and found that the reported emission changes for San Diego County were the same, on a percentage basis, as those for the SoCAB (54% NO<sub>x</sub> and 21% PM<sub>2.5</sub> reductions from 1993 to 2012). Emissions were much lower in the CHS communities north of Los Angeles — typically more than an order of magnitude lower than those in the SoCAB. Table 3 summarizes the 1993 emissions and 1993–2012 emission changes for Santa Barbara County, which were typical of the more northern study areas. Population and vehicle miles traveled (VMT) increased 51% during this time period. Countywide total emissions of NO<sub>x</sub>, SO<sub>x</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> all increased, but ROG emissions decreased, despite reductions in all on-road motor vehicle emissions (–57% NO<sub>x</sub> and –13% PM<sub>2.5</sub>). The emissions increases were primarily attributable to the growth of emissions from other mobile sources, a large proportion of which were likely emissions from oceangoing vessels calling on the ports of Los Angeles and Long Beach. At the ports, combined emissions of NO<sub>x</sub> and PM<sub>2.5</sub> increased ~160% during this time frame.

**Comparison of CHS Air Quality and Emissions Trends**

Ambient concentration trends in communities with high pollution levels were generally consistent with emission trends. This is perhaps most convincing for NO<sub>2</sub>, where both ambient levels and NO<sub>x</sub> emissions declined by ~54%. Trends in annual average ambient concentrations across the CHS communities were stronger for NO<sub>2</sub> and PM<sub>2.5</sub> than for PM<sub>10</sub> and O<sub>3</sub>. CHS communities with the highest NO<sub>2</sub> and PM<sub>2.5</sub> concentrations in the mid-1990s

exhibited the strongest downward trends over the 20-year period. For example, air quality trends in two communities with high NO<sub>2</sub> concentrations (Upland and Long Beach) and two communities with high PM<sub>2.5</sub> concentrations (Mira Loma and Riverside) are compared with trends in SoCAB emissions in Figure 7.

On average, annual NO<sub>2</sub> concentrations at Upland and Long Beach decreased 3.0% per year, slightly greater than the 2.8% annual decrease estimated for NO<sub>x</sub> emissions in the SoCAB from 1993–2011. NO<sub>2</sub> concentrations at sites farther inland (Mira Loma and Riverside) decreased at slower rates (1.6 to 2.4% per year) than estimated NO<sub>x</sub> emissions. The data from these four communities, which represent the western (Long Beach), central (Upland), and eastern (Riverside and Mira Loma) portions of the SoCAB region, bracketed the NO<sub>x</sub> emissions trend and showed consistent long-term trends in NO<sub>2</sub> air quality and NO<sub>x</sub> emissions. In Santa Barbara County, where the NO<sub>x</sub> emission barely changed (+0.6% per year) over this time period, the NO<sub>2</sub> concentrations did not show consistent long-term trends (see Lompoc, Santa Maria, and Santa Barbara in Figure 2).

Comparisons of data from these same four monitoring stations revealed higher rates of PM<sub>2.5</sub> concentration decreases than PM<sub>2.5</sub> emissions decreases over the 1994–2011 time period. Ambient basinwide PM<sub>2.5</sub> emissions decreased an average of 1%, but observed PM<sub>2.5</sub> concentrations decreased 3.9%, 3.4%, 3.2%, and 3.0% per year in Riverside, Long Beach, Mira Loma, and Upland, respectively. A large portion of ambient PM<sub>2.5</sub> in the SoCAB is secondary PM, as a result of gaseous NO<sub>x</sub>, ROG, and SO<sub>x</sub> emissions (Fine et al. 2004). The average rate of annual decrease in ambient PM<sub>2.5</sub> concentrations was mostly between the average annual rate of change of NO<sub>x</sub> emissions (2.9%) and ROG emissions (3.7%). The PM<sub>2.5</sub> air quality trends compared more favorably with NO<sub>x</sub> and ROG emissions trends than either PM<sub>2.5</sub> or PM<sub>10</sub> emissions trends over this time period. Reduction in ammonia emissions, primarily from the relocation of livestock operations to other parts of California, contributed to the downward PM<sub>2.5</sub> trends in Riverside and San Bernardino counties. To be realistic, however, it must be noted that these business relocations occurred not only because air regulators were concerned about ammonia emissions from agricultural farming enterprises, but also because of urbanization (economic development, population growth, and increasing land values).

Reconciliation of ambient O<sub>3</sub> concentration trends with emissions inventories is more challenging, because of O<sub>3</sub>’s secondary photochemical nature. Observed changes in annual O<sub>3</sub> levels in Lake Arrowhead, for example, were

**Table 3.** Estimated Emissions in Santa Barbara County (1993 to 2012)

Source Type	NO <sub>x</sub>	ROG	SO <sub>x</sub>	PM <sub>2.5</sub>	PM <sub>10</sub>
<b>1993 Emissions in Tons/Day</b>					
Stationary	9.0	13.8	1.6	0.5	0.9
Areawide	2.2	11.7	0.0	6.5	15.1
On-road motor vehicles	31.2	21.7	0.6	1.3	5.0
Other mobile sources	43.5	8.8	14.8	2.9	3.1
Total	86.0	56.0	17.1	11.3	24.1
<b>2012 Emissions in Tons/Day</b>					
Stationary	7.3	9.9	4.5	0.5	1.0
Areawide	2.1	10.8	0.0	6.6	16.5
On-road motor vehicles	13.4	5.9	0.1	1.2	5.6
Other mobile sources	73.2	8.5	35.6	5.6	5.8
Total	95.9	35.0	40.2	13.9	28.9
<b>1993–2012 Emission Changes in Tons/Day</b>					
Stationary	−1.8	−3.9	2.9	0.0	0.1
Areawide	−0.1	−1.0	0.0	0.1	1.4
On-road motor vehicles	−17.8	−15.8	−0.5	−0.2	0.6
Other mobile sources	29.7	−0.3	20.8	2.6	2.7
Total	10.0	−21.0	23.2	2.6	4.8
<b>1993–2012 Emission Changes in Percent</b>					
Stationary (%)	−20	−28	177	−3	6
Areawide (%)	−3	−8	−1	2	10
On-road motor vehicles (%)	−57	−73	−88	−13	11
Other mobile sources (%)	68	−4	140	90	87
Total (%)	12	−37	136	23	20

about half that expected, given the roughly 60% reductions in both ROG and NO<sub>x</sub> precursor emissions. However, if one subtracts the estimated background O<sub>3</sub> level (~30 to 40 ppb) (Fiore et al. 2014; Wang et al. 2009), changes in observed O<sub>3</sub> at peak stations were more consistent with emission trends. The apparent absence of O<sub>3</sub> trends in communities with moderate and lower ambient levels is inconsistent with changes in local precursor emissions and may be related to the effects of transported pollution, including increasing background O<sub>3</sub> in this period, or the nonlinearities in atmospheric chemistry that control inter-relationships between ROG, NO<sub>x</sub>, and O<sub>3</sub>.

**Regulatory Policies** Numerous regulatory policies and emissions reduction strategies were developed to address California’s air quality during this multi-year period. A summary of the key policies appears in Table 4. The multitude of on-road vehicle emissions mitigation efforts, including the low-emission vehicle (LEV) (I and II) program, drastically reduced passenger car, light-duty and medium-duty truck

emissions. Required gasoline reformulations starting in the early 1990s — in addition to the heavy-duty diesel vehicle emission reductions and fuel reformulation programs in the 2000s — seem to have been especially important in this period.

Regulatory policies that influenced emission reductions in the period from 1993 to 2012 originated with the Federal CAA of 1970 and subsequent CAA Amendments in 1977 and 1990. California mandated emission reductions from motor vehicles and stationary sources in the 1970s and 1980s, in accordance with the CAA. The focus was on light-duty vehicle (LDV) emissions and large stationary sources. Although substantial progress was made in the 1980s on reducing emission from large stationary sources (such as power plants and oil refineries in the SoCAB), overall progress towards achieving the compliance with the NAAQS was slow. It was clear that the SoCAB was not going to achieve NAAQS compliance by 1987, as required in the 1977 CCA amendments.

Several policy actions in the period from 1988 to 1990 greatly accelerated progress on responding to the SoCAB’s air pollution problem. The California Clean Air Act of 1988 directed the CARB “to achieve the maximum degree of emission reduction possible from vehicular and other mobile sources.” This led to the California LEV program, which was adopted in 1991. Also in 1988, the SCAQMD adopted an Air

Quality Management Plan (the SIP for SoCAB) that incorporated aggressive emission control strategies targeting essentially all sources, regardless of size (including, for example, consumer products) for reductions. It required introduction of zero-emission vehicles (a provision that was subsequently modified) and large (>80%) reductions in emissions to be achieved mostly with new “to-be-developed” technologies.

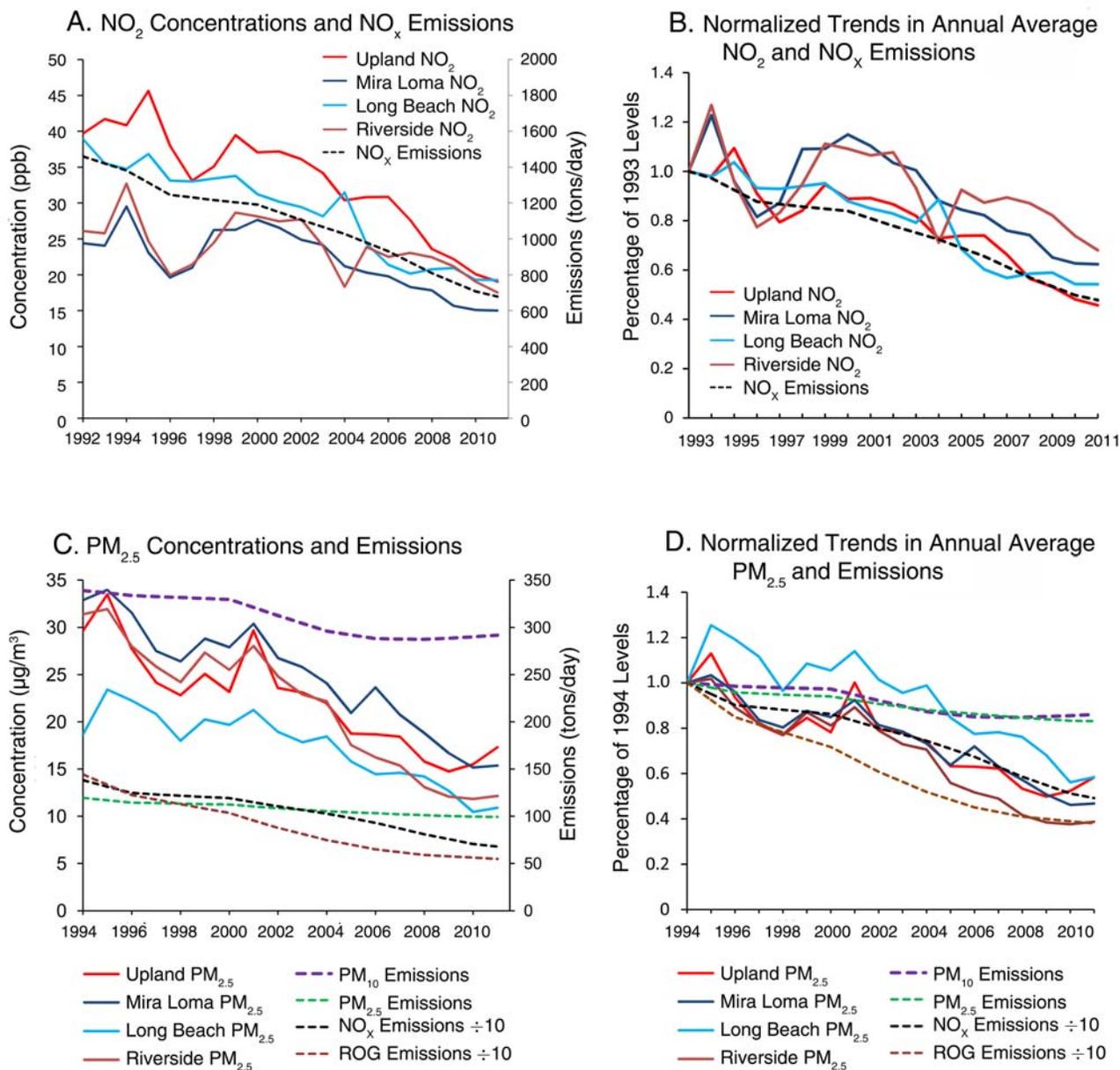


Figure 7. Comparison of NO<sub>2</sub> air quality and NO<sub>x</sub> emission trends, and PM<sub>2.5</sub> air quality and PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>x</sub>, and ROG emission trends in high-pollution communities. The normalized trends (right side) compare air quality and emissions with the baseline values (100%) in 1993 for NO<sub>2</sub> and 1994 for PM<sub>2.5</sub>.

**Table 4.** Major Regulatory Policies Affecting Pollution and Emission Trends in California

Regulatory Policy	Adoption Date
<b>On-Road Emissions</b>	
Low-emission vehicle standards for light-duty and medium-duty vehicles (LEV, LEV II)	1990, 1998
Reformulated gasoline	1988, 1990, 1991
On-board diagnostics standards for light-duty vehicles	1985, 1989
Medium-duty and heavy-duty truck gasoline emission standards	1995
Heavy-duty diesel truck engine emissions standards	1998, 2001
Clean diesel fuel requirements	2003
Financial incentives for replacement or retrofit high-polluting vehicles, engines & equipment (e.g., the Carl Moyer Program)	1998–2012
Cleaner port (drayage) trucks	2007
<b>Off-Road Emissions</b>	
Cleaner diesel fuel for ocean-going vessels, harbor craft, and trains	2004, 2008
Reduced port auxiliary engines and incinerator use, hoteling	2007
Cleaner locomotive engines in Southern California	1997, 2010
Stationary diesel engines standards for in-use agricultural engines	2007
<b>Stationary Point Sources</b>	
NO <sub>x</sub> and SO <sub>x</sub> reductions from Regional Clean Air Incentives Market (RECLAIM)	1994
New source review (NSR)	1990
Source-specific emissions standards	1988–2002
<b>Area Sources</b>	
Low-emission certificate programs for products and equipment	1988–2012
Unpaved and paved road dust control measures	2008
Water heater and small boiler emission standards	1999, 2004

Concurrently, the SCAQMD established the Technology Advancement Program to expedite the development, demonstration, and commercialization of cleaner technologies and clean-burning fuels.

Another major policy action was SCAQMD's adoption of the Regional Clean Air Incentives Markets (RECLAIM) program in the early 1990s (South Coast Air Quality Management District 2014). This program was designed to reduce NO<sub>x</sub> and SO<sub>x</sub> emissions from major industrial facilities by ~70% between 1994 and 2003. The RECLAIM program used a market-based approach in which businesses that beat their reduction targets could trade or sell their credits on the open market, whereas business that did not reduce emissions were required to acquire credits in the marketplace to continue operation. The market-based approach offered greater flexibility and a financial incentive to reduce air pollution beyond what clean air laws and traditional command-and-control rules required, yet still guaranteed annual reductions in air pollution until air quality standards were achieved.

CARB's identification of diesel PM as a toxic air contaminant in 1998 led to the adoption of a Diesel Risk Reduction Plan (CARB 2000) in 2000. It recommended control measures to achieve PM reduction goals of 75% by 2010 and 85% by 2020. The landmark plan led to (1) new regulatory standards for all new on-road, off-road, and stationary diesel-fueled engines and vehicles to reduce diesel PM emissions by ~90% from 2000 levels; (2) new retrofit requirements for existing on-road, off-road, and stationary diesel-fueled engines and vehicles that were determined to be technically feasible and cost-effective; and (3) new Phase 2 diesel fuel regulations to reduce the sulfur content levels of diesel fuel to no more than 15 ppm and thus to provide the quality of diesel fuel needed for the advanced diesel PM emission controls to function properly.

Adoption of the San Pedro Bay Ports Clean Air Action Plan in 2006 (U.S. EPA et al. 2006) provided yet another strategy for dramatically reducing air pollution emissions from port-related cargo movement in the ports of Long Beach and Los Angeles. It established plans to rapidly

reduce emissions from heavy-duty trucks servicing the ports as well as oceangoing vessels, cargo handling equipment, harbor craft, and rail/locomotives.

These major policy actions by the CARB, SCAQMD, and the ports during this period went beyond the requirements of the Federal CAA and accelerated progress toward clean air goals. However, the agencies and legislators decided that they needed additional programs to fund or co-fund emission reductions above and beyond that required by prevailing laws in order to accelerate implementation of new policies and technology. Accordingly, between 1988 and 2006, a broad array of programs was initiated to develop control technologies and fund or co-fund the replacement of on-road, off-road, and stationary sources with cleaner modern vehicles and equipment. More than \$1 billion were committed to accelerate emission reductions in the SoCAB through the SCAQMD’s Technology Advancement Program, the Carl Moyer Memorial Air Quality Standards Attainment Program, the Lower Emission School Bus Program, the Goods Movement Emission Reduction Program, the Air Quality Improvement Program, the Fleet Modernization Program, and the Surplus Off-Road Opt-In for NO<sub>x</sub> Program.

**Discussion of Air Quality Trends**

The finding that PM<sub>2.5</sub> air quality trends compared more favorably with NO<sub>x</sub> (and ROG) emission trends than either PM<sub>2.5</sub> or PM<sub>10</sub> emission trends is supported by aerosol composition data. Figure 8 shows trends in annual average

PM<sub>2.5</sub> nitrate concentrations at stations in selected CHS communities from 1994–2004 and nearest EPA’s Speciation Trends Network stations from 2001–2011. Although the paired sites are not collocated, they are aligned in the east–west direction of predominant wind flow and show similar concentration in years with concurrent measurements. The Mira Loma and Riverside-Rubidoux sites (which are 10 km apart) are historically the two sites with the highest nitrate concentrations in the SoCAB and from 1994–1995 to 2010–2011 annual PM<sub>2.5</sub> nitrate concentration decreased by 65%. From 1994–1995 to 2010, annual PM<sub>2.5</sub> nitrate concentrations decreased by 68%, and 59% at Upland/Fontana (13 km apart) and Long Beach/Anaheim (23 km apart), respectively. The changes in ambient nitrate at these sites are slightly greater than the NO<sub>x</sub> emission changes (–54%) and much greater than the primary PM<sub>2.5</sub> emission changes (-21%) in the SoCAB. They suggest the NO<sub>x</sub> emissions reductions made a substantial contribution to reductions in ambient PM<sub>2.5</sub> in the areas with high concentrations. The nitrate concentrations in Santa Maria during 1994–2004 were low and showed no temporal trend from 1994 to 2004, which is consistent with the small NO<sub>x</sub> emissions change (+12%) in Santa Barbara County. Unfortunately, it is not possible to assess comparable trends in PM<sub>2.5</sub> elemental carbon and organic carbon (EC/OC) at these pairs of stations because of the changes in EC/OC measurement techniques over this time period.

Our analyses suggest that dramatic improvements in ambient air quality occurred over the period from 1993 to 2012 in the Southern California region. These changes in

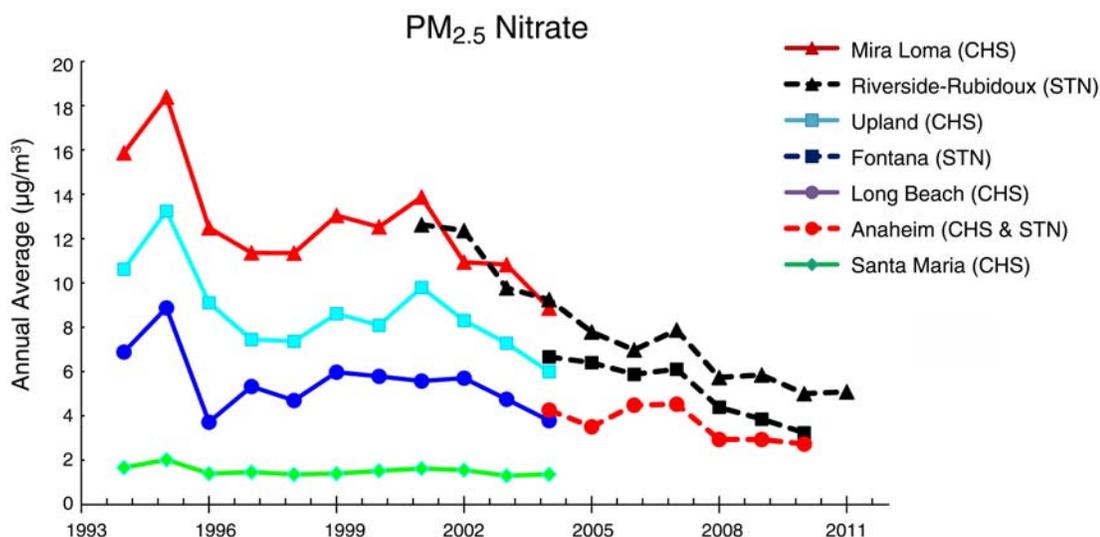


Figure 8. PM<sub>2.5</sub> nitrate air quality trends at CHS and Speciation Trends Network (STN) monitoring sites.

air quality are explainable by the similar decreases in emissions inventories over the same time period that were reported by CARB and other independent groups, and which we documented. Emissions reductions were the result of a multi-decade effort of aggressive air pollution reduction strategies undertaken by the State of California and the regional air quality agencies to address a wide variety of sources of pollution. The large changes in on-road emissions suggest that policies to reduce light and medium-duty gasoline and diesel vehicle emissions were especially effective in helping to achieve reductions in emissions and improve air quality in this period.

Because  $\text{NO}_x$  emission estimates are verifiable with independent estimation techniques and are considered more accurate than estimates for other pollutants, trends in  $\text{NO}_2$  levels and  $\text{NO}_x$  emissions are robust evidence of policy effectiveness. Emissions from on-road motor vehicles and large stationary sources are well-studied and more certain than other components of the emissions inventory. CARB has made substantial changes in the methods and data used to estimate emissions from other mobile sources in recent years. The new approach affects virtually all off-road mobile sources, including aircraft, trains, ocean-going vessels, commercial harbor craft, recreational boats, off-road recreational vehicles, off-road equipment, farm equipment, fuel storage and handling equipment, and cargo-handling equipment. Emissions estimates based on the new methodology were available starting in 2009, but they have not been backcast to prior years. These estimates are not currently part of the CEPAM projections. Thus, trends in the other-mobile-source category of emissions may be less certain than those for other categories.

**Emissions Inventories** Emissions inventories are inherently uncertain, because much of the fundamental data are estimated from sparse measurements of actual activities and emission factors. Numerous researchers have employed alternate approaches to evaluate emission inventory amounts and trends (Ban-Weiss et al. 2008; Bishop et al. 2010, 2012; Bishop and Stedman 2008; Dallmann and Harley 2010; Harley et al. 2005; McDonald et al. 2012, 2013; Pollack et al. 2013; Russell et al. 2010, 2012; Warneke et al. 2012). Most of these approaches emphasize on-road mobile source emissions, where emissions can be independently estimated from fuel-use data and vehicle emission factors based on fuel use determined from tunnel measurements and/or remote sensing of tailpipe emissions. Mobile emissions are often combined with other emissions to facilitate comparison with ambient air pollutant levels derived from surface observations and satellites.

McDonald and colleagues (2012) recently evaluated long-term trends in  $\text{NO}_x$  emissions for 1990 to 2010 in the SoCAB, which overlaps most of the period and area of our study. They compiled fuel-use data and vehicle emission factors based on fuel use from a large number of roadside remote sensing and tunnel studies. They found in-use LDV  $\text{NO}_x$  emission rates decreased steadily and dramatically during this period, declining from 14 to 4 g/kg fuel (or 71%). Heavy-duty vehicle (HDV) emission rates were constant from 1990–1997 and then decreased from 42 to 28 g/kg fuel (33%). Estimates of on-road LDV  $\text{NO}_x$  emissions in the SoCAB decreased by 65% between 1990 and 2010, whereas on-road HDV  $\text{NO}_x$  emissions initially increased, leveled, and then decreased (starting in 2006), resulting in little net change over this time period. In the early 1990s, gasoline engines were the dominant source (~75%) of on-road  $\text{NO}_x$  emissions. However, because LDV emission factors declined much faster than those for diesel HDV, the gasoline LDV and diesel HDV on-road  $\text{NO}_x$  emissions were comparable by 2007. Overall, McDonald and colleagues' (2012) estimates of on-road vehicle  $\text{NO}_x$  emissions decreased 53% from 1990–2010 and 49% from 1993–2010, slightly less than the 63% decrease derived from the CARB inventory for 1993–2012 (Table 2).

McDonald and colleagues also compared trends in total anthropogenic  $\text{NO}_x$  emissions with trends in ambient  $\text{NO}_x$  concentrations. Their comparison indicated that (1) on-road vehicle  $\text{NO}_x$  emissions were the dominant portion (~70 to 80%) of total anthropogenic  $\text{NO}_x$  emissions throughout this period, and that (2) trends in total anthropogenic  $\text{NO}_x$  emissions were consistent with trends in ambient concentrations.

Russell and colleagues (2010, 2012) compared satellite measurements of  $\text{NO}_2$  with CARB  $\text{NO}_x$  emissions inventories and ambient surface  $\text{NO}_2$  concentrations throughout California. From 2005 to 2011, satellite measurements of  $\text{NO}_2$  showed greater percentage reductions (40.3%, or 6.7% per year) than those for surface ambient concentrations or emission inventories in the SoCAB. The satellite  $\text{NO}_2$  data showed large differences between weekday and weekend measurements, which was interpreted as corroboration of the dominance of motor vehicle emissions in the overall inventory. It should be noted that the reductions reported from satellite measurements of  $\text{NO}_2$  were somewhat larger than what McDonald and colleagues found in emissions during this period.

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### PART 2: TRENDS IN AIR QUALITY AND RESPIRATORY HEALTH IN THE CHS

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#### OVERVIEW OF THE CHS DESIGN

The cohort resource for this investigation, the CHS, is a long-term study involving the recruitment of schoolchildren from communities across Central and Southern California (Figure 1) that were similar demographically but had differing ambient air pollution profiles. The CHS was initiated in 1993 and has continued, with periodic successive enrollments of elementary-school-aged children, to the present day. Since 1993, almost 12,000 schoolchildren have participated in the multi-year tracking effort. Between 1993 and 2011, five cohorts of children (identified as Cohorts A through E) were recruited into the CHS and tested annually to document lung-function growth, respiratory health status, and home-operating characteristics that might impact personal respiratory health growth (such as air conditioning and heating usage, water damage, the presence of pets, or the presence of smokers in the home).

Cohorts A and B were recruited as senior high students (nominal age 16 years) and middle school students (nominal age 13), respectively, and were followed annually until high school graduation at age 18. Cohorts C and D were recruited into the CHS as fourth-graders (nominal age, 10 years) and followed annually until high school graduation (nominal age 18). Cohort E was recruited in kindergarten and first-grade (nominal ages 5 to 7 years), and subjects were in senior high school (nominal ages, 14–15) at the time of this HEI-sponsored study's initiation, in the fall of 2011. A more complete review of CHS baseline design parameters can be found in previous publications (Peters et al. 1999a,b), but a brief summary is provided here for orientation.

The original CHS community selections were based on a quasi-factorial design that focused on outdoor O<sub>3</sub>, PM<sub>10</sub>, NO<sub>2</sub>, and strong acid as the pollutants of primary interest for health and air quality study. Regions of Southern California were selected with the aim of maximizing the variability and minimizing the correlations in these four pollutants. A pool of candidate communities was developed based on historic (1987–1989) routine air monitoring data and previously performed specialized monitoring studies. Where geographically proximal air monitoring data were not available to be assigned to a community, data interpolations from more distant monitoring sites were performed and an estimated value was assigned. In regions with pollution patterns of interest, communities with relatively stable student populations were identified for

consideration. Student stability was decided on the basis of a review of publicly available school district enrollment and retention data. This requirement of school and residential stability was thought to be necessary for a successful longitudinal investigation, but one potential unintended effect was to bias potential community selections towards a more middle-class socioeconomic status.

To address community-level sources of variability, we sought to maximize the number of participating communities within existing financial constraints. Some of the theoretical combinations of high and low ambient O<sub>3</sub>, PM<sub>10</sub>, NO<sub>2</sub>, and strong acids do not occur in the Southern California atmosphere, so a reduced number of combinations was sought for inclusion. Where possible, consideration was given to duplication of a specific pollutant combination to reduce the opportunity for local irregularities unduly biasing the overall schema. Ultimately, 12 communities (Santa Maria, Atascadero, Lompoc, Lancaster, Long Beach, San Dimas, Upland, Mira Loma, Riverside, Lake Arrowhead, Lake Elsinore, and Alpine) were selected in 1992 for study participation. Additional details on the original community selections may be found in Peters and colleagues (1999a). To augment the original 12 study communities for ongoing subsequent investigations, four additional communities (Santa Barbara, Anaheim, Glendora, and San Bernardino) were added in 2002. These were chosen from across the originally identified geographic regions, using data from the 2000 U.S. Census, and information from discussions with the various school districts' administrative personnel.

This HEI-sponsored investigation focuses on children initially recruited as parts of CHS Cohorts C, D, and E, in order to leverage complementary health data over similar time windows of biological development. Cohorts C and D were originally enrolled into the CHS when they were fourth-graders attending public elementary schools in 1992–1993 and 1995–1996, respectively, in 12 Southern Californian communities. Cohort E was established in 2002–2003, with the recruitment of public school students attending kindergarten or first-grade classes in 13 communities, nine of which were among the original 12 CHS communities (Table 5). All CHS communities were originally selected on the basis of differing air pollution profiles of O<sub>3</sub>, PM, NO<sub>2</sub>, and ambient acids; similar population demographics data as available from the 1990 or 2000 U.S. Census; and sympathetic school districts willing to participate in a multi-year program to assess children's respiratory health (see Peters et al. 1999a for additional details).

Over the course of the CHS, there have been several sources of financial support with different foci and project scopes of work. The financial resources necessary to complete annual testing on all study participants in all study

years at all study locations were not always available over the 20 years of study field operations, but the key population resource of schoolchildren was unwaveringly preserved. This unique resource was characterized by periodic testing of lung function or by means of administering questionnaires, and augmented by regional or specialty air monitoring sampling operations.

To provide the largest possible population data set to address the specific aims of the HEI-funded project, differing subpopulations of CHS participants were used to address the respective project aims. CHS lung-function data were available from the three study cohorts of interest in five overlapping communities across the three cohorts used in this study: Long Beach, San Dimas, Upland, Mira Loma, and Riverside. Questionnaire responses regarding respiratory symptoms were available in eight overlapping communities: the five previously identified for lung-function analyses (Long Beach, San Dimas, Upland, Mira Loma, and Riverside) and Santa Maria, Lake Elsinore, and Alpine. Although bronchitic symptoms data were collected in Lake Arrowhead — a rural community in the mountains east of Los Angeles (Figure 1) — the absence of home addresses required for geocoding prevented use of symptoms data from that community in this analysis of air pollutants.

### Institutional Review Board Approval and Participant Confidentiality

This study involved the direct voluntary interaction of human subjects, who were minors at the time of study participation. The study was performed by investigators from and under the oversight of the University of Southern California. Study protocols were reviewed and approved annually by the University of Southern California Institutional Review Board in conformance with its re-certification requirements. Regarding historical data collection in the CHS, written informed consent was obtained from all subjects prior to study participation. Because study participants were all minors at the time of study enrollment, the informed consent process included written consent provided by a parent or legal guardian and confirmed assent provided by the participant. Written questionnaire responses and data files containing subject identifiers were securely stored using locked filing cabinets and computers with multiple firewalls, restricted access, and strong password protection. Over the 20 years of health data collection, several project quality assurance officers have audited the integrity and rigor of the protections in place to maintain and preserve subject confidentiality and data validity. The procedures in place were repeatedly

**Table 5.** Children’s Health Study (CHS) Communities for Cohorts C, D, and E

CHS Community	Cohort C	Cohort D	Cohort E
Atascadero	+	+	
Santa Maria	+	+	+
Lompoc	+	+	
Santa Barbara			+
Lancaster	+	+	
Long Beach	+	+	+
San Dimas	+	+	+
Glendora			+
Upland	+	+	+
Anaheim			+
Mira Loma	+	+	+
Riverside	+	+	+
San Bernardino			+
Lake Arrowhead	+	+	+
Lake Elsinore	+	+	+
Alpine	+	+	+

reviewed and continue to preserve and protect data quality and confidentiality. With the advent of the HEI-sponsored investigation, another quality assurance officer was identified and assigned audit oversight regulatory control. Multiple internal audits, as well as external audits conducted by HEI quality assurance personnel, have provided assurance that the data set is appropriately documented and protected for both scientific credibility and human confidentiality considerations.

### Study Quality Assurance Evaluation and Reporting

A quality assurance project plan was developed to provide continued quality control of extracted data. The plan, submitted to HEI early in the project timeline, described the various components of the program, the research approaches that were undertaken in the performance of the study, the data management and analytical schemes that were employed, and the personnel involved in the study. Supporting documentation, including a data codebook detailing the health and air quality data variables in the existing study database, the data forms and field operations procedures used in the primary collection of the health data, and resumés for participating study personnel were all provided in the quality assurance project plan.

A quality assurance audit was conducted by RTI International in September 2013. Drs. Prakash Doraiswamy and Linda Brown visited the University of Southern California facility on September 23 and 24, met with the study research team, reviewed study paperwork, and assessed study documentation. The visit was prefaced by electronic requests by the HEI auditors for pre-audit documentation to review. The audit reviewed progress reports, personnel and staff, adequacy of equipment and facilities, internal quality assurance procedures, air quality data processing documentation, data processing, and backup procedures. Program codes were inspected to verify proper documentation. Analytic datasets and codebooks were examined. No errors were noted, but recommendations were made for documenting model development and quality assurance and quality control procedures and codes, as well as for developing a codebook for the lung-function dataset. Additional details are available in the section "HEI Quality Assurance Statement" later in this report.

## TRENDS IN AIR QUALITY AND LUNG FUNCTION

### Introduction

In prior investigations, we and others have linked exposure to ambient air pollution with lung-function impairment among children (Gauderman et al. 2002, 2004, 2007; Gehring et al. 2013; Gotschi et al. 2008; Molter et al. 2013;

Peters et al. 1999b; Urman et al. 2014). Reduced lung function in children has been associated with increased risk of developing asthma (Islam et al. 2007). Additionally, adverse effects of air pollution on the lungs in childhood can have long-term effects because lung function that is lower than predicted for a healthy adult has been found to be associated with increased risk of cardiovascular disease and mortality (Georgiopoulou et al. 2011; Ryan et al. 1999; Sin et al. 2005). Although progress has been made throughout the United States in reducing outdoor levels of several air pollutants, it is not known whether these reductions are associated with improvements in children's respiratory health.

As previously presented, Southern California has historically been plagued by high levels of air pollution because of the presence of a large motor vehicle fleet, numerous industries, the largest seaport complex in the world, and a natural landscape that traps polluted air over the Los Angeles Basin. With mounting scientific evidence of adverse health effects of air pollution, aggressive pollution-reduction policies have been enacted in this geographic region, including control strategies for mobile and stationary sources and reformulations of fuel and consumer products. As a result, air pollution levels have been trending downwards over the last several decades in Southern California.

Improvements in air quality over time provide the backdrop for a "natural experiment" to examine potential beneficial health effects. As part of the 20-year CHS, we recorded longitudinal lung-function measurements of three separate cohorts of children in the same four-year age range (11–15 years old) and in the same five study communities, but over different calendar periods. In this section of the final report, we examine whether the changes in levels of NO<sub>2</sub>, PM (PM<sub>10</sub> and PM<sub>2.5</sub>), and O<sub>3</sub> that occurred across these time spans are associated with changes in children's lung-function development.

### Study Methods

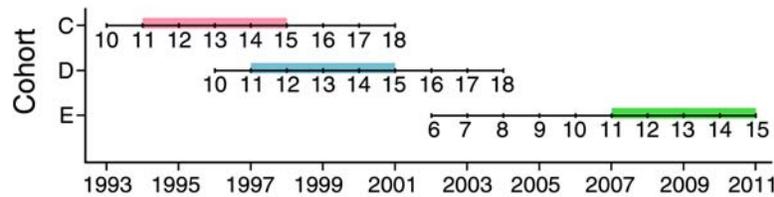
**Subjects** The analyses reported in this section were carried out among children recruited from three separate CHS cohorts (Figure 9), as described earlier. To facilitate direct comparisons across calendar periods, lung-function analyses were restricted to the five study communities (Long Beach, Mira Loma, Riverside, San Dimas, and Upland) in which lung-function testing was performed on all three cohorts (Figure 10). This sample totaled 2,120 children, including 669 in Cohort C, 588 in Cohort D, and 863 in Cohort E.

**Lung-Function Testing** Trained technicians coached CHS participants in performing valid lung-function maneuvers. From each maneuver, maximal FEV<sub>1</sub> and FVC were measured. These standardized measures of lung-function

performance are highly reproducible with minimal training and provide objective assessment of airway volumes and flows. Additional collected information included study participants' height and weight, asthma status, recent respiratory illness history, and smoking history at the time of lung-function testing.

Lung-function data for Cohorts C and D were collected using criteria from the 1994 American Thoracic Society (ATS) recommendations for spirometry (ATS 1995) to evaluate and accept performance maneuvers. For Cohort E, conformance with the 2005 ATS/European Respiratory Society (ERS) reproducibility guidelines (Miller et al. 2005) was used as an objective and credible basis for data

acceptability. For Cohorts C and D, lung-function testing was performed annually from fourth to twelfth grade (average ages 10 to 18 years) using rolling-seal spirometers (Spiroflow Model 132; P.K. Morgan Ltd., Gillingham, UK). In Cohort E, lung-function testing was performed every other year using pressure transducer-based spirometers (Screenstar, Morgan Scientific, Haverhill, Massachusetts, USA) when the children were approximately 11, 13, and 15 years old. Of the 2,120 children, 1,585 (74.8%) were tested at the beginning (age 11) and end (age 15) of the follow-up period, while the remaining 535 (25.2%) were tested at age 11 but not at age 15.



**Figure 9. Follow-up periods for Cohorts C, D, and E, including the years and average ages of follow-up.** Note: Shaded bars represent the overlapping age for which lung function measurements were collected across all three cohorts. (Reprinted from Lurmann et al. 2015 by permission of Taylor & Francis Ltd.)



**Figure 10. Locations of all CHS communities and the five specific communities (red dots) in which lung-function measurements were obtained for all three cohorts.**

Sensitivity analyses were conducted to assess whether the use of different spirometers (Spiroflow for Cohorts C and D and Screenstar for Cohort E) might have influenced pollution effect estimates. In a prior study, we measured FEV<sub>1</sub> and FVC on 59 children aged 17.3 to 19.5 years using both spirometers. These data were used to build two prediction models for Spiroflow FEV<sub>1</sub> and FVC values, respectively, as a function of the corresponding Screenstar values. That model was developed on older teenagers, and we applied it to the last year of observation in Cohort E (mean age 15) to obtain predicted Spiroflow-based FEV<sub>1</sub> and FVC. Using the age-15 cross-sectional data for all three cohorts, we estimated the effect of declines in air pollution on mean FEV<sub>1</sub> and FVC, first using the Screenstar measurements for Cohort E and then using the Spiroflow predictions for Cohort E.

**Questionnaires** At study enrollment and throughout the study, medical and residential history questionnaires were completed by parents or guardians and by study participants. Questionnaire administration was performed just prior to or immediately following lung-function testing. Questionnaires were used to obtain information about the child and his or her family (age, sex, race, ethnic background of child, insurance coverage, and education of parents), prior and current health conditions (such as asthma, bronchitis, and other cardiorespiratory issues), and other potential exposures (secondhand smoke, maternal smoking during the pregnancy period, or home mildew or mold from water damage). Additionally, questionnaires collected information regarding home operation (including use of gas or electricity for cooking, home use of air conditioning or heating, and the presence or use of fireplaces) as well as usual patterns of students' physical, temporal, and spatial activities.

**Air Pollutants** As described previously, ambient air pollution monitoring stations in each of the study communities have been continuously measuring regional air pollutants since 1993 (gases) and 1994 (PM). Hourly or daily concentrations of NO<sub>2</sub>, PM<sub>2.5</sub>, PM<sub>10</sub>, and O<sub>3</sub> concentrations were routinely collected using Federal Reference Method (FRM) or Federal Equivalent Method (FEM) instrumentation. A systematic quality assurance program was in place to review all data. Mean air pollution concentrations were calculated by community over the relevant periods of exposure for each cohort (1994–1997 for Cohort C, 1997–2000 for Cohort D, and 2007–2010 for Cohort E).

**Statistical Analyses** The goal of the analyses was to examine the association between long-term improvements in ambient air quality and changes in children's lung function development, as measured by FEV<sub>1</sub> and FVC increases

in children from age 11 to 15. All available lung-function measurements were used to estimate lung-function growth curves, including measurements at ages ranging from approximately 9 to 19 in Cohorts C and D and 10 to 16 in Cohort E. A previously developed linear spline model (Gauderman et al. 2007), with knots placed at ages 12, 14, and 16, was used to capture the nonlinear pattern of growth over adolescence (for details see Appendix A, which is available on the HEI Web site). The model included adjustments for sex, race, Hispanic ethnicity, height, height-squared, body mass index (BMI), BMI-squared, and presence of respiratory tract illness on the day of the lung-function test. The model was parameterized to yield estimates of pollutant effects on four-year lung-function growth (age 11 to 15) and on mean attained lung function at either age 11 or 15. This range was targeted as it covers the overlapping age period of lung-function testing across cohorts. Follow-up over this age range occurred from 1994–1998 in Cohort C, 1997–2001 in Cohort D, and 2007–2011 in Cohort E. The estimated health effect of each pollutant is reported as the expected difference in lung-function growth for a difference in exposure equal to the median of the five community changes in pollution over the study period. (Estimated differences in lung-function growth are scaled to the median of the five community-specific declines in each air pollutant, specifically to 14.1 ppb in NO<sub>2</sub>, 5.5 ppb in O<sub>3</sub> [10 AM–6 PM], 8.7 µg/m<sup>3</sup> in PM<sub>10</sub>, and 12.6 µg/m<sup>3</sup> in PM<sub>2.5</sub>).

In addition to examining lung-function growth in the four years from age 11 to 15, we analyzed the cross-sectional lung-function measurements obtained on 1,585 children at the end of this period (average age 15 years) to determine whether changes in air quality over time were associated with clinically important deficits in attained FEV<sub>1</sub> and FVC. Using data from all three cohorts, we developed a linear prediction model for FEV<sub>1</sub> that included adjustments for age, sex, race or ethnicity, height, height-squared, BMI, BMI-squared, and presence of respiratory illness. This model had *R*<sup>2</sup> values of 61% and 69% in age-15 FEV<sub>1</sub> and FVC measurements, respectively. For each child, we determined whether the observed/predicted ratio of FEV<sub>1</sub> and FVC fell below each of three cutoffs for defining low lung function: 90%, 85%, or 80%. Logistic regression was used to test for temporal trends in proportions with low lung function across cohorts after adjustment for community.

Associations were denoted as statistically significant for those that yielded a *P* value of less than 0.05, assuming a two-sided alternative hypothesis.

## Results

To investigate potential effects on lung-function level and growth, we assessed four-year growth trajectories to provide a comparable age time frame (11 to 15 years of age) for comparison across the three cohorts. We considered both lung flow and volume variables (FEV<sub>1</sub> and FVC), and restricted the analytic dataset to subjects that had multiple lung-function measurements and that were not missing any key covariates (age, sex, race, Hispanic ethnicity, height, BMI, respiratory illness, exercise prior to lung-function testing).

There were slightly more girls than boys (52% vs. 48%) in each of the three cohorts (Table 6). The mean age at baseline lung-function test was higher for Cohort E (11.3 years) than for Cohort C (10.9 years) and Cohort D (10.9 years). Age-specific mean height did not differ significantly across cohorts at ages 11, 13, or 15. There was a significantly higher proportion of Hispanic children in Cohort E (58%) compared with Cohorts C (31%) and D (33%). Cohort E also differed significantly from Cohorts C and D on several other factors, including less exposure to passive smoke and pets and a higher proportion of parents with health insurance.

Regional air quality has improved dramatically over the course of the CHS for some pollutants (Figure 3). For example, the four-year mean PM<sub>2.5</sub> levels in the highest PM community (Mira Loma) declined from 31.5 µg/m<sup>3</sup> for Cohort C to 17.8 µg/m<sup>3</sup> for Cohort E, a 43% reduction (Table 7). All five communities experienced large declines in both PM<sub>2.5</sub> and NO<sub>2</sub>. Changes in PM<sub>10</sub> and O<sub>3</sub> over time were more modest (Figure 3).

Across all three study cohorts, estimated mean FEV<sub>1</sub> in girls increased from 2,274 mL at age 11 to 3,150 mL at age 15, for an estimated average four-year growth of 876 mL (Table 8). In boys, estimated mean FEV<sub>1</sub> was 2,311 mL at age 11 and 3,831 mL at age 15, for an estimated average four-year growth of 1,520 mL. Similar magnitudes of growth were observed for FVC.

Increased four-year growth in both FEV<sub>1</sub> and FVC was associated with reduced levels of NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> in all five study communities (Figure 11). Averaging the effects across communities, mean four-year FEV<sub>1</sub> growth increased by 91.4 mL per decrease of 14.1 ppb in NO<sub>2</sub> ( $P < 0.001$ ), 65.5 mL per decrease of 8.7 µg/m<sup>3</sup> in PM<sub>10</sub> ( $P < 0.001$ ), and 65.5 mL per decrease of 12.6 µg/m<sup>3</sup> in PM<sub>2.5</sub> ( $P = 0.008$ ) (Table 9, last columns). At the beginning of the follow-up period (age 11 years), statistically significant differences in mean FEV<sub>1</sub> levels were associated with NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> (Table 9). However, the differences in mean FEV<sub>1</sub> levels at age 15 were even more pronounced following four years of growth with less pollution.

Analogous effects were observed for FVC. Changes in O<sub>3</sub> were not associated with FEV<sub>1</sub> or FVC growth or level.

The estimated pollution-related effects on four-year FEV<sub>1</sub> and FVC growth remained significant in sensitivity analyses (Table 10). For example, the associations observed between lung-function growth and NO<sub>2</sub> in Table 9 (shown as “base model” in Table 10) remained significant and of similar magnitude with additional adjustment for in-utero or secondhand smoke exposure; personal smoking; several indoor exposures including cats, dogs, and mold or mildew; health insurance; parental education; or asthma at baseline. We examined short-term difference in air pollutant levels by adjusting for O<sub>3</sub> (the pollutant that has recognized acute effects on lung function) on the day of the lung-function testing and found negligible change in effect estimates. There were statistically significant effects on lung-function growth in both boys and girls, although the magnitude of the air pollution effect was significantly larger in boys than in girls for both FEV<sub>1</sub> ( $P = 0.04$ ) and FVC ( $P = 0.001$ ). There were also significant pollution effects on growth in Hispanic white and non-Hispanic white children and in asthmatic and non-asthmatic children. Although the magnitude of the NO<sub>2</sub> effect was nearly twice as large in asthmatic compared with non-asthmatic children, the difference in effect between asthmatic and non-asthmatic children was not statistically significant for FEV<sub>1</sub> or FVC. Pollution-effect estimates were of similar magnitude to those in the base model when the sample was restricted to children with complete four-year follow-up. Sensitivity analyses of the other pollutants yielded analogous results to those of NO<sub>2</sub>. We found no significant association between growth in height and change in pollution over the study period (Table 11), indicating that our lung-function growth findings are not likely explainable by a secular trend in general development.

As shown in Table 9, mean attained levels of FEV<sub>1</sub> and FVC at age 15 were substantially larger for Cohort E compared to Cohorts C and D. Further analysis of lung function at age 15 also revealed statistically significant differences across cohorts in the proportion of children with low lung function (Figure 12). For example, at an observed/predicted cutoff of 80%, the proportions of children with low FEV<sub>1</sub> were 7.9% in Cohort C, 6.3% in Cohort D, and only 3.6% in Cohort E ( $P < 0.005$ ). Similar statistically significant trends were observed for FVC.

## Discussion

This study demonstrates an association between secular improvements in air quality in Southern California and measurable improvements in children’s lung-function development. Improved lung function was most strongly

## Effects of Air Quality Improvements on Children's Respiratory Health

**Table 6.** Demographic Characteristics of Children Contributing to Lung Function Analysis

Variable		All (N = 2120)	Cohort C (n = 669)	Cohort D (n = 588)	Cohort E (n = 863)	P Value <sup>a</sup>
Age at baseline <sup>b</sup>		11.0 (0.5)	10.9 (0.5)	10.9 (0.4)	11.3 (0.6)	< 0.001
Height (cm) <sup>b</sup>	Age 11	145.9 (6.9)	145.7 (6.8)	145.8 (6.8)	146.0 (7.1)	0.73
	Age 13	158.0 (7.3)	157.7 (7.4)	157.8 (7.4)	158.2 (7.2)	0.44
	Age 15	165.6 (6.9)	165.5 (6.9)	165.8 (7.1)	165.6 (6.7)	0.85
Male	No (%)	1,105 (52.1)	344 (51.4)	298 (50.7)	463 (53.7)	0.49
	Yes (%)	1,015 (47.9)	325 (48.6)	290 (49.3)	400 (46.3)	
Race	Asian (%)	157 (7.8)	61 (9.4)	47 (8.0)	49 (6.3)	< 0.001
	Black (%)	126 (6.3)	60 (9.2)	43 (7.4)	23 (3.0)	
	Mixed (%)	229 (11.4)	47 (7.2)	57 (9.7)	125 (16.1)	
	Other (%)	469 (23.4)	130 (20.0)	115 (19.7)	224 (28.9)	
	White (%)	1,027 (51.1)	351 (54.1)	323 (55.2)	353 (45.6)	
Hispanic ethnicity	No (%)	1,196 (57.9)	455 (69.0)	393 (67.1)	348 (42.4)	< 0.001
	Yes (%)	870 (42.1)	204 (31.0)	193 (32.9)	473 (57.6)	
Asthma at baseline	No (%)	1,646 (82.2)	536 (86.3)	465 (82.9)	645 (78.7)	< 0.001
	Yes (%)	356 (17.8)	85 (13.7)	96 (17.1)	175 (21.3)	
Parental education	Did not finish HS (%)	300 (14.8)	107 (16.5)	61 (10.7)	132 (16.3)	0.01
	HS diploma/some college (%)	1,167 (57.6)	372 (57.4)	352 (62.0)	443 (54.6)	
	College diploma or greater (%)	560 (27.6)	169 (26.1)	155 (27.3)	236 (29.1)	
Health insurance	No (%)	252 (12.3)	110 (16.9)	78 (13.5)	64 (7.9)	< 0.001
	Yes (%)	1,790 (87.7)	540 (83.1)	501 (86.5)	749 (92.1)	
In-utero smoke exposure	No (%)	1,793 (88.2)	532 (82.7)	494 (86.4)	767 (93.7)	< 0.001
	Yes (%)	241 (11.8)	111 (17.3)	78 (13.6)	52 (6.3)	
Secondhand smoke	No (%)	1,555 (77.9)	477 (73.7)	411 (73.7)	667 (84.2)	< 0.001
	Yes (%)	442 (22.1)	170 (26.3)	147 (26.3)	125 (15.8)	
Smoked 100 cigarettes by age 15	No (%)	2,077 (98.0)	643 (96.1)	573 (97.4)	861 (99.8)	< .0001
	Yes (%)	43 (2.0)	26 (3.9)	15 (2.6)	2 (0.2)	
Any pests <sup>c</sup> at home	No (%)	483 (25.3)	137 (22.8)	100 (18.6)	246 (31.9)	< .0001
	Yes (%)	1,428 (74.7)	464 (77.2)	438 (81.4)	526 (68.1)	
Any pets at home	No (%)	627 (30.4)	172 (25.7)	110 (18.7)	345 (42.8)	< .0001
	Yes (%)	1,437 (69.6)	497 (74.3)	478 (81.3)	462 (57.2)	
Dog ownership	No (%)	1,114 (54.0)	319 (47.7)	260 (44.2)	535 (66.3)	< .0001
	Yes (%)	950 (46.0)	350 (52.3)	328 (55.8)	272 (33.7)	
Cat ownership	No (%)	1,457 (70.6)	444 (66.4)	360 (61.2)	653 (80.9)	< .0001
	Yes (%)	607 (29.4)	225 (33.6)	228 (38.8)	154 (19.1)	
Carpet at home	No (%)	125 (6.1)	29 (4.5)	21 (3.6)	75 (9.2)	< .0001
	Yes (%)	1,917 (93.9)	621 (95.5)	558 (96.4)	738 (90.8)	
Mildew/mold at home	No (%)	1,484 (75.4)	484 (75.7)	428 (75.5)	572 (75.1)	0.96
	Yes (%)	484 (24.6)	155 (24.3)	139 (24.5)	190 (24.9)	
Water damage at home	No (%)	1,733 (85.2)	552 (84.9)	494 (85.8)	687 (84.9)	0.89
	Yes (%)	302 (14.8)	98 (15.1)	82 (14.2)	122 (15.1)	
Gas stove at home	No (%)	322 (15.7)	102 (15.6)	109 (18.8)	111 (13.7)	0.04
	Yes (%)	1,723 (84.3)	552 (84.4)	472 (81.2)	699 (86.3)	
Air conditioning at home	No (%)	425 (20.6)	156 (23.7)	143 (24.6)	126 (15.3)	< .0001
	Yes (%)	1,640 (79.4)	503 (76.3)	439 (75.4)	698 (84.7)	
Date of home construction	Before 1960 (%)	440 (25.3)	146 (26.1)	137 (28.1)	157 (22.8)	0.23
	1960s to 1970s (%)	692 (39.9)	215 (38.4)	184 (37.7)	293 (42.6)	
	1980 or later (%)	604 (34.8)	199 (35.5)	167 (34.2)	238 (34.6)	

Note: numbers might not add up to the total N because of missing values.

<sup>a</sup> P value comparing mean age and height and proportions of remaining variables across the three cohorts. The test for height includes adjustment for sex, race, and Hispanic ethnicity.

<sup>b</sup> Values for age and height are the mean (standard deviation).

<sup>c</sup> Pests include termites, spiders, ants, cockroaches, mice, and/or rats.

**Table 7.** Long-Term Average Concentrations of Air Pollutants in Five Communities Across Three CHS Cohorts for Use in Lung Function Analysis

Community	Cohort Exposure Period	Average of Air Pollutants by Cohort Exposure Period <sup>a</sup>			
		NO <sub>2</sub> (ppb)	O <sub>3</sub> (10AM–6PM, ppb)	PM <sub>10</sub> (µg/m <sup>3</sup> )	PM <sub>2.5</sub> (µg/m <sup>3</sup> )
Long Beach	C: 1994–1997	34.4	28.6	37.5	21.3
	D: 1997–2000	32.9 (–4.5%)	28.8 (0.7%)	35.9 (–4.2%)	19.7 (–7.5%)
	E: 2007–2010	20.3 (–41.0%)	31.4 (10.0%)	28.4 (–24.2%)	13.0 (–38.9%)
Mira Loma	C: 1994–1997	23.3	56.2	66.5	31.5
	D: 1997–2000	25.3 (8.5%)	49.3 (–12.3%)	66.0 (–0.7%)	27.6 (–12.2%)
	E: 2007–2010	16.7 (–28.3%)	48.4 (–13.9%)	52.6 (–20.8%)	17.8 (–43.3%)
Riverside	C: 1994–1997	24.7	61.9	42.1	29.3
	D: 1997–2000	25.7 (4.0%)	54.1 (–12.5%)	41.5 (–1.4%)	25.7 (–12.2%)
	E: 2007–2010	21.4 (–13.2%)	54.5 (–11.9%)	33.4 (–20.7%)	13.1 (–55.3%)
San Dimas	C: 1994–1997	36.6	52	36.9	24.5
	D: 1997–2000	32.4 (–11.6%)	41.4 (–20.5%)	32.5 (–12.0%)	19.6 (–19.9%)
	E: 2007–2010	21.5 (–41.3%)	46.6 (–10.5%)	29.9 (–19.1%)	11.9 (–51.6%)
Upland	C: 1994–1997	39.4	48.8	42.9	28.7
	D: 1997–2000	36.2 (–8.1%)	40.9 (–16.1%)	39.9 (–7.1%)	23.8 (–17.2%)
	E: 2007–2010	23.4 (–40.7%)	47.5 (–2.6%)	34.7 (–19.2%)	16.1 (–43.9%)

<sup>a</sup> Mean pollutant level over the indicated 4-yr period in each community (values in parentheses are the percent change compared to Cohort C, 1994–1997).

**Table 8.** Estimated Mean Lung Function Level and Growth in Girls and Boys<sup>a</sup>

Outcome	Girls			Boys		
	Age		4-yr Growth	Age		4-yr Growth
	11 yr	15 yr		11 yr	15 yr	
FEV <sub>1</sub> (mL)	2,274 (2,251 to 2,297)	3,150 (3,121 to 3,178)	876 (859 to 893)	2,311 (2,288 to 2,335)	3,831 (3,794 to 3,869)	1,520 (1,497 to 1,543)
FVC (mL)	2,581 (2,554 to 2,607)	3,573 (3,540 to 3,606)	992 (974 to 1,011)	2,708 (2,680 to 2,737)	4,483 (4,438 to 4,527)	1,774 (1,749 to 1,800)

<sup>a</sup> Estimated mean lung function was calculated by fitting a spline model containing only age with knots at ages 12, 14, and 16, and the age term parameterized such that it estimates the growth in lung function between ages 11 and 15. The model was fitted twice for boys and girls: once with age centered at age 11 and once with age centered at age 15. The intercepts and the growth term along with their 95% confidence intervals (shown in parentheses) were extracted from these models ( $\alpha_a$  and  $\alpha_b$  from Equation 11 in Appendix A, available on the HEI Web site).

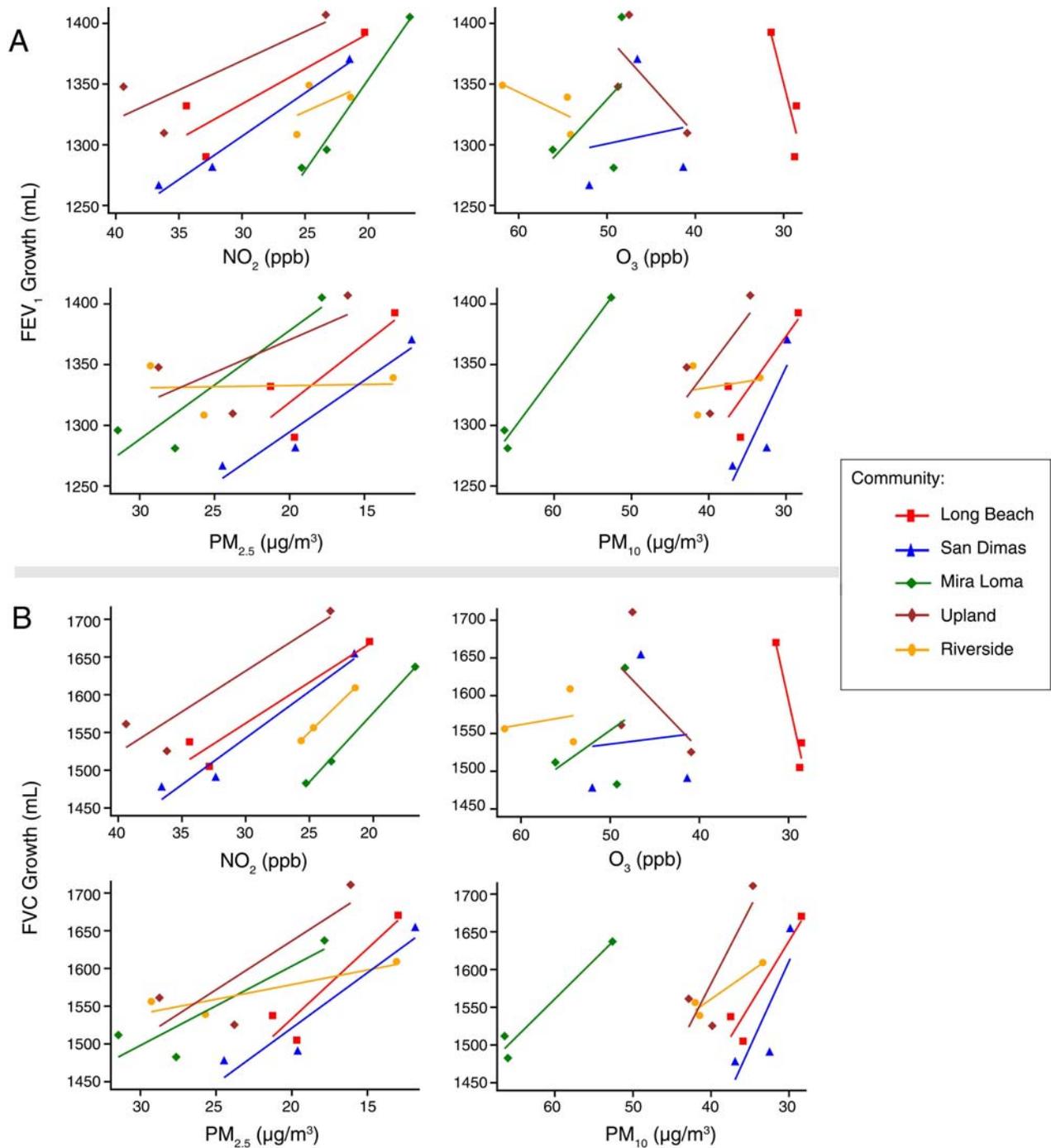


Figure 11. Community-average four-year growth in (A) FEV<sub>1</sub> and (B) FVC from age 11 to 15 versus the corresponding community-average levels of four pollutants.

**Table 9.** Estimated Difference in Four-Year Lung Function Growth for Average Decreases in Ambient Pollutant Levels<sup>a</sup>

Lung Function / Pollutant	Level at Age 11			Level at Age 15			Growth, Age 11 to 15		
	Difference (95% CI)	<i>P</i> Value		Difference (95% CI)	<i>P</i> Value		Difference (95% CI)	<i>P</i> Value	
<b>FEV<sub>1</sub></b>									
NO <sub>2</sub>	119.2 (76.5 to 161.9)	< 0.001		210.6 (156.0 to 265.2)	< 0.001		91.4 (47.9 to 134.9)	< 0.001	
O <sub>3</sub> (10AM–6PM)	15.0 (–38.5 to 68.6)	0.58		8.3 (–82.9 to 99.6)	0.86		–6.7 (–51.0 to 37.5)	0.77	
PM <sub>10</sub>	87.7 (50.2 to 125.2)	< 0.001		153.2 (97.7 to 208.6)	< 0.001		65.5 (27.2 to 103.7)	< 0.001	
PM <sub>2.5</sub>	100.0 (58.9 to 141.2)	< 0.001		165.5 (95.4 to 235.6)	< 0.001		65.5 (17.1 to 113.8)	0.008	
<b>FVC</b>									
NO <sub>2</sub>	131.3 (91.0 to 171.6)	< 0.001		300.2 (240.0 to 360.3)	< 0.001		168.9 (127.0 to 210.7)	< 0.001	
O <sub>3</sub> (10AM–6PM)	7.6 (–50.2 to 65.4)	0.80		0.3 (–126.0 to 126.5)	0.99		–7.3 (–79.3 to 64.6)	0.84	
PM <sub>10</sub>	93.8 (54.0 to 133.6)	< 0.001		206.8 (124.6 to 289.1)	< 0.001		113.1 (60.0 to 166.1)	< 0.001	
PM <sub>2.5</sub>	110.1 (69.8 to 150.4)	< 0.001		237.0 (147.2 to 326.7)	< 0.001		126.9 (65.7 to 188.1)	< 0.001	

<sup>a</sup> Estimated differences in lung function growth are scaled to the median of the five community-specific declines in each air pollutant, specifically to 14.1 ppb in NO<sub>2</sub>, 5.5 ppb in O<sub>3</sub> (10AM–6PM), 8.7 µg/m<sup>3</sup> in PM<sub>10</sub>, and 12.6 µg/m<sup>3</sup> in PM<sub>2.5</sub>.

**Table 10.** Sensitivity Analysis of the Effect of Decreased NO<sub>2</sub> Levels on Four-Year Lung Function Growth

Model	FEV <sub>1</sub> Growth, Age 11 to 15		FVC Growth, Age 11 to 15	
	Difference (95% CI)	<i>P</i> Value	Difference (95% CI)	<i>P</i> Value
Base Model (NO <sub>2</sub> ) <sup>a</sup>	91.4 (47.9 to 134.9)	< 0.001	168.9 (127.0 to 210.7)	< 0.001
<b>Additional Adjustments</b>				
Base + education	90.7 (47.6 to 133.9)	< 0.001	168.4 (126.8 to 210.0)	< 0.001
Base + insurance	89.1 (45.6 to 132.7)	< 0.001	166.5 (127.4 to 205.7)	< 0.001
Base + in-utero smoke	90.7 (47.3 to 134.1)	< 0.001	168.6 (126.8 to 210.5)	< 0.001
Base + secondhand smoke	90.6 (47.4 to 133.7)	< 0.001	168.5 (126.8 to 210.2)	< 0.001
Base + personal tobacco smoking	90.9 (47.5 to 134.4)	< 0.001	167.8 (126.9 to 208.7)	< 0.001
Base + acute O <sub>3</sub>	94.0 (51.9 to 136.0)	< 0.001	169.7 (128.4 to 210.9)	< 0.001
Base + asthma	92.6 (49.3 to 136.0)	< 0.001	168.1 (126.4 to 209.9)	< 0.001
Base + pests	89.2 (46.4 to 131.9)	< 0.0001	169.2 (127.2 to 211.2)	< 0.0001
Base + pets	87.4 (44.1 to 130.7)	< 0.0001	167.4 (125.1 to 209.6)	< 0.0001
Base + dog	90.7 (46.3 to 135.1)	< 0.0001	169.9 (126.9 to 213.0)	< 0.0001
Base + cat	88.7 (45.2 to 132.1)	< 0.0001	165.8 (124.5 to 207.1)	< 0.0001
Base + carpet	88.6 (45.8 to 131.5)	< 0.0001	167.8 (126.1 to 209.5)	< 0.0001
Base + mildew/mold	91.2 (47.4 to 135.0)	< 0.0001	168.6 (126.7 to 210.6)	< 0.0001
Base + water damage	91.2 (47.8 to 134.7)	< 0.0001	168.7 (127.0 to 210.4)	< 0.0001
Base + gas stove	92.0 (48.4 to 135.6)	< 0.0001	170.0 (128.0 to 212.0)	< 0.0001
Base + air conditioning	90.7 (47.3 to 134.2)	< 0.0001	168.4 (126.9 to 209.9)	< 0.0001
Base + date of home construction	91.8 (48.1 to 135.5)	< 0.0001	168.7 (126.9 to 210.4)	< 0.0001
<b>Subgroups</b>				
Girls only	70.9 (29.3 to 112.5)	< 0.001	113.0 (71.4 to 154.6)	< 0.001
Boys only	112.4 (43.1 to 181.8)	0.002	236.3 (165.4 to 307.2)	< 0.001
Non-Hispanic white	84.2 (21.3 to 147.1)	0.009	168.8 (109.3 to 228.4)	< 0.0001
Hispanic white	104.4 (42.8 to 165.9)	0.0009	179.0 (107.3 to 250.7)	< 0.0001
Non-smokers (until age 15)	96.3 (52.3 to 140.2)	< 0.0001	174.3 (133.5 to 215.0)	< 0.0001
Non-asthmatics only	82.2 (35.1 to 129.4)	< 0.001	139.2 (97.0 to 181.4)	< 0.001
Asthmatics only	150.8 (43.2 to 258.5)	0.006	306.9 (195.0 to 418.9)	< 0.001
Complete data at ages 11 and 15	87.8 (45.3 to 130.2)	< 0.001	161.7 (122.0 to 201.3)	< 0.001

<sup>a</sup> Base model is equivalent to the effect estimates shown for NO<sub>2</sub> in Table 9.

associated with lower levels of particulate pollution (PM<sub>2.5</sub> and PM<sub>10</sub>) and NO<sub>2</sub>. These associations were observed in boys and girls, Hispanic white and non-Hispanic white children, and asthmatic and non-asthmatic children, suggesting that all children have the potential to benefit from improvements in air quality.

We also found strong association between air pollution and clinically low FEV<sub>1</sub> and FVC at age 15. In general, the age range of 11 to 15 captures a period in which lungs are developing rapidly for both boys and girls. Lung-function development continues in girls until their late teens and in boys until their early 20s, but at a much-reduced rate compared with

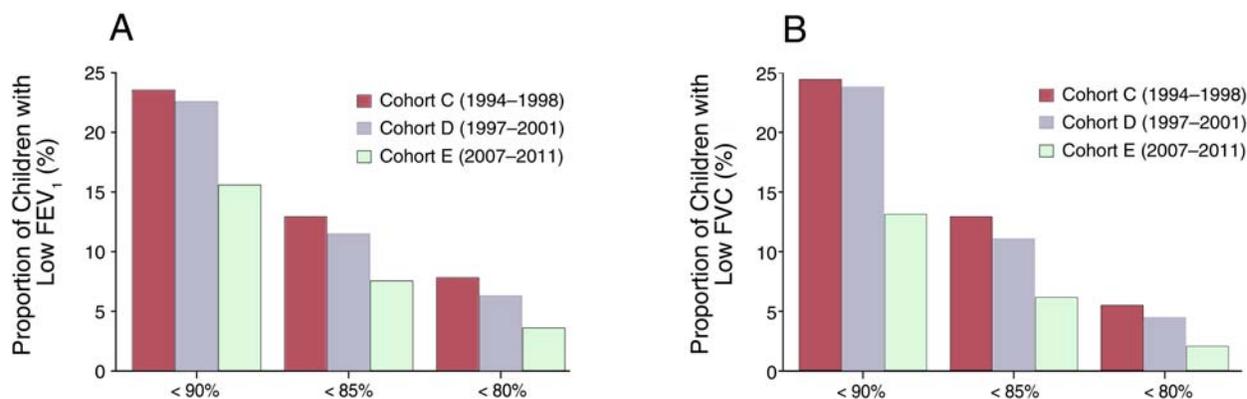
this earlier adolescent period (Burrows et al. 1983; Wang et al. 1993). It is therefore likely that the improved function we observed in the less-exposed children will persist into their adulthood. A higher level of lung function in early adulthood may decrease the risk of respiratory conditions (McKean et al. 2001). However, the greatest benefit of improvements in lung-function growth may occur later in life, as it has been shown that greater lung function in adulthood can contribute to lower risks of premature death and other adverse health outcomes (Ashley et al. 1975; Friedman et al. 1976; Hole et al. 1996; Kannell et al. 1983; Knudman et al. 1999; Schroeder et al. 2003; Schunemann

**Table 11.** Estimated Difference in Four-Year Height Growth for Average Decreases in Ambient Pollutant Levels<sup>a,b</sup>

Pollutant	Level at Age 11		Level at Age 15		Growth, Age 11 to 15	
	Difference (95% CI)	P Value	Difference (95% CI)	P Value	Difference (95% CI)	P Value
NO <sub>2</sub>	0.26 (−0.65 to 1.16)	0.58	−0.13 (−0.91 to 0.66)	0.75	−0.39 (−1.12 to 0.34)	0.29
O <sub>3</sub> (10AM–6PM)	0.18 (−0.39 to 0.74)	0.55	0.18 (−0.30 to 0.67)	0.46	0.01 (−0.44 to 0.46)	0.97
PM <sub>10</sub>	0.16 (−0.54 to 0.86)	0.66	−0.07 (−0.68 to 0.53)	0.81	−0.24 (−0.81 to 0.34)	0.42
PM <sub>2.5</sub>	0.07 (−0.73 to 0.87)	0.87	−0.06 (−0.75 to 0.62)	0.85	−0.14 (−0.83 to 0.56)	0.70

<sup>a</sup> Estimated differences in height growth (in cm) are scaled to the median of the five community-specific declines in each air pollutant, specifically to 14.1 ppb in NO<sub>2</sub>, 5.5 ppb in O<sub>3</sub> (10AM–6PM), 8.7 µg/m<sup>3</sup> in PM<sub>10</sub>, and 12.6 µg/m<sup>3</sup> in PM<sub>2.5</sub>.

<sup>b</sup> We analyzed the association between height growth and changes in air quality to determine whether the pollution-related associations we observed with lung function growth might be attributable to a more general time trend in physiological development. We used the same spline-based approach as was used for lung function (see “Statistical Modeling” in Appendix A, available on the HEI Web site) to model the relationship between height and air quality. This model included adjustments for sex, race, Hispanic ethnicity, and study community. As shown above, neither height growth nor mean height at age 11 or 15 are significantly associated with the change in any of the pollutants.



**Figure 12.** Proportion of children with lung function below 90%, 85%, or 80% of predicted at age 15 years in Cohorts C, D, and E for (A) FEV<sub>1</sub> and (B) FVC.

et al. 2000). Consistent with the growth effects we have observed in children, there is evidence that reduced pollution exposure in adulthood can slow the decline in lung function (Lepeule et al. 2014) and increase life expectancy (Laden et al. 2006; Pope et al. 2009).

In Southern California, motor vehicles are a primary source of PM<sub>2.5</sub>, PM<sub>10</sub>, and NO<sub>2</sub> through direct tailpipe emissions as well as downwind physical and photochemical reactions of vehicular emissions (McDonald et al. 2012; Sardar et al. 2005). Gasoline- and diesel-powered engines contribute to high levels of these pollutants. Improved emission standards for both types of vehicles have contributed to the observed declines in air pollutants. Previous control strategies implemented in the 1970s and 1980s focused primarily on reducing levels of O<sub>3</sub>, a pollutant with a long history of demonstrated acute health effects (Bascom et al. 1996). Although levels of O<sub>3</sub> continued to decline in the 1990s and 2000s, the changes were less than for NO<sub>2</sub> and PM and we did not observe O<sub>3</sub>-related effects on lung-function growth. This finding is consistent with our previous report that decreased lung-function growth was related to increased exposure to NO<sub>2</sub> and PM, but not to O<sub>3</sub> (Gauderman et al. 2004). Only a few other studies have addressed the long-term effects of O<sub>3</sub> on lung function in children, and results have been inconsistent (Tager 1999). Because of high correlations in reductions of PM<sub>2.5</sub>, PM<sub>10</sub>, and NO<sub>2</sub> (Table 12), we could not disentangle independent associations of these pollutants. Many other studies have also been unable to identify the health effects of specific pollutants that are constituents of a multi-pollutant mixture (Gehring et al. 2013; Liu et al. 2009). However, the results of our investigation make it clear that broad-based efforts to improve general air quality are associated with substantial and measurable public health benefits.

A main directive of the CAA was to establish "...ambient air quality standards...allowing an adequate margin of

safety...requisite to protect the public health...." A basic tenet of the CAA is that changes in airborne pollutant levels can lead to improved public health, and that the scientific evidence needed to determine the appropriate levels for those standards can be determined. Our observation of improving air quality with subsequent improvements in longitudinal respiratory health outcomes may provide objective evidence in support of that basic tenet.

The data necessary to conduct this study were collected over a period of nearly two decades. Strengths of the study include the use of consistent protocols for collecting health, covariate, and air quality data over the entire study period. Although the extended follow-up period can be viewed as a study strength, it also presented several challenges. A change in the spirometers used over the course of the study was unavoidable but raises the issue of instrumental comparability. To address this, we conducted additional analyses to demonstrate that our findings are robust to the use of different spirometers. In Table 13, we show that the use of transducer-based spirometer (Screenstar) measurements in Cohort E for the primary analyses did not lead to any systematic biases in the pollution effects reported elsewhere in this report.

The change from annual testing in Cohorts C and D to every-other-year testing in Cohort E, because of budgetary constraints, might have caused concern about cohort dropout. In general, bias can occur in a cohort study if dropout depends simultaneously on both outcome and exposure. In our study, however, subject attrition during the follow-up period was not jointly associated with baseline lung function and several measures of exposure, including cohort membership and cohort-specific mean levels of NO<sub>2</sub> and PM (the pollutants that showed significant associations with lung-function growth). Additionally, the magnitude and significance of our observed growth effects were similar in those with complete follow-up

**Table 12.** Partial Correlations (Adjusted for Community) of Long-Term Cohort-Specific Mean Pollutant Levels Across Five Communities Used in the Analysis of Lung Function

Pollutant	O <sub>3</sub> (ppb)	PM <sub>10</sub> (µg/m <sup>3</sup> )	PM <sub>2.5</sub> (µg/m <sup>3</sup> )
NO <sub>2</sub>	0.02	0.82	0.82
O <sub>3</sub>		0.33	0.39
PM <sub>10</sub>			0.93

**Note:** All correlations greater than 0.4 were statistically significant ( $P < 0.05$ ). Correlations are based on the pollutant values found in Table 7.

(Table 10), making it unlikely that selective dropout is responsible for our observed associations.

The shift in ethnicity across cohorts to a more Hispanic population, synchronous with general trends occurring more broadly in Southern California (U.S. Census 2000, 2010) raises potential concerns about confounding by ethnic-specific factors. Also, because this is an observational study, it is possible that one or more additional factors associated with both lung-function growth and change in air quality over time could confound our pollution analyses. However, we conducted many sensitivity analyses and found that none of these factors appreciably impacted our estimates or inferences. Furthermore, because average height growth did not vary over the study period, one might conclude that the change in lung-function growth is not the result of a general constitutional reduction in growth, with improvement in air quality serving as an important contributing factor.

Another limitation of our study is the lack of a pure “control” community, that is, a community in which there was no change in pollution over the study period. However, we did study five different communities, with differing magnitudes of improvement in air quality, which collectively serve as five replicate experiments of our within-community temporal trend experiment. We conducted an additional analysis to demonstrate that the expected gain in lung function over time within any one community was aligned with the magnitude of improvement in air quality within that community (Figure 13). The trends in these effects suggest that if we did have a pure control community, we would expect little change in lung-function growth. This figure also suggests that even modest improvements in air quality can lead to improved health, although with only five communities we caution that we do not have adequate resolution to make definitive conclusions about the form of the exposure–response relationship.

**Table 13.** Cross-Sectional Analysis of Lung Function at Age 15 to Examine Sensitivity to the Use of Different Spirometers<sup>a</sup>

Outcome / Pollutant	Cohort E: Measured Lung Function <sup>b</sup>		Cohort E: Modeled Lung Function <sup>c</sup>	
	Difference (95% CI)	<i>P</i> Value	Difference (95% CI)	<i>P</i> Value
<b>FEV<sub>1</sub></b>				
NO <sub>2</sub>	200.0(142.7 to 257.3)	< 0.001	209.3(153.7 to 265.0)	< 0.001
O <sub>3</sub> (10AM–6PM)	–12.4(–48.1 to 23.3)	0.49	–10.2(–44.9 to 24.6)	0.57
PM <sub>10</sub>	120.8(75.7 to 166.0)	< 0.001	130.3(86.4 to 174.2)	< 0.001
PM <sub>2.5</sub>	132.9(82.4 to 183.4)	< 0.001	143.6(94.6 to 192.7)	< 0.001
<b>FVC</b>				
NO <sub>2</sub>	293.0(231.5 to 354.6)	< 0.001	342.0(282.3 to 401.7)	< 0.001
NO <sub>2</sub>	–13.7(–52.7 to 25.2)	0.49	20.2(–18.0 to 58.3)	0.30
O <sub>3</sub> (10AM–6PM)	180.8(132.0 to 229.6)	< 0.001	245.7(198.6 to 292.8)	< 0.001
PM <sub>10</sub>	218.1(163.7 to 272.4)	< 0.001	306.9(254.7 to 359.0)	< 0.001

<sup>a</sup> For Cohorts C and D, lung function testing was performed using rolling-seal spirometers (Spiroflow Model 132; P.K. Morgan Ltd., Gillingham, UK), while in Cohort E, lung function testing was performed using pressure transducer-based spirometers (Screenstar, Morgan Scientific, Haverhill, Massachusetts, USA). Sensitivity analyses were conducted to assess whether the use of different spirometers (Spiroflow in Cohorts C and D, Screenstar in Cohort E) might have influenced pollution effect estimates. In a prior study, we measured FEV<sub>1</sub> and FVC on 59 children aged 17.3 to 19.5 years using both spirometers. These data were used to build two prediction models for Spiroflow FEV<sub>1</sub> and FVC, respectively, as a function of the corresponding Screenstar values. That model was developed on older teenagers, and thus we applied it to the last year of observation in Cohort E (mean age 15) to obtain predicted Spiroflow-based FEV<sub>1</sub> and FVC. Using the age-15 cross-sectional data for all three cohorts, we estimated the effect of declines in air pollution on mean FEV<sub>1</sub> and FVC, first using the Screenstar measurements for Cohort E and then using the Spiroflow predictions for Cohort E (Table 12). Statistically significant associations were observed for both FEV<sub>1</sub> and FVC with NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> (all with *P* < 0.001) regardless of the reference spirometer for Cohort E. This suggests that use of Screenstar measurements in Cohort E for the primary analyses did not lead to any systematic biases in the pollution effects reported elsewhere in this report.

<sup>b</sup> Measured values using the ScreenStar spirometer for Cohort E (Spiroflow spirometer used for Cohorts C and D).

<sup>c</sup> Modeled values used for Cohort E, based on a prediction model for Spiroflow spirometer measurements as a function of ScreenStar spirometer values. Measured values from the Spiroflow were used for Cohorts C and D.

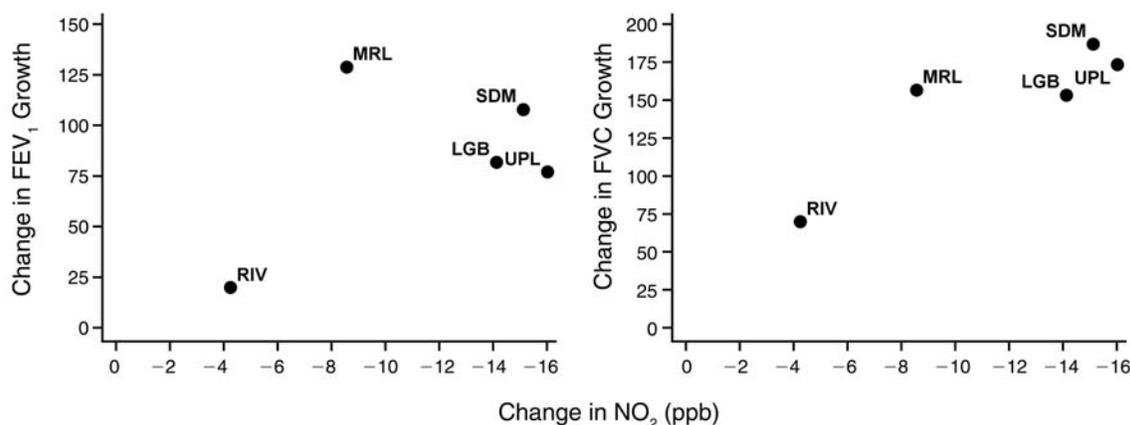


Figure 13. Predicted change in 4-year lung-function growth (vertical change in the trend lines of Figure 11) versus the change in average NO<sub>2</sub> concentrations over the study period (horizontal change in the trend lines of Figure 11) for each community. LGB=Long Beach, MRL=Mira Loma, RIV=Riverside, SDM=San Dimas, and UPL=Upland

We have demonstrated that improved air quality in Southern California is associated with statistically and clinically significant improvements in childhood lung-function growth. The pollutants we found to be associated with lung-function growth — NO<sub>2</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> — are products of primary fuel combustion and are likely to be present at increased levels in most urban environments. These pollutants were among those effectively reduced through targeted policy strategies. The magnitude of our observed effects and the importance of lung function over the course of the human lifetime justify the efforts that have been made to improve air quality.

## AIR QUALITY TRENDS AND RESPIRATORY SYMPTOMS

### Introduction

Bronchitis and chronic bronchitic symptoms in children are common yet underappreciated aspects of clinically important morbidity (Aalto et al. 2005; Braun-Fahrlander et al. 1997; Dockery et al. 1989, 1996; Heinrich et al. 2000; Jedrychowski and Flak 1998; McConnell et al. 1999, 2003). Evidence from a number of studies indicates that exposure to elevated concentrations of ambient air pollution, often at levels below regulatory standards, is associated with large increases in the prevalence of bronchitic symptoms among children with asthma (Dockery and Pope 1994; Dockery et al. 1989; McConnell et al. 2006a, 2003).

As discussed above, Southern California has reported high levels of ambient air pollution attributable to

emissions from vehicular traffic, industrial sources, two very large ports, and complex photochemical reactions. In the last 20 years, significant improvements in air quality have been observed because of a broad spectrum of air pollution reduction policies and strategies. We hypothesized that the reduction of PM<sub>10</sub>, PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub> concentrations observed across Southern California was associated with improvements in chronic respiratory symptoms in children (Bayer-Oglesby et al. 2005).

In this section of the report, we investigated the effects of improving air quality on the prevalence of bronchitic symptoms in children with or without asthma in eight Southern California communities. We examined data from the Southern California CHS that included 20 years of continuous air quality monitoring data and respiratory outcome information from successive cohorts of children followed during 1993–2012.

### Methods and Study Design

As discussed above in the Lung Function section, the health database for this investigation is the CHS, a long-term study of schoolchildren from demographically similar communities with differing ambient air pollution profiles across Central and Southern California. We summarize our methods below, and further details can be found above in the Methods section of the Lung Function section.

Twelve Southern California communities were originally selected to represent a historically diverse pollution profile of regional levels of NO<sub>2</sub>, PM<sub>10</sub>, O<sub>3</sub>, and acid vapor (Peters et al. 1999b). Three successively recruited cohorts were used in the current study. Nine communities (Alpine,

Lake Arrowhead, Lake Elsinore, Long Beach, Mira Loma, Riverside, San Dimas, Santa Maria, and Upland) had participants in all three cohorts, hereafter referred to as Cohorts C, D, and E. The symptoms analyses involved only eight of these nine communities because of incompleteness of data needed to assign air pollution levels in Lake Arrowhead. We further excluded 297 subjects who were newly diagnosed with asthma during the follow-up period. The final analysis data set included 4,602 participants (1,008, 1,067, and 2,527 children from Cohorts C, D, and E, respectively) who had data from two or more annual follow-up questionnaires. All parents or guardians of participating children provided written informed consent. The study protocol was approved by the Institutional Review Board of the University of Southern California.

**Respiratory Symptoms Assessment** Our approach stems from previous observations suggesting that asthmatic children are a susceptible group at higher risk for bronchitic symptoms compared with non-asthmatic children (McConnell et al. 1999, 2003). Bronchitic symptoms were assessed annually using a follow-up questionnaire, as previously described (McConnell et al. 2003, 2006a). A child was considered to have had chronic bronchitic symptoms during the previous 12 months, based on the parent's and/or child's report of a daily cough for three months in a row, congestion or phlegm other than when accompanied by a cold, or bronchitis. To assess bronchitic symptoms — bronchitis, cough, and phlegm — we analyzed data from cohort participants residing in the eight CHS communities that included 20 years of continuous air quality monitoring data and respiratory outcome information from successive cohorts of children followed during 1993–2012. To assess the robustness of the main findings, we also conducted extensive sensitivity analysis by restricting our analyses to those with overlapping ages (i.e., ages 10 to 15 years) for Cohorts C, D, and E.

For Cohorts C and D, children were considered to have a history of asthma before age 10 if there was a “yes” answer to the question on the baseline questionnaire “Has a doctor ever diagnosed this child as having asthma?” For Cohort E, a child was considered to have a history of asthma before age 10 if an asthma diagnosis was made before age 10 based on annual assessment starting from age 5–7. In the models, subjects were classified according to whether they had asthma before age 10 (asthma group) or did not have asthma before age 10 and during the follow-up period (non-asthma group) (McConnell et al. 2003, 2006a).

**Air Pollution Measurements and Metrics** As described above, air pollution monitoring stations were established

in each of the study communities. For each year of follow-up, measurements were made for O<sub>3</sub>, NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>, as described previously (Gauderman et al. 2000; Peters et al. 1999b). We computed annual averages of the 24-hour PM<sub>10</sub>, PM<sub>2.5</sub>, and NO<sub>2</sub>, and of the 10:00 AM to 6:00 PM averages of O<sub>3</sub>. Community-specific one-year lagged annual averages of the 24-hour PM<sub>10</sub>, PM<sub>2.5</sub>, and NO<sub>2</sub> and of the 10:00 AM to 6:00 PM averages of O<sub>3</sub> were used to compute the cohort-specific mean levels for the relevant period of follow-up (Cohort C: 9-year 1992–2000 average; Cohort D: 9-year 1995–2003 average; and Cohort E: 10-year 2002–2011 average) in each community.

Individual subjects' exposure assignments were based on the central site monitoring data from the community where the subjects resided. Each station monitored hourly levels of O<sub>3</sub>, PM<sub>10</sub>, NO<sub>2</sub>, and PM<sub>2.5</sub>, which were collected using a variety of samplers and instruments over time and standardized to reference methods. We selected the 10:00 AM to 6:00 PM metric for O<sub>3</sub> concentration because O<sub>3</sub> has a marked diurnal pattern, with highest concentrations occurring during midday and afternoon periods, when children were likely to be outside and, therefore, more exposed. Annual averages of PM<sub>2.5</sub> were computed from hourly, daily, and/or two-week average measurements. A systematic quality assurance program was implemented to review all data and correct, adjust, or reject any data of suspect quality. In cases where we invalidated data because there were questions of quality, interpolation methodologies using nearby monitoring sites and historical data were used to provide imputed values. PM<sub>10</sub> average pollutant concentrations from 1994 were used for Alpine, Riverside, and Upland for 1992 and 1993 because of missing data. Similarly, PM<sub>2.5</sub> average pollutant concentrations from 1994 were used for 1992 and 1993, for all eight communities, because of missing data. Data review teams from regional monitoring agencies and the study research team from the University of Southern California sequentially reviewed and approved data for acceptance into the study database.

**Additional Covariates from Questionnaires** From the baseline and follow-up questionnaires, we evaluated potential confounders or modifiers of the effects of air pollution, including annual information on exposure to secondhand smoke in the home (SHS) and baseline information on the ownership of a dog, cat, or any pet (including dogs and cats), sex, race/ethnicity, and housing conditions.

## Statistical Methods and Data Analysis — Respiratory Symptoms

**Symptoms Analyses** The main objective of the symptoms analysis was to assess the impact of changing levels of ambient air pollution on bronchitic symptoms in children during the CHS period of observation. We examined the distributions of demographic as well as other personal and housing characteristics within each cohort, at study entry, using descriptive statistics and tests for overall associations. Furthermore, to examine the trend in air pollution levels changing from the earlier cohorts (C and D) to the later cohort (E) within each community, we described the cohort-specific averages in air pollutants within each community.

We used a multilevel logistic modeling strategy described in previous studies (Berhane et al. 2004; McConnell et al. 2003, 2006a,b) to examine the association between cohort- and community-specific pollution levels and binary (Yes/No) longitudinal data on bronchitic symptoms. The analyses included a random-effects assignment to account for serial dependency within study participants and clustering effects of individuals by cohort. Effect estimates were scaled to the corresponding median of the eight community-level average changes in pollution level, corresponding to each pollutant, from the Cohort C to Cohort E study periods. Time-dependent covariates included SHS exposure in the home, age (centered at 10 years), and cubic spline terms of age with knots at 10 and 15 years of age, to account for the non-linear association with bronchitic symptoms. All of the final models were adjusted for age, sex, race/ethnicity, and exposure to SHS during the follow-up period. In addition, the models for NO<sub>2</sub> were also adjusted for exposure to roaches at home as it was a confounder for the association of NO<sub>2</sub> with bronchitic symptoms. These models also included a fixed-effect for community, which was used to make inferences about effects of secular changes in air pollution levels (with one year lag to conform to the bronchitic symptom outcomes that were assessed for the preceding 12 months) across the span of the observation period (1992–2011) on bronchitic symptoms. We fitted models with effects stratified by asthma status because there were significant differences in prevalence of bronchitic symptoms between subjects in the “asthma” and “non-asthma” groups. We also examined effect modification by sex, dog ownership, and SHS exposure. Models that tested effect modification by sex and dog ownership used data from 4,442 children, because of missing relevant questionnaire data. In all models, missing data were assumed to be missing at random. Because missingness in the adjustment variables was very modest, we used a missing indicator method as

needed for any adjustment variable in order to avoid loss of sample size (Diggle et al. 1994). Two-pollutant models were fitted whenever the correlation between covariates were found to be sufficiently low in order to avoid multicollinearity.

All analyses assumed a two-sided alternative hypothesis at a 0.05 level of significance. All models were fitted using R software (version i386 3.0.2), via the “glmer” function in the “lme4” package for logistic mixed-effects regression models. To assess the sensitivity of results under various software platforms, key models were also refitted via the SAS software package (SAS 9.3) using the GLIMMIX procedure. Additional information regarding the statistical modeling approach can be found in Appendix A (available online at HEI Web site).

## Results

There were similar numbers of girls and boys overall (49% versus 51%) and across all cohorts (Table 14). The proportion of Hispanic children increased from 30% for Cohort C to 36% for Cohort D and 58% for Cohort E. Cohort E also differed significantly from Cohorts C and D on several other factors, with a lower proportion of exposure to SHS or history of in-utero exposure to maternal smoking, and lower prevalence of ownership of cats, dogs or any other pets; as well as higher prevalence of asthma at age 10 (23% vs. 15%). Additionally, Cohort E had larger proportions of children with health insurance, living in homes with gas stoves, and who were obese or overweight at age 10; as well as a lower proportion of children who had carpeting in the house and who had parents with a high school diploma. A higher proportion of Cohort E also completed a Spanish-language questionnaire.

Overall, there was a declining trend in air pollution levels across the three cohorts over a period spanning 1994–2011 (Figure 4). For NO<sub>2</sub> and O<sub>3</sub>, a declining trend in pollution levels in all eight communities was observed with the lowest average levels observed for Cohort E, with the exception of Long Beach and Santa Maria where O<sub>3</sub> levels were higher in Cohort E (see Table 15 and Figure 14). Decreases were larger in communities with the highest levels of pollutants. Similar declines were observed for PM<sub>2.5</sub>, with the exception of Alpine. Changes in levels of PM<sub>10</sub> were smaller in most communities over the study period with modestly increased levels in some communities.

We found that decreases in ambient air pollutant levels of NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> were associated with substantial reductions in bronchitic symptoms at ages 10 and 15 with and without asthma (Table 16). The reductions in bronchitic symptoms were larger in children with asthma — a group that had a significantly higher overall prevalence of

## Effects of Air Quality Improvements on Children's Respiratory Health

**Table 14.** Demographic Characteristics of Children Contributing to Bronchitic Symptoms Analysis

Characteristic	All (N = 4602)	Cohort C (n = 1008)	Cohort D (n = 1067)	Cohort E (n = 2527)	P Value <sup>b</sup>	
Age <sup>a</sup> at baseline (yr)	8.0 (1.7)	9.9 (0.6)	9.7 (0.6)	6.6 (0.7)	< 0.001	
BMI <sup>a</sup> (kg/m <sup>2</sup> ) at age 10	18.7 (3.7)	18.4 (3.3)	18.2 (3.5)	19.1 (3.9)	< 0.01	
Categorized BMI at age 10	BMI percentile < 85	2,356 (67.4)	669 (73.1)	684 (72.1)	1,003 (61.4)	< 0.01
	85 ≤ BMI percentile < 95	534 (15.2)	132 (14.4)	131 (13.8)	271 (16.6)	
	95 ≤ BMI percentile	608 (17.4)	114 (12.5)	134 (14.1)	360 (22.0)	
Male	No (%)	2,268 (49.3)	493 (48.9)	530 (49.7)	1,245 (49.3)	0.94
	Yes (%)	2,334 (50.7)	515 (51.1)	537 (50.3)	1,282 (50.7)	
Race	Asian (%)	212 (4.9)	60 (6.1)	63 (5.9)	89 (4.0)	< 0.001
	Blacks (%)	182 (4.2)	49 (5.0)	56 (5.3)	77 (3.4)	
	Mixed (%)	491 (11.5)	67 (6.8)	105 (9.9)	319 (14.2)	
	Other (%)	1,060 (24.7)	184 (18.6)	228 (21.5)	648 (28.9)	
	White (%)	2,342 (54.6)	627 (63.5)	608 (57.4)	1,107 (49.4)	
Hispanic ethnicity	No (%)	2,412 (53.4)	695 (69.8)	678 (63.8)	1,039 (42.3)	< 0.001
	Yes (%)	2,105 (46.6)	301 (30.2)	384 (36.2)	1,420 (57.7)	
Asthma status at age 10	Asthma (%)	892 (19.4)	150 (14.9)	164 (15.4)	578 (22.9)	< 0.001
	Non-asthma (%)	3,710 (80.6)	858 (85.1)	903 (84.6)	1,949 (77.1)	
Parental education	Did not finish HS (%)	754 (17.1)	144 (14.6)	136 (13.4)	474 (19.6)	0.001
	HS diploma/some college (%)	2,705 (61.2)	625 (63.4)	647 (63.7)	1,433 (59.3)	
	College diploma or greater (%)	958 (21.7)	217 (22.0)	233 (22.9)	508 (21.0)	
Health insurance	No (%)	599 (13.3)	163 (16.6)	162 (15.4)	274 (11.1)	< 0.001
	Yes (%)	3,909 (86.7)	821 (83.4)	889 (84.6)	2,199 (88.9)	
In-utero smoke exposure	No (%)	3,963 (88.7)	807 (82.1)	890 (85.3)	2,266 (92.9)	< 0.001
	Yes (%)	503 (11.3)	176 (17.9)	153 (14.7)	174 (7.1)	
Exposure to secondhand smoke (at first observation)	No (%)	3,831 (85.1)	738 (74.5)	803 (76.4)	2,290 (93.0)	< 0.001
	Yes (%)	672 (14.9)	252 (25.5)	248 (23.6)	172 (7.0)	
Any pests <sup>c</sup> at home	No (%)	1,145 (27.2)	194 (20.9)	189 (19.6)	762 (32.9)	< 0.001
	Yes (%)	3,070 (72.8)	736 (79.1)	777 (80.4)	1,557 (67.1)	
Roaches at home	No (%)	3,709 (88.0)	769 (82.7)	817 (84.6)	2,123 (91.5)	< 0.001
	Yes (%)	506 (12.0)	161 (17.3)	149 (15.4)	196 (8.5)	
Any pets at home	No (%)	1,631 (36.1)	262 (26.0)	236 (22.1)	1,133 (46.3)	< 0.001
	Yes (%)	2,892 (63.9)	746 (74.0)	831 (77.9)	1,315 (53.7)	
Dog ownership	No (%)	2,676 (59.2)	479 (47.5)	481 (45.1)	1,716 (70.1)	< 0.001
	Yes (%)	1,847 (40.8)	529 (52.5)	586 (54.9)	732 (29.9)	
Cat ownership	No (%)	3,318 (73.4)	640 (63.5)	684 (64.1)	1,994 (81.5)	< 0.001
	Yes (%)	1,205 (26.6)	368 (36.5)	383 (35.9)	454 (18.5)	
Carpet at home	No (%)	216 (4.8)	32 (3.2)	43 (4.1)	141 (5.8)	< 0.001
	Yes (%)	4,261 (95.2)	959 (96.8)	1,004 (95.9)	2,298 (94.2)	
Mildew / mold at home	No (%)	3,294 (76.4)	714 (73.8)	789 (76.8)	1,791 (77.4)	0.07
	Yes (%)	1,016 (23.6)	254 (26.2)	238 (23.2)	524 (22.6)	
Water damage at home	No (%)	3,813 (85.7)	828 (84.1)	920 (87.4)	2,065 (85.6)	0.11
	Yes (%)	636 (14.3)	156 (15.9)	133 (12.6)	347 (14.4)	
Gas stove at home	No (%)	916 (20.6)	252 (25.6)	282 (27.0)	382 (15.7)	< 0.001
	Yes (%)	3,539 (79.4)	733 (74.4)	762 (73.0)	2,044 (84.3)	
Spanish questionnaire	No (%)	3,870 (84.1)	931 (92.4)	930 (87.2)	2,009 (79.5)	< 0.001
	Yes (%)	732 (15.9)	77 (7.6)	137 (12.8)	518 (20.5)	
Bronchitic symptoms at age 10	No (%)	2,919 (83.4)	782 (80.5)	797 (80.2)	1,340 (87.4)	< 0.001
	Yes (%)	581 (16.6)	190 (19.5)	197 (19.8)	194 (12.6)	
Bronchitic symptoms at age 15	No (%)	1,848 (79.0)	525 (76.8)	576 (77.1)	747 (82.4)	0.01
	Yes (%)	490 (21.0)	159 (23.2)	171 (22.9)	160 (17.6)	

Note: numbers might not add up to the total N because of missing values.

<sup>a</sup> Values for age and BMI are the mean (standard deviation).

<sup>b</sup> Examining differences between cohorts based on Chi-square test (for categorical variables) and *F* test (for continuous variables).

<sup>c</sup> Pests include termites, spiders, ants, cockroaches, mice, and/or rats.

bronchitic symptoms (Figure 15). Note that the results reported in Table 16 present estimates of the reductions in bronchitic symptoms averaged across all the community-specific effects depicted in Figure 15 (at age 10), scaled to the median of the eight community-level average changes in pollution levels during the period between Cohorts C and E. Among children with asthma, the reductions in prevalence of bronchitic symptoms at age 10 were 21% ( $P < 0.01$ ) for NO<sub>2</sub>, 34% ( $P < 0.01$ ) for O<sub>3</sub>, 39% ( $P < 0.01$ ) for PM<sub>10</sub>, and 32% ( $P < 0.01$ ) for PM<sub>2.5</sub> corresponding to reductions of 4.9 ppb, 3.6 ppb, 5.8 µg/m<sup>3</sup>, and 6.8 µg/m<sup>3</sup>, respectively. Among children without asthma, the corresponding reductions in prevalence of bronchitic symptoms

were smaller at 16% ( $P < 0.01$ ), 15% ( $P < 0.05$ ), 20% ( $P < 0.01$ ), and 21% ( $P < 0.01$ ), for NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>, respectively (Table 16). Similar reductions in bronchitic symptoms were also observed at age 15. Plots of the predicted changes in prevalence of bronchitic symptoms by changes in air pollution levels across the study period showed that relatively larger changes in prevalence of bronchitic symptoms were observed in communities with larger changes in air pollutant levels (Figure 16) indicating that decreases in symptoms were unlikely because of an artifact of temporal confounding acting across communities. For example, in the asthma group, a 12-µg/m<sup>2</sup> decline in PM<sub>2.5</sub> for children in Riverside was associated with a

**Table 15.** Long-Term Average Concentrations of Air Pollutants in Eight Communities Across Three CHS Cohorts for Use in Bronchitic Symptoms Analysis

Community	Cohort Exposure Period	Mean of Air Pollutants by Cohort Exposure Period <sup>a</sup>			
		NO <sub>2</sub> (ppb)	O <sub>3</sub> (ppb)	PM <sub>10</sub> (µg/m <sup>3</sup> )	PM <sub>2.5</sub> (µg/m <sup>3</sup> )
Alpine	C: 1992–2000	13.2	56	23.9	9.8
	D: 1995–2003	12.9 (–2.7%)	53.4 (–4.6%)	25.5 (6.9%)	9.9 (0.2%)
	E: 2002–2011	9.6 (–27.5%)	52.1 (–6.9%)	25.2 (5.5%)	10.2 (3.7%)
Lake Elsinore	C: 1992–2000	18.2	54.8	34.9	15.5
	D: 1995–2003	17.6 (–3.5%)	53.6 (–2.2%)	34.1 (–2.3%)	14.3 (–7.4%)
	E: 2002–2011	13.9 (–23.8%)	51.4 (–6.1%)	35.3 (1.2%)	10.8 (–30.2%)
Long Beach	C: 1992–2000	34.5	29.4	37	20
	D: 1995–2003	32.1 (–6.9%)	28.7 (–2.4%)	36.6 (–1.2%)	20.3 (1.1%)
	E: 2002–2011	23.5 (–31.8%)	30.4 (3.4%)	30.4 (–18%)	14.8 (–26%)
Mira Loma	C: 1992–2000	24.6	53.8	66.2	30.5
	D: 1995–2003	24.4 (–1.1%)	49.8 (–7.5%)	66.6 (0.6%)	28.8 (–5.7%)
	E: 2002–2011	19.2 (–22%)	48.2 (–10.4%)	55.6 (–16.1%)	20.8 (–31.9%)
Riverside	C: 1992–2000	25.8	59.2	42.1	28.5
	D: 1995–2003	25.2 (–2.3%)	55.2 (–6.8%)	42.3 (0.4%)	26.5 (–7.2%)
	E: 2002–2011	22.0 (–14.7%)	54.7 (–7.6%)	37.2 (–11.7%)	16.8 (–41.1%)
San Dimas	C: 1992–2000	35.4	50.8	38.1	23.3
	D: 1995–2003	33.1 (–6.6%)	44.4 (–12.7%)	33.7 (–11.4%)	21.1 (–9.5%)
	E: 2002–2011	23.5 (–33.5%)	45 (–11.6%)	30 (–21.1%)	14.7 (–37.1%)
Santa Maria	C: 1992–2000	11.2	29.6	21.4	9.1
	D: 1995–2003	11.2 (0.3%)	30.5 (2.8%)	22 (2.9%)	9.4 (2.7%)
	E: 2002–2011	9.2 (–17.7%)	31.1 (4.9%)	22.7 (5.9%)	7.9 (–13.1%)
Upland	C: 1992–2000	39.0	47.7	42.9	27.3
	D: 1995–2003	37.3 (–4%)	43.7 (–8%)	40 (–7%)	25.9 (–5%)
	E: 2002–2011	27.5 (–29%)	45.4 (–5%)	35.2 (–18%)	18.8 (–31%)

<sup>a</sup> Mean pollutant level over the indicated exposure period in each community (values in parentheses are the percent change compared to Cohort C, 1992–2000).

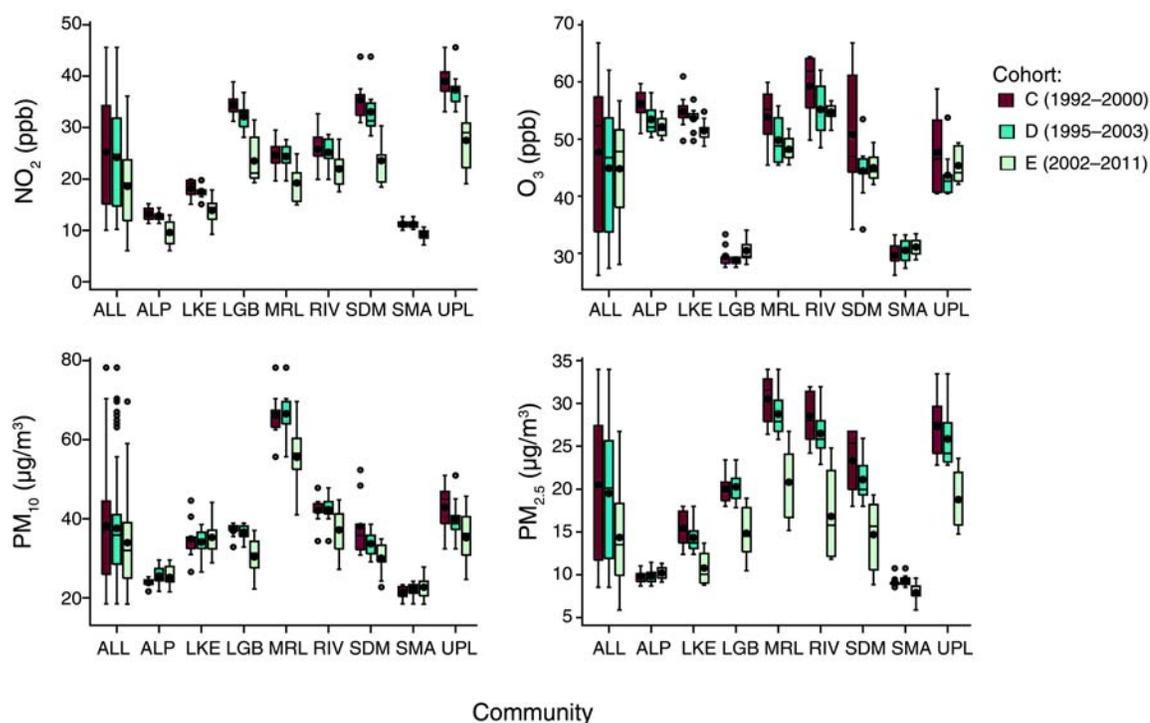


Figure 14. Box plots of annual average air pollutant concentrations by cohorts and communities. ALL = all communities, ALP = Alpine, LKE = Lake Elsinore, LGB = Long Beach, MRL = Mira Loma, RIV = Riverside, SDM = San Dimas, SMA = Santa Maria, and UPL = Upland.

Table 16. Reductions in Bronchitic Symptoms as a Function of Improvements in Air Quality by Asthma Status

Air Pollutant	Asthma		Non-Asthma	
	OR / Range <sup>a</sup> (95% CI)	P Value	OR / Range <sup>a</sup> (95% CI)	P Value
<b>At Age 10</b>				
NO <sub>2</sub> <sup>b</sup>	0.79 (0.67 to 0.94)	< 0.01	0.84 (0.76 to 0.92)	< 0.01
O <sub>3</sub> <sup>c</sup>	0.66 (0.50 to 0.86)	< 0.01	0.85 (0.74 to 0.97)	0.02
PM <sub>10</sub> <sup>c</sup>	0.61 (0.48 to 0.78)	< 0.01	0.80 (0.70 to 0.92)	< 0.01
PM <sub>2.5</sub> <sup>c</sup>	0.68 (0.53 to 0.86)	< 0.01	0.79 (0.69 to 0.91)	< 0.01
<b>At Age 15</b>				
NO <sub>2</sub> <sup>b</sup>	0.76 (0.64 to 0.89)	< 0.01	0.78 (0.71 to 0.86)	< 0.01
O <sub>3</sub> <sup>c</sup>	0.66 (0.50 to 0.86)	< 0.01	0.85 (0.75 to 0.98)	0.02
PM <sub>10</sub> <sup>c</sup>	0.61 (0.48 to 0.77)	< 0.01	0.78 (0.68 to 0.89)	< 0.01
PM <sub>2.5</sub> <sup>c</sup>	0.64 (0.50 to 0.82)	< 0.01	0.71 (0.61 to 0.81)	< 0.01

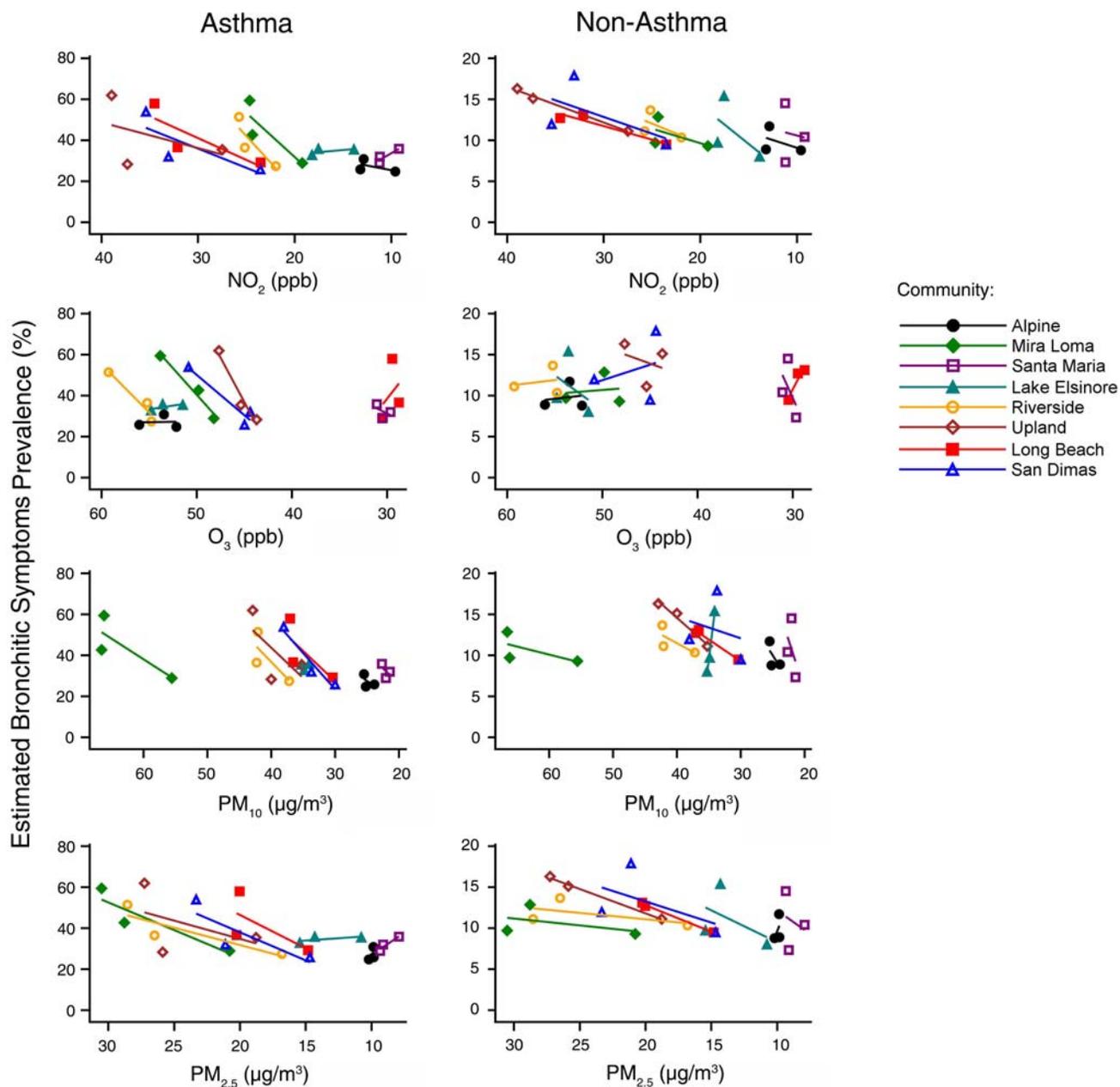
<sup>a</sup> Odds ratios (ORs) are for the median range of decrease in each pollutant (i.e., change in long-term mean air pollutant in Cohort E to that in Cohort C) across the 8 communities (4.9 and 3.6 ppb for NO<sub>2</sub> and O<sub>3</sub>, and 5.8 and 6.8 µg/m<sup>3</sup> for PM<sub>10</sub> and PM<sub>2.5</sub>, respectively). 95% CI entries refer to 95% confidence intervals.

<sup>b</sup> Odds ratio (OR), by asthma status, adjusted for age, sex, race/ethnicity, longitudinal exposure to secondhand smoke, and roaches at baseline.

<sup>c</sup> Odds ratio (OR), by asthma status, adjusted for age, sex, race/ethnicity and longitudinal exposure to secondhand smoke.

20% reduction in bronchitic symptom prevalence, while in Alpine, a decline of  $0.5 \mu\text{g}/\text{m}^2$  was associated with a small change in the prevalence of bronchitic symptoms. Corresponding results at age 15 were either similar or slightly larger (Table 16).

Extensive sensitivity analyses were conducted to test the robustness of study findings by limiting the analysis (1) to those children without SHS or in-utero tobacco smoke exposure, (2) to those with pets, (3) to those with parents completing English language questionnaire only,



**Figure 15. Estimated bronchitic symptom prevalences versus long-term average air pollutant concentrations among CHS children by asthma status.** The estimated bronchitic symptoms prevalences at age 10 obtained from longitudinal analyses with adjustments for sex, race/ethnicity, age, and SHS exposure, for CHS children with asthma (left panels) and without asthma (right panels). Long-term averaging periods for air pollutant concentrations can be found in Figure 4 and Table 15.

(4) to those children without any asthma medication use, or (5) to those children with complete data during follow-up. Additional analyses were conducted stratified by whether participants were non-obese or normal weight, by ethnicity (Hispanic whites or non-Hispanic whites only), sex, dog ownership, cat ownership, parental level of education, or exposure to SHS. The estimated reductions in

bronchitic symptoms were robust to any of these restrictions (Table 17). Models limited to data with overlapping ages for all three cohorts (i.e., between ages of 10 and 15 years) also showed reductions in bronchitic symptoms (Table 18) and were similar to those shown in Table 16.

To test whether the effects of improvements in air quality on bronchitic symptoms were modified by additional

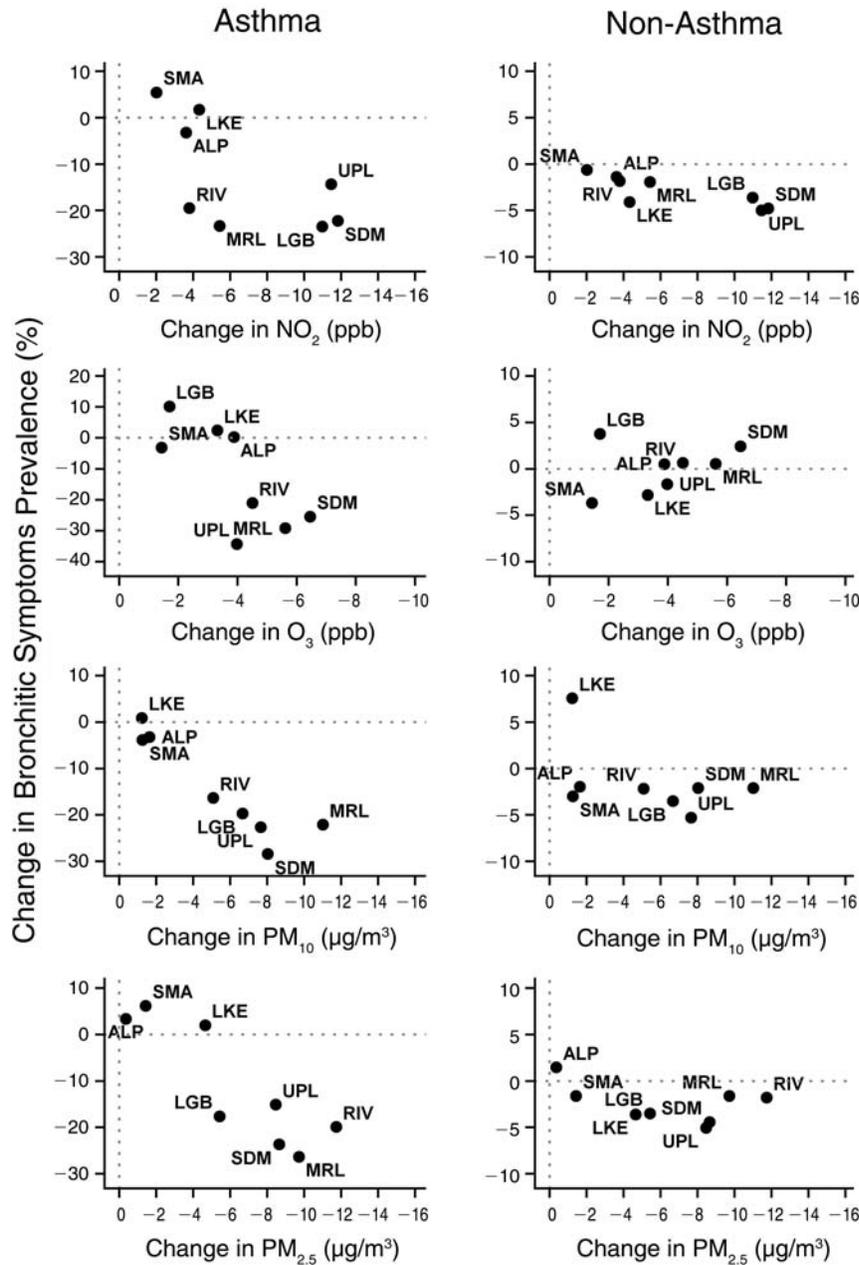


Figure 16. Predicted change in bronchitic symptoms prevalence at age 10 (vertical change in the trend lines of Figure 15) versus the change in average air pollutants over the study period (horizontal change in the trend lines of Figure 15) for each community. ALP = Alpine, LKE = Lake Elsinore, LGB = Long Beach, MRL = Mira Loma, RIV = Riverside, SDM = San Dimas, SMA = Santa Maria, and UPL = Upland.

factors, we fitted models that included interaction terms for sex, dog ownership, parental level of education, cat ownership, or exposure to SHS. In the asthma group, the effects of NO<sub>2</sub> and PM<sub>2.5</sub> were significantly larger in males and among children with family dog ownership (Table 19). None of the other interaction tests were found to be statistically significant. Due to high multi-collinearity between NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> (Table 20), multi-pollutant models were only possible for O<sub>3</sub> (with each of NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>). Results from these two-pollutant models revealed that the effects of O<sub>3</sub> became non-significant whereas the effects of each of the other pollutants remained significant and even became slightly stronger (Table 21).

## Discussion

Our findings from respiratory symptoms analysis demonstrate that reductions in levels of ambient air pollution over the past 20 years in Southern California were associated with significant reductions in bronchitic symptoms in asthmatic and non-asthmatic children. Reductions were proportionally larger in asthmatic children and were similar when examined at 10 and 15 years of age during the follow-up period (Table 16). The higher prevalence of bronchitic symptoms in children with asthma makes them more likely beneficiaries of air quality improvements. Among asthmatics, the reductions in bronchitic symptoms tended to be larger in boys and those from households with dogs. Our results are consistent with findings from a multi-community Swiss study of 9,591 children that showed that moderate improvements in air quality led to significant reductions in respiratory symptoms, based on cross-sectional health assessments between 1992 and 2001 (Bayer-Oglesby et al. 2005).

Reductions in bronchitic symptoms were larger in communities that showed higher improvements in air quality levels (Figure 16), indicating that the findings were robust to temporal confounding (Pope 1991). Our findings were found to be insensitive to subgroup analysis by several factors that could contribute to differential biases and/or potential over- or underestimation of study findings (Table 17). Any temporal trends in asthma diagnosis, prevalence, severity, or medication use are unlikely to account for these findings, as our models also included spline terms for age, to account for any long-term temporal trends of bronchitic symptoms. The linear relationship between change in air quality and changes in prevalence across all communities are consistent with an effect of air pollution reduction, and not a temporal correlated factor confounding the results (Figure 16).

Several studies have shown that areas with increased concentrations of regulated regional air pollution levels

have increased prevalence of bronchitis (Dockery et al. 1989, 1996; McConnell et al. 1999). Some studies have also shown that yearly variations in pollutant concentrations are strongly and positively associated with bronchitis prevalence, especially among children with asthma (McConnell et al. 2003, 2006a). Few previous studies have evaluated whether trends in reductions in air pollution levels over decades have led to reductions in bronchitic symptoms. Results from two repeated surveys in former East Germany showed that within-community reductions in total suspended particulates and SO<sub>2</sub> levels following reunification were associated with substantial reductions in total bronchitis prevalence and other non-allergic respiratory symptoms (Heinrich 2003; Heinrich et al. 2000).

Although confounding by other temporal community characteristics or trends in respiratory outcomes across cohorts could explain these results, the consistency of associations in diverse populations and study designs and the biological patterns of susceptibility observed in studies of air pollution and bronchitis suggest that the associations and the benefits observed in our study reflect air pollution reductions. Larger reductions in prevalence of bronchitic symptoms in children with asthma and with dogs as pets have been observed in previous analyses of the *within*-cohort variability in pollution concentrations across years in the CHS (McConnell et al. 2003, 2006a). These differences were predicted based on the known susceptibility of children with asthma to the pollutants studied and the higher levels of endotoxin, which has been shown to potentiate pollutant exposures in the homes of children with dogs. We considered unrecognized confounding as an explanation for the interaction with dogs. For example, children with dogs may have less eosinophilic asthma. However, we found no relationship with fractional exhaled nitric oxide (FeNO, a marker for eosinophilic asthma) and dogs in this cohort, making this explanation unlikely.

A major strength of our findings is the consistency of protocols used in collecting bronchitic symptoms and covariate information, as well as air pollution monitoring throughout the long study period. The findings do have some limitations: the outcome measure is based on relatively imprecise assessment of health outcomes defined using questionnaire-based reporting of symptoms. However, these outcomes have been widely used in previous epidemiological studies and have shown robust associations with regional pollutants (Dockery et al. 1989, 1996; Heinrich et al. 2000; McConnell et al. 1999, 2003, 2006a). The components of the bronchitic symptom outcomes used in this study are suggestive of chronic, indolent symptoms that may follow an illness, acute exacerbation of asthma, or chronic inflammation, which would likely be

## Effects of Air Quality Improvements on Children's Respiratory Health

**Table 17.** Sensitivity Analysis of the Reductions in Bronchitic Symptoms (at Age 10) as a Function of Improvements in Air Quality by Asthma Status

Air Pollutants / Sensitivity Analysis Group	Subjects ( <i>n</i> )	Asthma		Non-Asthma	
		OR / Range <sup>a</sup> (95% CI)	<i>P</i> Value	OR / Range <sup>a</sup> (95% CI)	<i>P</i> Value
<b>NO<sub>2</sub><sup>b</sup></b>					
All subjects	4,602	0.79 (0.67 to 0.94)	0.01	0.84 (0.76 to 0.92)	< 0.01
Subjects without SHS or in-utero smoke exposure	2,519	0.87 (0.69 to 1.09)	0.22	0.82 (0.71 to 0.94)	< 0.01
Subjects with pets	2,892	0.88 (0.72 to 1.07)	0.19	0.81 (0.72 to 0.91)	< 0.01
Nonobese subjects	3,465	0.81 (0.67 to 0.99)	0.04	0.84 (0.75 to 0.94)	< 0.01
Normal-weight subjects	2,529	0.79 (0.62 to 0.99)	0.04	0.87 (0.76 to 0.99)	0.04
English questionnaire users only	3,870	0.81 (0.69 to 0.96)	0.02	0.88 (0.79 to 0.97)	0.01
Hispanic whites	2,081	0.92 (0.68 to 1.26)	0.61	0.74 (0.63 to 0.89)	< 0.01
Non-Hispanic whites	1,883	0.79 (0.62 to 1.00)	0.05	0.79 (0.69 to 0.91)	< 0.01
Subjects without any medication use	3,671	0.85 (0.59 to 1.23)	0.38	0.79 (0.71 to 0.88)	< 0.01
Subjects with complete data	1,207	0.71 (0.54 to 0.91)	0.01	0.79 (0.68 to 0.92)	< 0.01
<b>O<sub>3</sub><sup>c</sup></b>					
All subjects	4,602	0.67 (0.51 to 0.87)	< 0.01	0.85 (0.74 to 0.98)	0.02
Subjects without SHS or in-utero smoke exposure	2,519	0.74 (0.49 to 1.13)	0.17	0.82 (0.67 to 1.02)	0.07
Subjects with pets	2,892	0.69 (0.50 to 0.95)	0.02	0.81 (0.69 to 0.95)	0.01
Nonobese subjects	3,465	0.60 (0.44 to 0.82)	< 0.01	0.81 (0.70 to 0.95)	0.01
Normal-weight subjects	2,529	0.58 (0.41 to 0.82)	< 0.01	0.90 (0.75 to 1.07)	0.24
English questionnaire users only	3,870	0.70 (0.53 to 0.91)	0.01	0.87 (0.76 to 1.01)	0.06
Hispanic whites	2,081	0.64 (0.37 to 1.08)	0.09	0.81 (0.63 to 1.05)	0.11
Non-Hispanic whites	1,883	0.64 (0.44 to 0.93)	0.02	0.88 (0.73 to 1.06)	0.17
Subjects without any medication use	3,671	0.65 (0.36 to 1.17)	0.15	0.82 (0.71 to 0.95)	0.01
Subjects with complete data	1,207	0.61 (0.39 to 0.94)	0.03	0.91 (0.71 to 1.16)	0.42
<b>PM<sub>10</sub><sup>c</sup></b>					
All subjects	4,602	0.62 (0.49 to 0.79)	< 0.01	0.81 (0.71 to 0.92)	< 0.01
Subjects without SHS or in-utero smoke exposure	2,519	0.71 (0.49 to 1.03)	0.07	0.73 (0.60 to 0.89)	< 0.01
Subjects with pets	2,892	0.74 (0.55 to 0.99)	0.04	0.74 (0.63 to 0.88)	< 0.01
Nonobese subjects	3,465	0.60 (0.45 to 0.80)	< 0.01	0.81 (0.69 to 0.95)	0.01
Normal-weight subjects	2,529	0.60 (0.43 to 0.85)	< 0.01	0.85 (0.71 to 1.02)	0.09
English questionnaire users only	3,870	0.61 (0.48 to 0.79)	< 0.01	0.85 (0.73 to 0.98)	0.02
Hispanic whites	2,081	0.63 (0.42 to 0.96)	0.03	0.71 (0.58 to 0.88)	< 0.01
Non-Hispanic whites	1,883	0.66 (0.46 to 0.96)	0.03	0.79 (0.64 to 0.98)	0.03
Subjects without any medication use	3,671	0.67 (0.39 to 1.14)	0.14	0.76 (0.66 to 0.88)	< 0.01
Subjects with complete data	1,207	0.56 (0.39 to 0.81)	< 0.01	0.72 (0.58 to 0.89)	< 0.01
<b>PM<sub>2.5</sub></b>					
All subjects <sup>c</sup>	4,602	0.69 (0.54 to 0.88)	< 0.01	0.80 (0.69 to 0.92)	< 0.01
Subjects without SHS or in-utero smoke exposure	2,519	0.79 (0.56 to 1.11)	0.18	0.72 (0.59 to 0.88)	< 0.01
Subjects with pets	2,892	0.81 (0.61 to 1.08)	0.15	0.73 (0.61 to 0.87)	< 0.01
Nonobese subjects	3,465	0.70 (0.53 to 0.94)	0.02	0.76 (0.64 to 0.89)	< 0.01
Normal-weight subjects	2,529	0.66 (0.47 to 0.92)	0.01	0.81 (0.67 to 0.98)	0.03
English questionnaire users only	3,870	0.69 (0.54 to 0.89)	< 0.01	0.86 (0.75 to 1.00)	0.06
Hispanic whites	2,081	0.72 (0.47 to 1.10)	0.13	0.66 (0.52 to 0.83)	< 0.01
Non-Hispanic whites	1,883	0.74 (0.51 to 1.06)	0.10	0.81 (0.65 to 1.00)	0.05
Subjects without any medication use	3,671	0.77 (0.43 to 1.38)	0.38	0.72 (0.62 to 0.83)	< 0.01
Subjects with complete data	1,207	0.56 (0.39 to 0.80)	0.00	0.74 (0.59 to 0.92)	0.01

<sup>a</sup> ORs are for the median range across the eight communities (4.9 and 3.6 ppb for NO<sub>2</sub> and O<sub>3</sub>, and 5.8 and 6.8 µg/m<sup>3</sup> for PM<sub>10</sub> and PM<sub>2.5</sub>, respectively).

<sup>b</sup> OR adjusted for age, sex, race/ethnicity, longitudinal secondhand smoke, and roaches at baseline.

<sup>c</sup> OR adjusted for age, sex, race/ethnicity, and longitudinal secondhand smoke.

**Table 18.** Reductions in Bronchitic Symptoms (at Age 10) as Air Quality Improved Among CHS Children, by Asthma Status, Based Only on Data for Ages Common to All Cohorts (i.e., Between Ages 10 and 15)

Air Pollutants	Asthma		Non-Asthma	
	OR / Range <sup>a</sup> (95% CI)	P Value	OR / Range <sup>a</sup> (95% CI)	P Value
NO <sub>2</sub> <sup>b</sup>	0.90 (0.80 to 1.02)	0.10	0.84 (0.78 to 0.91)	< 0.01
O <sub>3</sub> <sup>c</sup>	0.78 (0.65 to 0.92)	< 0.01	0.94 (0.86 to 1.02)	0.14
PM <sub>10</sub> <sup>c</sup>	0.74 (0.61 to 0.88)	< 0.01	0.81 (0.73 to 0.90)	< 0.01
PM <sub>2.5</sub> <sup>c</sup>	0.80 (0.67 to 0.95)	0.01	0.81 (0.73 to 0.90)	< 0.01

<sup>a</sup> The averaging periods for exposure in this analysis were as follows: 1992–1997 for Cohort C, 1995–2000 for Cohort D, and 2006–2011 for Cohort E. Odds ratios (ORs) are scaled to 4.9 and 3.6 ppb for NO<sub>2</sub> and O<sub>3</sub>, and 5.8 and 6.8 µg/m<sup>3</sup> for PM<sub>10</sub> and PM<sub>2.5</sub>, respectively, for effects to be comparable to those in Table 16. 95% CI entries refer to 95% confidence intervals.

<sup>b</sup> Odds ratio (OR), by asthma status, adjusted for age, sex, race/ethnicity, longitudinal exposure to secondhand smoke, and roaches at baseline.

<sup>c</sup> Odds ratio (OR), by asthma status, adjusted for age, sex, race/ethnicity, and longitudinal exposure to secondhand smoke.

**Table 19.** Reductions in Bronchitic Symptoms as Air Quality Improved (1993–2012) by Age, Sex, Dog Ownership, and Asthma Status

Effect Modifiers	NO <sub>2</sub> <sup>a</sup>		O <sub>3</sub> <sup>b</sup>		PM <sub>10</sub> <sup>b</sup>		PM <sub>2.5</sub> <sup>b</sup>	
	OR <sup>c</sup> (95% CI)	Inter-action P Value <sup>d</sup>	OR <sup>c</sup> (95% CI)	Inter-action P Value <sup>d</sup>	OR <sup>c</sup> (95% CI)	Inter-action P Value <sup>d</sup>	OR <sup>c</sup> (95% CI)	Inter-action P Value <sup>d</sup>
<b>Asthma 10-yr old</b>								
Boys	0.72 (0.60 to 0.86) <sup>f</sup>	0.01	0.66 (0.50 to 0.86) <sup>f</sup>	0.61	0.59 (0.46 to 0.76) <sup>f</sup>	0.27	0.55 (0.42 to 0.72) <sup>f</sup>	0.02
Girls	0.86 (0.71 to 1.03)		0.64 (0.49 to 0.85) <sup>f</sup>		0.64 (0.50 to 0.82) <sup>f</sup>		0.82 (0.62 to 1.09)	
Had dog	0.71 (0.6 to 0.85) <sup>f</sup>	0.01	0.70 (0.54 to 0.91) <sup>f</sup>	0.18	0.60 (0.47 to 0.77) <sup>f</sup>	0.06	0.57 (0.43 to 0.74) <sup>f</sup>	0.03
No dog	0.85 (0.7 to 1.02)		0.65 (0.49 to 0.86) <sup>f</sup>		0.67 (0.51 to 0.88) <sup>f</sup>		0.79 (0.59 to 1.06)	
<b>Non-Asthma 10-yr old</b>								
Boys	0.82 (0.74 to 0.91) <sup>f</sup>	0.18	0.85 (0.74 to 0.98) <sup>e</sup>	1.00	0.80 (0.70 to 0.92) <sup>f</sup>	0.71	0.78 (0.67 to 0.92) <sup>f</sup>	0.20
Girls	0.84 (0.76 to 0.93) <sup>f</sup>		0.83 (0.73 to 0.96) <sup>e</sup>		0.81 (0.71 to 0.93) <sup>f</sup>		0.79 (0.68 to 0.92) <sup>f</sup>	
Had dog	0.83 (0.74 to 0.92) <sup>f</sup>	0.20	0.84 (0.74 to 0.97) <sup>e</sup>	0.28	0.83 (0.72 to 0.95) <sup>f</sup>	0.34	0.79 (0.67 to 0.92) <sup>f</sup>	0.44
No dog	0.85 (0.77 to 0.95) <sup>f</sup>		0.88 (0.77 to 1.02)		0.80 (0.70 to 0.94) <sup>f</sup>		0.81 (0.69 to 0.96) <sup>e</sup>	
<b>Asthma 15-yr old</b>								
Boys	0.70 (0.59 to 0.84) <sup>f</sup>	0.02	0.69 (0.53 to 0.91) <sup>f</sup>	0.16	0.59 (0.46 to 0.76) <sup>f</sup>	0.14	0.56 (0.43 to 0.73) <sup>f</sup>	0.03
Girls	0.83 (0.69 to 1.00) <sup>e</sup>		0.67 (0.50 to 0.88) <sup>f</sup>		0.63 (0.49 to 0.81) <sup>f</sup>		0.75 (0.56 to 0.99) <sup>e</sup>	
Had dog	0.70 (0.59 to 0.84) <sup>f</sup>	0.03	0.68 (0.52 to 0.88) <sup>f</sup>	0.15	0.60 (0.47 to 0.76) <sup>f</sup>	0.06	0.54 (0.41 to 0.71) <sup>f</sup>	0.03
No dog	0.82 (0.68 to 0.99) <sup>e</sup>		0.65 (0.49 to 0.85) <sup>f</sup>		0.67 (0.51 to 0.88) <sup>f</sup>		0.72 (0.54 to 0.96) <sup>e</sup>	
<b>Non-Asthma 15-yr old</b>								
Boys	0.78 (0.71 to 0.87) <sup>f</sup>	1.00	0.85 (0.74 to 0.98) <sup>e</sup>	1.00	0.77 (0.68 to 0.89) <sup>f</sup>	0.49	0.72 (0.61 to 0.84) <sup>f</sup>	0.34
Girls	0.78 (0.71 to 0.87) <sup>f</sup>		0.84 (0.73 to 0.96) <sup>e</sup>		0.78 (0.68 to 0.90) <sup>f</sup>		0.69 (0.60 to 0.81) <sup>f</sup>	
Had dog	0.80 (0.72 to 0.89) <sup>f</sup>	0.58	0.85 (0.74 to 0.97) <sup>e</sup>	1.00	0.80 (0.70 to 0.92) <sup>f</sup>	0.38	0.74 (0.63 to 0.86) <sup>f</sup>	0.68
No dog	0.80 (0.72 to 0.89) <sup>f</sup>		0.87 (0.75 to 1.00) <sup>e</sup>		0.78 (0.68 to 0.91) <sup>f</sup>		0.73 (0.62 to 0.86) <sup>f</sup>	

<sup>a</sup> Odds ratio (OR) adjusted for age, sex, race/ethnicity, longitudinal secondhand smoke, and roaches at baseline.

<sup>b</sup> Odds ratio (OR) adjusted for age, sex, race/ethnicity, and longitudinal secondhand smoke.

<sup>c</sup> Odds ratios (ORs) are for the median range of decrease in each pollutant across the eight communities (4.9 and 3.6 ppb for NO<sub>2</sub> and O<sub>3</sub>, and 5.8 and 6.8 µg/m<sup>3</sup> for PM<sub>10</sub> and PM<sub>2.5</sub>, respectively). 95% CI entries refer to 95% confidence intervals.

<sup>d</sup> P values for tests of interaction effects between air pollutants and effect modifiers.

<sup>e</sup> P < 0.05.

<sup>f</sup> P < 0.01.

**Table 20.** Partial Correlations (Adjusted for Community) of Long-Term Cohort-Specific Mean Pollutant Levels Across Eight Communities Used in the Analysis of Bronchitic Symptoms

	O <sub>3</sub> (ppb)	PM <sub>10</sub> (µg/m <sup>3</sup> )	PM <sub>2.5</sub> (µg/m <sup>3</sup> )
NO <sub>2</sub>	0.38	0.80	0.84
O <sub>3</sub>		0.47	0.54
PM <sub>10</sub>			0.88

**Note:** All correlations were statistically significant ( $P < 0.05$ ). Correlations are based on the pollutant values found in Table 15.

**Table 21.** Reductions in Bronchitic Symptoms (at Age 10) as Air Quality Improved Among CHS Children by Asthma — Two-Pollutant Models

Air Pollutants	Asthma		Non-Asthma	
	OR / Range <sup>a</sup> (95% CI)	<i>P</i> Value	OR / Range <sup>a</sup> (95% CI)	<i>P</i> Value
NO <sub>2</sub> <sup>b</sup> + O <sub>3</sub> <sup>b</sup>				
NO <sub>2</sub>	0.79 (0.66 to 0.94)	0.01	0.76 (0.69 to 0.85)	< 0.01
O <sub>3</sub>	0.74 (0.55 to 0.99)	0.04	0.95 (0.83 to 1.10)	0.52
PM <sub>10</sub> <sup>c</sup> + O <sub>3</sub> <sup>c</sup>				
PM <sub>10</sub>	0.66 (0.51 to 0.87)	< 0.01	0.78 (0.68 to 0.91)	< 0.01
O <sub>3</sub>	0.81 (0.60 to 1.09)	0.16	0.95 (0.82 to 1.10)	0.50
PM <sub>2.5</sub> <sup>c</sup> + O <sub>3</sub> <sup>c</sup>				
PM <sub>2.5</sub>	0.65 (0.49 to 0.87)	< 0.01	0.69 (0.58 to 0.81)	< 0.01
O <sub>3</sub>	0.81 (0.59 to 1.11)	0.18	1.00 (0.85 to 1.17)	0.98

<sup>a</sup> Odds ratios (ORs) are for the median range of decrease in each pollutant across the eight communities (4.9, and 3.6 ppb for NO<sub>2</sub> and O<sub>3</sub>, and 5.8 and 6.8 µg/m<sup>3</sup> for PM<sub>10</sub> and PM<sub>2.5</sub>, respectively). 95% CI entries refer to 95% confidence intervals.

<sup>b</sup> Odds ratio (OR), by asthma status, adjusted for age, sex, race/ethnicity, longitudinal exposure to secondhand smoke, and roaches at baseline.

<sup>c</sup> Odds ratio (OR), by asthma status, adjusted for age, sex, race/ethnicity, and longitudinal exposure to secondhand smoke.

remembered well by subjects. Additionally, questionnaire-based reporting of respiratory symptoms might also reflect repeated acute exacerbation, but acute bronchitis has been reported to have a marked impact on quality of life in adults and in children, and to persist for several weeks, so such episodes also would be likely to be remembered well (Brandt et al. 2012; Verheij et al. 1995).

It is possible that false positive misclassification of asthma might have resulted in an underestimation of the true effect of air pollution in children with asthma, given that asthmatic children were more sensitive than children without asthma. The misclassification of personal exposure

based on community monitors may also have resulted in some underestimation of the magnitude of associations. However, because concentrations of PM<sub>2.5</sub> and PM<sub>10</sub> vary gradually with geographic distance in Southern California, exposure misclassification for children who attend school in their communities is unlikely to produce a large attenuation of effects. O<sub>3</sub> concentration gradients were limited across the study communities, but there are large indoor–outdoor concentration differences that depend on housing characteristics and operation. The resulting exposure misclassification would likely result in artificially low effect estimates for O<sub>3</sub>.

Finally, reporting bias is an unlikely explanation for the observed within-community between-cohorts associations because any awareness of long-term trends in air pollution within a community is unlikely to have been a determinant of bronchitis reporting. The shift in ethnic composition across the three cohorts towards more Hispanic ethnicity and lower socioeconomic status is a potential source of bias. However, bias in our estimates from this change in ethnic distribution is not likely to have a major impact, as sensitivity analyses based on models that considered only Hispanic children gave similar results to those that included all children.

Our findings have substantial public health, economic, and policy implications. They supply powerful evidence of air quality improvement effectiveness through emission control strategies over the last few decades in California and elsewhere in improving public health, especially in some of the most vulnerable segments of society, such as children and those with asthma (Henschel et al. 2012). Reductions in bronchitic symptoms are likely to have resulted in substantial economic savings in health care cost because (1) there were fewer exacerbations of asthma and subsequently reduced emergency room visits and hospitalizations and (2) there was decreased school absenteeism by children and fewer work-days lost by parents in caring for their sick children (Brandt et al. 2012). These findings provide tangible and strong evidence for the public health benefits of air quality standards and the regulatory programs to achieve and maintain compliance with the standards.

We have shown that substantial reductions in bronchitic symptoms are likely the direct results of air quality improvements in Southern California and that there are significantly positive societal and economic implications from regulatory actions to improve air quality. The examined air pollutants are common by-products of fuel combustion ubiquitous in many urban environments across the globe. Because the sources contributing to air pollution might vary by geographic region, research to replicate these findings in other settings would be useful as part of the emerging body of evidence indicating that effective policies to improve air quality result in significant improvements in public health.

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## SUMMARY DISCUSSION

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Our research addresses a question central to public health and environmental regulations: Are observed improvements in ambient air quality reflected in improved health outcomes in the exposed population? Data

presented from this study indicate that cleaning up the air has improved public health.

Using almost two decades of pollutant emissions and air monitoring data, we examined whether air pollution-driven policies enacted during the CHS time frame (1993–2012) led to reductions in outdoor pollutant concentrations. We also asked whether changes in respiratory symptoms and lung function were consistent with mechanisms hypothesized to underlie epidemiologic associations between ambient air pollution and respiratory morbidity.

Significant reductions in certain ambient air pollutants were observed, including ~55% reductions in annual average NO<sub>2</sub> and PM<sub>2.5</sub> in the communities with the highest concentrations of these pollutants during the study period. In our longitudinal study of schoolchildren, we concomitantly observed important changes in measures of bronchitic symptoms and lung function (FEV<sub>1</sub> and FVC). Improved lung function was most strongly associated with lower levels of particulate pollution (PM<sub>2.5</sub> and PM<sub>10</sub>) and NO<sub>2</sub>. These associations were observed in both sexes and in children with and without asthma, suggesting that improvements in air quality have the potential to benefit all children.

Although significant reductions in bronchitic symptoms were observed for children with or without asthma, observed reductions were larger among children with asthma. These results imply that all children benefit from improvements in air quality, but asthmatic children may especially benefit, because exacerbations of the disease are reduced. Among asthmatic children, reductions in bronchitic symptoms (and hence asthma exacerbations) tended to be larger in boys and in those children from households with dogs.

Our findings complement prior studies investigating reductions in air pollution and their associations with changes in cardiorespiratory health outcomes (Friedman et al. 1976; Peel et al. 2010; Rich et al. 2012). Extending other previous studies, we have demonstrated that measured health outcomes showed significant changes with associated pollutant changes and that these changes were primarily policy-driven.

In Southern California, motor vehicles are a primary source of PM<sub>2.5</sub>, PM<sub>10</sub>, and NO<sub>2</sub>, both through direct tail-pipe emissions and downwind physical and photochemical reactions of vehicular emissions (McDonald et al. 2012; Sardar et al. 2005). Both gasoline- and diesel-powered engines contribute to high levels of these pollutants, and improved emission standards for both types of vehicles have contributed to the observed declines in air pollutants. The high correlation in reductions of PM<sub>2.5</sub>, PM<sub>10</sub>, and NO<sub>2</sub> across our study communities prevented us from distinguishing between independent effects of these pollutants.

Many other studies have also had difficulties in identifying the health effects of specific pollutants that are constituents of multi-pollutant mixtures (Gehring et al. 2013; Liu et al. 2009). Short-term exposure to O<sub>3</sub> has been previously linked to acute changes in lung function, but evidence of long-term exposure effects has been less conclusive (U.S. EPA 2013); our lung function findings are consistent with these observations.

### CHANGES IN AIR QUALITY AND LINKAGE TO POLICIES

The linkage between air pollution control policies, emissions, and air quality is conceptually simple but often difficult to quantify in real-world situations. The complexity stems from the large number of policies developed, the variability in timing and speed of rollout for some policies' activation and application, and the lack of direct continuous measurements of most emission sources. Emission control programs and regulations affect many different types of sources and are implemented over time with various degrees of stringency, compliance, and effectiveness. Regulatory requirements can have rigid and well-defined timelines or may be phased in gradually over time. Rules are sometimes modified based on in-use experiences and technological developments. With hundreds of different regulations influencing the time course of on-road mobile, off-road mobile, stationary, and area-wide sources in any year, it is impossible to track the effectiveness of any individual control measure. Furthermore, the effects of controls are not likely to be uniform in space or time for anything other than the most widespread sources (e.g., LDV). Atmospheric chemistry and changing background concentrations may also cause nonlinearities in relationships between precursor emissions, such as NO<sub>x</sub> and ROG, and ambient concentrations of secondary pollutants such as O<sub>3</sub>, NO<sub>2</sub>, and secondary PM. Hence, the regulatory assessment approach for this study was necessarily qualitative and required aggregation of temporally overlapping policy actions.

The magnitude of the SoCAB emission reductions achieved should rightly be considered a substantial achievement of public policy. In the face of population growth and increased VMT, emissions in the Los Angeles area during this time frame would likely have increased and air quality would have suffered, were it not for the broad range of aggressive air pollution control policies put into place. The breadth of reductions across all major pollutants and categories of emissions suggests that the policies put into place have been comprehensive and successful. The observation that PM<sub>2.5</sub> air quality trends over this time period compared more favorably with NO<sub>x</sub>

and ROG emission trends than with either PM<sub>2.5</sub> or PM<sub>10</sub> emission trends may have implications for other geographical areas.

### STRENGTHS AND LIMITATIONS

Based on our prior research, the assembled research team, the data resources available through the CHS, and the support of regional and state air quality management agencies (the State of California Air Resources Board and the South Coast Air Quality Management District), we were ideally positioned to address a fundamental public health question and develop scientifically credible responses for it. With regard to children's health, our research group is in an excellent position to address this public health question, with broad experience with a unique longitudinal resource (the CHS). The health effects among this population from modest differences in air pollution have been previously well established (Avol et al. 2001; Gauderman et al. 2004; McConnell et al. 2003), so it was appropriate that these public health questions were addressed in this setting.

Collecting lung-function performance data repeatedly in children from their elementary through high school years was a substantial strength of the study. Both the precision with which measurements were made and the large number of subjects who participated in the data collection efforts positioned us to detect relatively small changes in lung-function performance with a comfortable level of statistical confidence.

Ready availability of carefully collected, quality-assured, and location-relevant air monitoring data was another study advantage. Our ongoing collaborative relationships with regional air quality agencies facilitated the deployment of necessary monitoring instrumentation and the collection of critical air quality data. Control of possible sources of exposure misclassification errors is a fundamental part of any credible research study, and the inherent exposure design of the CHS — with community-located central-site air monitoring stations — provided relevant exposure data for the study without having to rely on data from stations more geographically removed and spatially distant from subjects' residential and school locations.

We do recognize, however, that our approach was not without challenges and limitations. Improvements in ambient air quality and reductions in PM and NO<sub>x</sub> emissions are the result of decades of regulatory effort involving a number of overlapping, complementary, and successive policies, controls, and approaches. Identifying a discrete association of a specific regulation with an apportioned reduction in pollutant emissions or air

quality improvement was a formidable, and perhaps insurmountable, challenge. The history of pollution control regulation has been one of multiple concurrent legislative actions (completely consistent with an emphasis for timely improvement of public health) rather than a one-at-a-time type approach (which might better reflect a systematic application of the scientific method). A mid-study change in spirometry instrumentation also raised some challenges, which we have sought to address through a calibration substudy. In a similar manner, changes in air monitoring instrumentation, sampling location, and emission models were addressed by co-location studies.

Another potential limitation is temporal confounding from demographic shifts in the population and other temporal trends that may have occurred throughout the entire study period, such as changes in the physiological development of children, shifts in asthma treatment, and differences in the prevalence of exposure to SHS. We investigated the potential for residual temporal confounding through various sensitivity analyses. We found no difference in height across the cohorts suggesting that improved physiological development does not explain the improvement in lung function. Models were carefully adjusted for several factors, including Hispanic ethnicity, asthma status, and SHS; we additionally presented models restricted to particular subgroups (e.g., Hispanic white, Non-Hispanic white, asthmatic children, non-asthmatic children, and subjects not on asthma medication). All of our associations were robust to these sensitivity analyses, suggesting that these factors are unlikely to have confounded our results. Lastly, we noted that larger than expected gains in lung function and changes in prevalence of bronchitic symptoms were observed in communities that had the largest improvement in air quality, which further suggested that our reported associations were not simply the result of temporal confounding.

Overall, our study also had several substantial strengths. These included a prospective study design, which enabled evaluation of effects of secular trends in air pollution across several cohorts from the same communities on trends in bronchitic symptoms; participation of a large, ethnically diverse population of children; exploitation of a wide range of exposures to complex multipollutant mixtures available in Southern California and representing the full range in the United States; and testing whether the associations varied by patterns in susceptibility factors (e.g., asthma and sex).

## CONCLUSIONS

This study investigated the respiratory health outcomes observed in three consecutive cohorts of children in public

schools over an almost 20-year period during a period of dramatic reductions in air pollutant emissions and substantive improvement in air quality for several contaminants of regulatory interest. We found that a wide array of regulatory policies, which focused on mobile, stationary, and area sources, led to dramatic reductions in emissions in California from 1990 to 2011.

During this period of time, three successive cohorts of children were tested to assess lung-function growth and respiratory symptoms during comparable four-year study periods, as they aged from 11 to 15 years. Improvements in four-year growth of both FEV<sub>1</sub> and FVC were associated with declining levels of NO<sub>2</sub> ( $P < 0.0001$ ), PM<sub>2.5</sub> ( $P < 0.01$ ), and PM<sub>10</sub> ( $P < 0.001$ ). Significant improvements in lung-function growth were observed in both boys and girls and among asthmatic and non-asthmatic children. The proportions of children with clinically low FEV<sub>1</sub> (defined as <80% predicted) at age 15 declined significantly, from 7.9% to 6.3% to 3.6% across the three time periods, respectively, as the air quality improved ( $P < 0.005$ ). Among asthmatic children, the reductions in prevalence of bronchitic symptoms were 21% ( $P < 0.01$ ) for NO<sub>2</sub>, 34% ( $P < 0.01$ ) for O<sub>3</sub>, 39% ( $P < 0.01$ ) for PM<sub>10</sub>, and 32% ( $P < 0.01$ ) for PM<sub>2.5</sub> corresponding to reductions of 4.9 ppb, 3.6 ppb, 5.8 µg/m<sup>3</sup>, and 6.8 µg/m<sup>3</sup>, respectively, at age 10.

These strong associations persisted after adjustment for several potential confounders. Collectively, these findings provide strong evidence for continued efforts to reduce airborne pollution with the reasonable expectation that improvements in air quality will be reflected in improved public health.

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## IMPLICATIONS OF FINDINGS

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Epidemiologic findings of associations between air pollution and respiratory disease and death are largely driven by studies of the elderly and those with cardiorespiratory diseases. In our study, we observed changes linking air pollution with respiratory disease outcomes across three groups of children, ages 10 to 15 years, from wide-ranging backgrounds and communities of varying air pollution profiles. As documented in this report, improvements in regional air quality over a 20-year period across Southern California were associated with improvements in measured lung-function performance and bronchitic symptoms among children growing up in the region. As air quality improved, the proportion of children with clinically poor lung function decreased and the exacerbation of asthmatic symptoms among asthmatic children was reduced.

Our analyses add to the evidence base that air pollution affects respiratory health, independent of commonly recognized risk factors (e.g., old age and predisposing diseases). As the complementary analyses document, the implementation of a broad array of air quality-oriented regulatory policy initiatives led to decreases in assorted emissions from both stationary and mobile sources. These policy-driven emission reductions were reflected in steadily improving regional air quality across the region.

Our findings have broad public health implications, suggesting that improved air quality not only benefits susceptible populations (as shown in previous studies), but can also reduce the burden of respiratory disease (documented here by improved lung-function performance and decreases in specific respiratory symptoms) among both healthy and asthmatic children. This observation has important implications for long-term health. By linking the reported health outcomes to air quality and to implemented regulatory policies, we have shown the direct and high impact these regulations can have on public health.

These results also support previous assessments indicating that air quality improvement over the last several decades, attributable to air pollution regulations, may account for as much as 15% of an overall increase in life expectancy in U.S. metropolitan areas (Rich et al. 2012). The results of our study strongly support continued aggressive regulatory policy interventions, which have been valuable and should be maintained to improve public health. Despite the substantial accomplishments in emissions reduction and air quality improvement to date, the Los Angeles region remains in violation of the PM<sub>2.5</sub> and O<sub>3</sub> NAAQS. Additional emissions reductions will be needed in order to achieve regulatory compliance.

Our study provides clear evidence that sustained efforts on behalf of air pollution improvements provide health benefits to a wide portion of the general population and that improvements in early-life respiratory development can potentially result in reduced healthcare costs later in life. Therefore, both long-term health strategies and short-term health concerns strongly support continued efforts to improve community air quality levels for all members of the public.

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### ACKNOWLEDGMENTS

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We thank the families, students, school staff and administrators without whom this data would not have been attainable. We especially thank the staffs of both the CARB and the SCAQMD for their support in documenting the policies, emissions, and activities reported herein, especially Todd Sax and Cynthia Marvin of CARB, and Elaine Chang and

Laki Tisopulos of SCAQMD. This project was performed under a contract with the Health Effects Institute (#4910-RFA11-1/12-4), with additional support from a National Institute of Environmental Health Sciences (NIEHS) Center Grant (#5 P30 ES07048-19) and NIEHS program project (#5P01ES011627-10) and a contract with CARB (#94-331). The authors have considered their activities and report no conflicts of interest. The contents of this report are solely the responsibility of the authors and do not necessarily represent the official views of any funding agencies who have supported this body of research in the past or present.

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## HEI QUALITY ASSURANCE STATEMENT

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The conduct of this study was subjected to independent audits by RTI International staff members Drs. Linda Morris Brown and Prakash Doraiswamy. These staff members are experienced in quality assurance oversight for air quality monitoring, emission inventories and modeling, and related epidemiological studies. Other participants on the RTI QA oversight team included Dr. Lei Li, a statistician who reviewed the statistical aspects of the draft final report.

The QA oversight program consisted of an on-site audit at the University of Southern California (USC), Department of Preventive Medicine, Keck School of Medicine of USC, Los Angeles, California, and a final review of the draft final report of the study. The USC on-site audit was performed by Drs. Brown and Doraiswamy. The review of the final report was performed by Drs. Brown, Li, and Doraiswamy. The audits included review of study documentation and reports, and discussions with key project staff of study activities for conformance to the study protocol and standard operating procedures. The dates of the audits and reviews are listed below, along with a description of what was reviewed.

### September 23–24, 2013

The auditors conducted an on-site audit at the Department of Preventive Medicine, Keck School of Medicine, USC, Los Angeles, California. The audit reviewed the following study components: progress reports; personnel and staff; adequacy of equipment and facilities; internal quality assurance procedures; air quality data processing documentation; data processing; and backup procedures. Program codes were inspected to verify proper documentation. Analytic data sets and codebooks were examined. The audit included an observation of the demonstration of the script executions, comparison of SAS and R outputs, file tree structure on the server, and model diagnostics. The audit also evaluated contingencies in place and future analysis plans. No errors were noted, but recommendations were made for documenting model development and QA/QC procedures and codes and developing a codebook for the lung function data set.

### April–May 2016

The RTI QA oversight audit team consisting of Drs. Brown, Li, and Doraiswamy reviewed the draft final report for the project. No serious quality-related issues were identified during the review.

Written reports of each activity were provided to HEI. 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 draft final report, except as noted in the comments\*, appears to be an accurate representation of the study.



Linda Morris Brown, MPH, DrPH, Epidemiologist,  
Quality Assurance Auditor



Prakash Doraiswamy, PhD, Air Quality Specialist,  
Quality Assurance Auditor

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## APPENDIX AVAILABLE ON THE WEB

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Appendix A, Ambient Air Quality Measurements and Supplemental Methods, contains supplemental material not included in the printed report. It is available on the HEI Web site at [www.healtheffects.org/publications](http://www.healtheffects.org/publications).

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## ABOUT THE AUTHORS

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**Frank Gilliland**, M.D. Ph.D., is a physician and epidemiologist and Hastings Professor in the Department of Preventive Medicine, Keck School of Medicine, University of Southern California. He has extensive experience in studies of environmental contribution to health and disease. He serves as the project director of the Southern California Environmental Health Sciences Center. He is the principal investigator of this study and the Children's Health Study.

**Edward Avol**, M.S., is a professor in the Department of Preventive Medicine at University of Southern California and served as the deputy director of the Children's Health Study under John Peters. He is an expert on respiratory health, air pollution, and the public health impacts of traffic exposure. He contributed to the study concept, proposal formulation, the identification and outlining of policy impacts on pollutant trends and resultant health effects, and served as co-principal investigator on this project.

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\*The auditors' comments on the draft final report were addressed as part of the editorial process.

**Rob McConnell**, M.D., is a professor of preventive medicine at University of Southern California's Keck School of Medicine and director of the Children's Environmental Health Center. He has researched the effects of air pollution on the development and exacerbation of asthma and is the co-principal investigator for the Children's Health Study. His work includes the study of associations between O<sub>3</sub> and traffic emissions with the development of asthma. His interests also include the effects of psychosocial stress and other social characteristics on asthma.

**Kiros Berhane**, Ph.D., is professor of biostatistics in the Department of Preventive Medicine, University of Southern California. He was one of the senior biostatisticians for this project and oversaw the statistical analyses relevant to symptoms assessment. He participated in experimental design activities, directed the data management activities, and conducted statistical analyses.

**W. James Gauderman**, Ph.D., is a professor and chief of biostatistics in the Department of Preventive Medicine, University of Southern California. For two decades, he has investigated the association between urban air pollution and children's respiratory health as a co-investigator for the Children's Health Study. In the current investigation, he led analyses related to lung function performance evaluation.

**Fred W. Lurmann**, M.S., is chairman of Sonoma Technology, Incorporated, and manager of exposure assessment studies. He has been involved with collection, management, and analysis of data for the assessment of exposure to air pollution for more than 40 years. He oversaw all work in this study related to regulatory policy assessment and air quality data evaluation.

**Robert Urman**, Ph.D., completed his doctoral degree in the Department of Preventive Medicine at the University of Southern California during the preparation of this report. His research has focused on lung function effects of outdoor air pollution. In the current study, he contributed analyses, insights, text, and perspective to all elements of the lung function evaluations of the respective Children's Health Study cohorts.

**Roger Chang**, Ph.D., completed his doctoral degree in the Department of Preventive Medicine at the University of Southern California during the preparation of this report. His research contribution in this study focused on biostatistical assessments of respiratory symptoms.

**Edward B. Rappaport**, M.P.H., is a statistician in the Department of Preventive Medicine at the University of Southern California. For more than 20 years he has had primary responsibilities related to the assembly and management of Children's Health Study questionnaire, lung function, and air quality datasets. He was responsible for the main health and air quality datasets used for this study.

**Stephen Howland**, M.S., is a research coordinator in the Department of Preventive Medicine at the University of Southern California. He has contributed more than twenty years of critical effort to the Children's Health Study. In the current study, he served as project quality assurance officer and was responsible for preparation of all quality assurance documentation related to the study.

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### OTHER PUBLICATIONS RESULTING FROM THIS RESEARCH

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Berhane K, Chang C-C, McConnell R, Gauderman WJ, Avol E, Rappaport E, et al. 2016. Association of changes in air quality with bronchitic symptoms in children in California, 1993–2012. *JAMA* 315:1491–1501. doi: 10.1001/jama.2016.3444.

Gauderman WJ, Urman R, Avol E, Berhane K, McConnell R, Rappaport E, et al. 2015. Association of improvements in air quality with lung function in children. *N Engl J Med* 372(10):905–913; doi: 10.1056/NEJMoa1414123.

Lurmann F, Avol E, Gilliland F. 2015. Emissions reduction policies and recent trends in Southern California's ambient air quality. *J Air Waste Manag Assoc* 65(3):324–335; doi: 10.1080/10962247.2014.991856.

Research Report 190, *The Effects of Policy-Driven Air Quality Improvements on Children's Respiratory Health*, F. Gilliland et al.

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## INTRODUCTION

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The Health Effects Institute has a long history of funding research to assess the health outcomes of actions to improve air quality. HEI initially funded studies that evaluated local actions that were implemented relatively rapidly; for example, banning the sale of coal for heating in Ireland or reducing traffic or local and regional emissions during a unique event, such as the Olympic Games (Dockery et al. 2013; Peel et al. 2010; Rich et al. 2012; Zhang et al. 2013). After assessing the results from this first wave of studies, HEI issued Request for Applications (RFA\*) 11-1, "Assessing the Health Outcomes of Air Quality Actions," in 2011. The goals of the RFA were to fund research to (1) evaluate regulatory and other actions at the national or regional level implemented over multiple years; (2) evaluate complex sets of actions targeted at improving air quality in large urban areas, including those in the vicinity of major ports; or (3) develop methods to support such health outcomes research.

In response, Dr. Frank Gilliland of the University of Southern California submitted an application "The Effects of Policy-Driven Air Quality Improvements on Children's Respiratory Health." The proposed study aimed to build on an ongoing cohort study, the National Institute of Environmental Health Sciences (NIEHS)-funded Children's Health Study (CHS), which Gilliland and colleagues had been working with for many years. In the CHS, the investigators annually or biennially assessed the lung-function growth and respiratory health status of thousands of Southern California schoolchildren, who were recruited in

different cohorts over the course of the study. The children lived in communities that had different air pollution characteristics but similar demographics. Health information was then linked to data on individual air pollutants collected from fixed-site monitors. Gilliland and colleagues indicated that multiple regulations to curb emissions of airborne pollutants had been introduced both nationally and statewide over the last several years. For the proposed HEI study, the investigators wanted to explore whether changes in ambient pollutant levels in Southern California resulted from the implementation of these regulations and whether these changes were associated with improvements in children's respiratory health (measured as growth of their lung function and a decrease in symptoms of bronchitis).

HEI's Research Committee thought the design of the study, based on the data collected during the CHS, was strong and recommended the study for funding. However the Committee noted that a limitation of the proposal was the lack of plans to analyze direct linkage between regulatory actions and health outcomes, such as the use of counterfactual scenarios (i.e., what would have happened if the regulations had not been put in place) and the Committee recommended that the investigators include this in their analytical plan.

This Commentary provides the HEI Review Committee's evaluation of the study. It 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.

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## BACKGROUND

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### EFFECTS OF AIR POLLUTION ON RESPIRATORY FUNCTION IN ADULTS AND CHILDREN

Many studies in adults have shown that long-term exposure to air pollution has multiple adverse cardiorespiratory effects, including increased risks for respiratory disease (particularly incidence of asthma [Jacquemin et al. 2015]) and increased risk for cardiorespiratory morbidity and mortality (e.g., Brook et al. 2010; Brunekreef et al. 2009; Krewski et al. 2009; Turner et al. 2016; Wolf et al. 2015).

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Dr. Frank Gilliland's 2-year study, "The effects of policy-driven air quality improvements on children's respiratory health," began in May 2012. Total expenditures were \$561,772. The draft Investigators' Report from Gilliland and colleagues was received for review in August 2014. A revised report, received in September 2015, was provisionally accepted for publication in October 2015, pending further revisions. A second revision of the report, received in December 2015, was accepted for publication in February 2016. During the review process, the HEI 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 Commentary.

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 this volume.

Children are considered more susceptible than adults to the effects of air pollution because their lungs are still developing and because they may be exposed to higher levels of pollutants than adults — in comparison with adults, children breathe faster and generally spend more time outdoors engaged in strenuous activities. Lung-function development continues in girls until the late teens. In boys, lung-function development continues until the early 20s but at a much-reduced rate compared with the earlier adolescent period (Burrows et al. 1983; Wang et al. 1993). Thus, the level of lung function at age 18 is a good reflection of lung development in healthy individuals of either sex until that age. From a public health perspective the lung function of the young adult is also critical because it is a marker of future health — lung function lower than that predicted for a healthy adult is associated with increased risk of cardiovascular disease and mortality (Georgiopoulou et al. 2011; Ryan et al. 1999; Sin et al. 2005).

#### THE CHILDREN'S HEALTH STUDY

The CHS is a landmark long-term study of the health effects in children of exposures to outdoor air pollution in multiple communities in Southern California that began in 1992. The CHS investigators made annual assessments of lung-function growth and respiratory health status in thousands of schoolchildren in Southern California. To date, almost 12,000 children, in five different cohorts, have been recruited at different stages of the study. The "Methods" section below further characterizes the specific cohorts in the study. The health information obtained from the thousands of assessments was then linked to data on individual air pollutants that had been collected from fixed-site monitors in each community.

CHS results before those of the current study have already provided important insights. They have shown that long-term exposure of children to elevated levels of air pollution had adverse effects on the development of their lung function (Gauderman et al. 2000, 2002, 2004). Gauderman and colleagues (2000) showed that, over the course of the 4-year study, exposure of the participants (who initially were entering the fourth grade) to ambient particulate matter (PM)  $\leq 10 \mu\text{m}$  in aerodynamic diameter (PM<sub>10</sub>), PM  $\leq 2.5 \mu\text{m}$  in aerodynamic diameter (PM<sub>2.5</sub>), nitrogen dioxide (NO<sub>2</sub>), or inorganic acid vapor — but not ozone (O<sub>3</sub>) — was associated with a deficit in the growth of lung function. Lung function was measured as forced expiratory volume in 1 second (FEV<sub>1</sub>), forced vital capacity (FVC), maximal midexpiratory flow (MMEF), and forced expiratory flow at 75% maximum expiration (FEF<sub>75</sub>). The investigators calculated that the estimated growth rate for

children in the most polluted communities compared with the least polluted communities showed a cumulative reduction of 3.4% in FEV<sub>1</sub> and 5.0% in MMEF over the 4-year study period. The estimated deficits were generally larger for children who spent more time outdoors. Gauderman and colleagues (2002) substantially replicated these findings in a second cohort of fourth-graders.

Evaluating the data from assessments of children made over an 8-year period, from the ages of 10 to 18, Gauderman and colleagues (2004) showed that exposure to NO<sub>2</sub>, acid vapor, PM<sub>2.5</sub>, and elemental carbon (EC) were associated with deficits in the growth of FEV<sub>1</sub> (10% on average) and of other spirometric measures. These deficits were judged to be clinically relevant at the age of 18; for example, the estimated proportion of 18-year-old participants with a low FEV<sub>1</sub> (defined as a ratio of observed to expected FEV<sub>1</sub> of less than 80%) was 4.9 times as great at the *highest* level of exposure to PM<sub>2.5</sub> than at the *lowest* level of exposure (7.9% versus 1.6%). For the same 8-year period, Gauderman and colleagues (2007) also showed that children who lived within 500 meters of a freeway also had deficits in FEV<sub>1</sub> and MMEF compared with children who lived at least 1500 meters away. Taken together, these studies suggested that abnormally low lung function in adolescents was more likely to be found in participants who lived in communities with high pollutant levels — particularly those with high PM and NO<sub>2</sub> levels.

Furthermore, publications from the CHS investigators indicated that children's exposure to outdoor pollution in Southern California was also associated with increased symptoms of airway disease. The prevalence of chronic bronchitic symptoms was increased twofold among children with asthma (McConnell et al. 1999, 2003). The investigators found positive associations between bronchitis and exposure to PM<sub>10</sub>, between phlegm and exposure to multiple air pollutants (particularly NO<sub>2</sub>) but not O<sub>3</sub> (McConnell et al. 1999), and between bronchitic symptoms and yearly variability of PM<sub>10</sub>, organic carbon (OC), NO<sub>2</sub>, and O<sub>3</sub> (McConnell et al. 2003). McConnell and colleagues (2002) also reported increased incidence of new diagnoses of asthma among children exercising in areas with high O<sub>3</sub> levels.

In addition, McConnell and colleagues (2002) showed that among children with no history of asthma, who were followed for up to 5 years, the relative risk of developing asthma in those children playing three or more sports in communities with high O<sub>3</sub> concentrations was 3.3-fold higher than that in children playing no sports. Sports participation had no effect in areas of low O<sub>3</sub> concentration. Time spent outside was associated with a higher incidence of asthma in areas of high but not low O<sub>3</sub>. Exposure to

pollutants other than O<sub>3</sub> did not alter the effects of engaging in outdoor sports activities.

Avol and colleagues (2001) showed that if children moved out of their CHS community, they showed a small increase in lung function measured as MMEF (i.e., lung function improved) if they moved to an area with *lower* PM<sub>10</sub> and a decrease (i.e., lung function worsened) if they moved to an area with *higher* PM<sub>10</sub>. In this sense, the current study may be considered an extension of the work of Avol and colleagues (2001); that is, it focuses on lung development in children who did not move out of their communities but who were expected to have been exposed to declining levels of multiple air pollutants, including PM<sub>10</sub>, over several years as the result of regulatory actions.

As outlined in the sections below, the overall goals of the study were to determine whether decreases in emissions and levels of key outdoor air pollutants occurred over the course of the study, whether those changes resulted from regulatory policies introduced, and whether the decreases in levels of air pollutants had a positive impact on the children's health.

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## DESCRIPTION OF STUDY

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### SPECIFIC AIMS

The study had the following specific aims:

1. To develop a list of air quality regulations enforced between 1993 and 2012 for mobile, stationary, and area source emissions in Southern California and to link the regulations to improvements in measured air quality;
2. To determine whether improvements in long-term PM<sub>10</sub>, PM<sub>2.5</sub>, and NO<sub>2</sub> in ambient levels in CHS communities resulted in increased lung-function level and growth; and
3. To determine whether improvements in long-term PM<sub>10</sub>, PM<sub>2.5</sub>, and NO<sub>2</sub> ambient levels within CHS communities resulted in decreased chronic bronchitic symptoms among children with and without asthma.

### STUDY DESIGN

#### Regulatory Policies and Emissions Estimates

Gilliland and colleagues used information from the California Air Resources Board (CARB) and the South Coast Air Quality Management District (SCAQMD), the two key agencies responsible for air emission regulations and programs affecting Southern California communities, to make

estimates of how emissions of air pollutants changed over the 1993–2011 time period in Southern California. As the investigators acknowledged, multiple regulations were introduced during this time period, many of which overlapped. Gilliland and colleagues focused on identifying the major policies responsible for changes in annual average NO<sub>2</sub> and PM<sub>2.5</sub> concentrations, because they had previously reported associations between these pollutants and children's respiratory health (e.g., Gauderman et al. 2004 and McConnell et al. 2003). They then estimated emission reductions using “backcasted” emissions inventory data.

Though the focus was primarily on changes in emissions of oxides of nitrogen (NO<sub>x</sub>) and PM, the investigators also studied emissions of oxides of sulfur (SO<sub>x</sub>) because both NO<sub>x</sub> and SO<sub>x</sub> are important precursors of PM<sub>2.5</sub>, and NO<sub>x</sub> is a precursor of O<sub>3</sub>. The investigators also evaluated reactive organic gases (ROG), which are precursors of PM<sub>2.5</sub>. As defined by the CARB Emissions Inventory Branch, ROG are total organic gases minus “exempt compounds,” which include methane and multiple chlorofluorocarbons and hydrofluorocarbons (California Air Resources Board 2009).

The investigators also evaluated air quality measurements from monitors in each community and then semi-quantitatively compared them with trends and spatial patterns in emissions.

#### Study Participants

The participants belonged to three cohorts (Cohorts C, D, and E) of the five total cohorts of schoolchildren recruited into the CHS. Participants in Cohorts A and B were not used because they were recruited as senior high and middle school students, respectively.

The goal of the current study was to evaluate changes in participants' lung function and respiratory symptoms in the communities that had data for children of the same ages across all three cohorts and that had collected continuous pollution measurements over the 20 years of the CHS. Thus, participants were drawn from five of the 16 CHS communities for the lung-function analysis (Long Beach, San Dimas, Upland, Mira Loma, and Riverside) and from eight CHS communities for the respiratory symptoms — the same five communities for the lung-function analysis plus three others (Santa Maria, Lake Elsinore, and Alpine). Commentary Table 1 shows some of the key characteristics of the participants in the three cohorts whose lung function and respiratory symptoms were analyzed.

**Commentary Table 1.** Characteristics of the Participants Studied in Cohorts C, D, and E<sup>a</sup>

Cohort	Participants in Each Substudy		Year Recruited (Grade, Nominal Age at Recruitment)	Years of Health Information Used
	Lung Function	Respiratory Symptoms		
C	669	1008	1992–1993 (4th, 10 yr)	4th–12th grade, through 2001
D	588	1067	1995–1996 (4th, 10 yr)	4th–12th grade, through 2004
E	863	2527	2002–2003 (Kindergarten and 1st, 5–7 yr)	4th–12th grade, through 2014
C + D + E	2120	4602		

<sup>a</sup> Collection of health information for both substudies (lung function and respiratory symptoms) from participants in Cohorts C and D was completed before the current study started. Data were previously obtained from the original 12 CHS communities (Atascadero, Santa Maria, Lompoc, Long Beach, San Dimas, Upland, Mira Loma, Riverside, Lake Arrowhead, Lake Elsinore, Lancaster, and Alpine). Four more communities (Anaheim, Glendora, San Bernardino, and Santa Barbara) were added later to the CHS.

For Cohorts C and D, follow-up health data were already available from prior assessments. In the current study, new lung-function data for participants in Cohort E were collected in the five communities with prior lung-function data, and new respiratory symptoms data were collected in all eight included communities.

#### HEALTH DATA AND EXPOSURE ASSESSMENT

Commentary Table 2 shows the key pollutant and health data collected and analyzed across Cohorts C, D, and E and the primary and sensitivity analyses conducted in the two major substudies — the assessments of the associations between changes in pollutant levels and (1) differences in the children's lung-function growth and (2) differences in the development and progression of the children's respiratory symptoms.

##### Lung Function

Gilliland and colleagues obtained lung-function data — specifically, FEV<sub>1</sub> and FVC — by spirometry every year for participants from Cohorts C and D (average ages 10 to 18 years old) and every other year for participants from Cohort E (approximately 11, 13, and 15 years old). At the time that lung function was tested, the investigators also collected information on each participant's height and weight, asthma status, recent respiratory illness, and smoking history.

For this analysis the investigators evaluated only those participants in all cohorts (total number 2,120) who had had multiple lung-function measurements to derive lung growth curves, and for whom data on multiple additional covariates were available; key covariates included sex, ethnicity, and exposure to possible indoor factors (such as pests, mildew, or having a dog or cat).

In a separate sensitivity analysis the investigators used measurements of lung function (i.e., FEV<sub>1</sub> and FVC) collected from all participants for whom they had data at ages 11 and 15 (1,585 of the original 2,120) to determine whether changes in air pollutant levels were associated with what they defined as “clinically important deficits” in FEV<sub>1</sub> and FVC, that is, less than 90%, 85%, or 80% of expected function for that age, taking into account such factors as ethnicity, sex, age, height, and BMI (see “Statistical Methods” section below for details).

##### Symptoms and Other Health-Relevant Information

Gilliland and colleagues collected responses to annual questionnaires about each child's health status and other relevant information over the previous 12 months from children in the eight communities in which investigators had collected continuous pollution measurements over 20 years.

**Commentary Table 2.** Key Features of the Measurements and Analyses Performed for the Lung Function and Symptoms Substudies

	Lung Function Analyses		Respiratory Symptoms Analyses	
	Primary	Sensitivity	Primary	Sensitivity
Health metric	FEV <sub>1</sub> and FVC, measured every yr or every 2 yr, depending on cohort <sup>a</sup>		Bronchitic symptoms reported in annual questionnaire from ages 10 to 18 <sup>b</sup>	
Pollutants measured	NO <sub>2</sub> , PM <sub>2.5</sub> , PM <sub>10</sub> , O <sub>3</sub>		NO <sub>2</sub> , PM <sub>2.5</sub> , PM <sub>10</sub> , O <sub>3</sub>	
Pollutant averaging period	4 yr <sup>c</sup>		9 or 10 yr, depending on cohort <sup>d</sup>	
Modeling approach	Estimate effects of individual pollutants on 4-year growth of FEV <sub>1</sub> and FVC from ages 11 to 15		Estimate associations between cohort- and community-specific levels of individual pollutants and respiratory symptoms	
Major effect estimate	1.Expected difference in lung function growth for a difference in exposure to a pollutant equal to the median of the 5 community changes in each pollutant over the study period. 2.% in each cohort with low FEV <sub>1</sub> or FVC at age 15 <sup>e</sup>	1(a). Inclusion of individual covariates, including level of parental education, SHS, insurance, asthma and pets, complete data at ages 11 and 15 <sup>f</sup> 1(b). Height growth <sup>g</sup> 1(c). Use of different spirometers <sup>h</sup>	Scaled to the corresponding median of the 8 community-level average changes in pollutant level, for each pollutant, from the Cohort C (highest exposure) to Cohort E (lowest exposure) study period.	1.Asthma vs. nonasthma <sup>i</sup> 2.Inclusion of individual covariates <sup>j</sup> , including SHS exposure in the home, pets, race/ethnicity, complete data 3.By age overlapping across all cohorts (ages 10–15) <sup>k</sup> 4.By age, sex, dog ownership <sup>l</sup> , and asthma status.
Subject-specific covariates in models	Sex, race, Hispanic ethnicity, community		Sex, race/ethnicity, pet ownership, asthma status, <sup>m</sup> community	
Time-dependent covariates in models	Age, height, BMI, respiratory illness on day of testing		Age (centered at 10), SHS exposure in the home	
Knot break points — ages in models	12, 14, 16	12, 14, 16	10 and 15	10 and 15

<sup>a</sup> Lung function testing performed annually for Cohorts C and D, between average ages 10 and 18; every 2 yr for Cohort E, between approximate ages 11, 13, and 15.

<sup>b</sup> Symptoms described in year prior to the administration of the annual questionnaire.

<sup>c</sup> Averaging period: Cohort C, 1994–1997; Cohort D, 1997–2000; Cohort E, 2007–2010.

<sup>d</sup> Cohort C, 1992–2000; Cohort D, 1995–2003; Cohort E, 2002–2011.

<sup>e</sup> 1585 Participants of original 2120 tested at ages 11 and 15.

<sup>f</sup> All covariates listed in IR Table 10.

<sup>g</sup> See IR Table 11.

<sup>h</sup> See IR Table 13. Based on a model constructed from prior data from 59 children ages 17.3–19.5 years whose FEV<sub>1</sub> and FVC had been measured using the two spirometers used in the current study.

<sup>i</sup> See IR Table 16.

<sup>j</sup> See IR Table 17.

<sup>k</sup> See IR Table 18; data from only the ages that overlapped in all 3 cohorts, i.e., ages 10–15. Cohort C, 1992–1997; Cohort D, 1995–2000; Cohort E, 2006–2011.

<sup>l</sup> See IR Table 19. Models to test effect modification by sex and dog ownership had 4442 participants.

<sup>m</sup> NO<sub>2</sub> models adjusted for cockroaches in the home.

Of particular interest were (1) symptoms associated with chronic bronchitis (i.e., bronchitis, cough, and phlegm) and (2) asthma status. The definition of asthma differed among the cohorts: in Cohorts C and D, a child was considered to have a history of asthma before age 10 if he or she answered “yes” to the question, “Has a doctor ever diagnosed this child as having asthma?”; in Cohort E, a history of asthma before age 10 was based on an annual assessment starting from ages 5 to 7.

Questionnaires were also used to obtain information about the child and his or her family (medical and residential history questionnaires were completed by parents or guardians at study enrollment and by study participants during the current study). These included age, sex, race, ethnic background, insurance coverage, and education of parents, as well as prior and current health conditions, such as asthma, bronchitis, and other cardiorespiratory conditions. The questionnaires also provided information on other potential sources of pollutant exposure for the participant (environmental tobacco smoke, in-utero smoke, mildew or mold from water damage at home, or presence of pets); home features, including use of gas or electricity for cooking, air conditioning, or heating, and the presence and use of fireplaces; and usual patterns of the participant's physical, temporal, and spatial activities.

### Exposure Assessment

Beginning in 1994, the investigators collected measurements of levels of outdoor pollutants at one central site in each CHS community. They collected hourly or daily readings of NO<sub>2</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> concentrations. They used the 10:00 AM to 6:00 PM mean concentration of O<sub>3</sub> as an average of O<sub>3</sub> exposure because O<sub>3</sub> concentrations have strong diurnal variation.

Gilliland and colleagues then calculated daily and monthly averages for each pollutant. From the monthly averages they calculated averages in each community for all the years relevant to the particular substudy, that is, 4 years for the lung function substudy and 9 years (Cohorts C and D) or 10 years (Cohort E) for the respiratory symptoms substudy.

Because bronchitic symptoms were defined in the year before the parents or children responded to the questionnaire, the investigators used a one-year lagged annual average for each pollutant in that substudy. They then calculated a cohort-specific mean level for each community across the relevant years.

### Statistical Methods and Data Analysis

Commentary Table 2 also shows the primary and sensitivity analyses that were conducted in both the lung-function and respiratory symptoms substudies.

**Associations Between Changes in Levels of Air Pollutants and Lung-Function Growth** The main goal of the analysis in the lung-function substudy (2,120 participants analyzed) was to estimate the effects of a decrease of individual pollutants on 4-year lung-function growth (over the ages 11 to 15). Because lung-function growth is nonlinear, the investigators used a linear spline model they had previously developed (Gauderman et al. 2007) with knots at ages 12, 14, and 16 to construct growth curves for lung function — as measured by FEV<sub>1</sub> and FVC — over the entire ages of the cohorts (approximately 9 to 19 years in Cohorts C and D and 10 to 16 years in Cohort E) in the five communities in which they had measured children's lung function. The model included adjustments for factors such as sex, race, Hispanic ethnicity, height, and BMI. Further details of the models and how they were used are presented in Appendix A to the Investigators' Report (IR), available on the HEI Web site.

The investigators estimated the health effect of each pollutant as the expected difference in lung-function growth associated with a difference in exposure equal to the median of the five community-specific cross-cohort declines in the 4-year averages of each air pollutant.

A second goal of the lung-function growth analysis was to determine in cross-sectional analyses whether the proportion of children with clinically important deficits in FEV<sub>1</sub> and FVC at age 15 differed (1,585 participants, tested at ages 11 and 15) in relation to declines in air pollution. To do this, Gilliland and colleagues developed a linear prediction model for these lung-function measures that included adjustments for factors that included age, sex, race and ethnicity, height, BMI, and BMI squared. They determined for each child whether the observed-to-predicted ratio of FEV<sub>1</sub> and FVC fell below each of three cutoffs they used to define low lung function: 90%, 85%, or 80%. They used logistic regression to model the cross-cohort temporal trends in proportion of the participants with low lung function after adjustment for community.

In all analyses, an association with a *P* value < 0.05 was considered statistically significant, assuming a two-sided alternative hypothesis.

**Associations Between Changes in Levels of Air Pollutants and Respiratory Symptoms** The main goal of the analysis in the respiratory symptoms substudy was to estimate the effects of individual pollutant declines on bronchitic

symptoms (i.e., bronchitis, cough, and phlegm) in children across the entire CHS period. Thus, data were analyzed from all individuals (4,602 total) for whom respiratory (bronchitic) symptoms data were available for 9 or 10 years in eight communities that also had pollutant data for all three cohorts (that is, pollutant data collected over the entire 20-year study period, 1992–2011). The analysis took into account the decreasing trend in air pollution levels from the earlier Cohorts C and D to the more recently recruited Cohort E.

Gilliland and colleagues used a multilevel logistic modeling strategy they had used previously (Berhane et al. 2004; McConnell et al. 2003, 2006a) to assess associations between cohort- and community-specific multiyear average pollution levels and longitudinal data on bronchitic symptoms. In the models, the investigators included random effects to account for serial dependency within study participants and clustering effects of individuals by cohort. They also included time-dependent covariates such as age (centered at 10 years) and exposure to second-hand smoke (SHS) in the home and cubic spline terms of age with knots at 10 and 15 years old to account for the non-linear associations of age with bronchitic symptoms. All the final models were adjusted for possible effect modification by various factors, including age, sex, race or ethnicity, dog or cat ownership, and exposure to SHS. Models for NO<sub>2</sub> were also adjusted for exposure to cockroaches at home.

The models also included a fixed effect for community, which the investigators used to make inferences about the effects on bronchitic symptoms of secular changes in air pollution levels across the span of the entire period from 1992 to 2011. Community-specific one-year lagged annual averages of the 24-hour PM<sub>10</sub>, PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub> were used to compute the cohort-specific mean levels for the relevant period of follow-up in each community.

Because the prevalence of bronchitic symptoms was much higher in subjects with asthma, Gilliland and colleagues also fitted models with effects stratified by asthma status. In these analyses, the investigators focused on changes in the participants' symptoms over the age range of 10 to 15 years, the ages that overlapped in all three cohorts. Gilliland and colleagues also examined effect modification by SHS exposure and sex and dog ownership (sex and dog ownership analysis used data from only 4,442 children, because of missing questionnaire data).

The investigators wrote: "Effect estimates were scaled to the corresponding median of the eight community-level average changes in pollution level, corresponding to each pollutant, from the Cohort C to Cohort E study periods." That is, the investigators used the median of the community-specific differences obtained by subtracting the 9- or

10-year average in the highest exposed cohort, Cohort C, from the 9- or 10-year average in the lowest exposed cohort, Cohort E. As in the lung-function analyses, an association with a *P* value <0.05 was considered statistically significant, assuming a two-sided alternative hypothesis.

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## SUMMARY OF RESULTS

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### LEVELS OF OUTDOOR AIR POLLUTANTS

#### NO<sub>2</sub> and PM<sub>2.5</sub>

In communities that had high levels of NO<sub>2</sub> (>25 ppb in 5 of the 12 communities) at the start of the study, annual average levels of NO<sub>2</sub> showed a large decreasing trend across the 20 years of the study (IR Figure 2). In Upland, for example, NO<sub>2</sub> levels decreased by 53%, from 41 ppb in 1992 to 19 ppb in 2011. Five communities that had lower annual levels of NO<sub>2</sub> at the start of the study (10–25 ppb) showed smaller decreasing trends across the study (e.g., from 10 to 7 ppb [28%] in Santa Maria). Two communities with very low starting levels showed no change in NO<sub>2</sub> across the entire period.

The five communities included in the lung-function substudy (IR Figure 3) had mainly high starting levels of NO<sub>2</sub> and showed decreases in it from early to later in the study (comparing Cohort C with Cohort E over the 4-year averaging period). All eight communities included in the respiratory symptoms substudy (IR Figure 4) showed decreasing trends in NO<sub>2</sub> levels across the time of the study, but the trends were small in communities with low starting levels of NO<sub>2</sub>.

The pattern of decreases in PM<sub>2.5</sub> levels across communities was almost identical to the pattern of changes in NO<sub>2</sub> (IR Figures 2, 3, and 4) — that is, a large decreasing trend in five communities with high starting levels (>25 µg/m<sup>3</sup>), a smaller decreasing trend in five communities with lower starting levels (10–25 µg/m<sup>3</sup>), and little or no change in two communities with low starting levels (<10 µg/m<sup>3</sup>).

#### O<sub>3</sub> and PM<sub>10</sub>

Reductions in O<sub>3</sub> and PM<sub>10</sub> levels were seen across the study in some communities (IR Figure 2), but these were smaller than the decreases in PM<sub>2.5</sub> and NO<sub>2</sub>, even in the most highly polluted communities. In Riverside, for example, one of the two CHS communities with the highest O<sub>3</sub> levels, daytime O<sub>3</sub> decreased by 12% (64.3 to 56.7 ppb) and PM<sub>10</sub> decreased by 24% (42.4 to 32.4 µg/m<sup>3</sup>). However, in communities with moderate to lower outdoor levels of O<sub>3</sub> and PM<sub>10</sub>, the changes in levels of these pollutants

were more variable. In some communities, no statistically significant changes in O<sub>3</sub> levels were observed across the study (IR Figure 2). In the five communities examined in the lung-function substudy, small decreases or no changes in O<sub>3</sub> and PM<sub>10</sub> levels were noted (IR Figure 3). In the respiratory symptoms substudy (IR Figure 4), average O<sub>3</sub> levels showed a decreasing trend across the study, except in Long Beach and Santa Maria, where levels were higher in Cohort E, at the end of the study. Changes in PM<sub>10</sub> levels were also small in the respiratory symptoms substudy.

### EMISSIONS OF AIR POLLUTANTS

Emissions decreased in almost all categories of air pollutants over the study period (1993–2012 [IR Figure 5 and Table 2]). In the South Coast Air Basin (SoCAB), total estimated emissions decreased by 54% for NO<sub>x</sub>, 65% for ROG, 40% for SO<sub>x</sub>, 21% for PM<sub>2.5</sub>, and 15% for PM<sub>10</sub>. For all pollutants in 1993 the principal emissions sources were in the “on-road mobile sources” category, and the largest reductions in *total* emissions were seen in this category in 2012, especially for NO<sub>x</sub> and ROG (reductions of > 500 tons/day). In addition, on-road motor vehicle SO<sub>x</sub> emissions decreased by more than 90%. Large percentage reductions were also reported for stationary-source NO<sub>x</sub> (64%) and ROG (69%) emissions.

For communities included in the CHS but outside SoCAB, the investigators indicated that the percent reductions in emissions of the same set of air pollutants in San Diego County (south of SoCAB) over the period 1993–2012 were similar to those found in the SoCAB (data not shown). In Santa Barbara County (north of SoCAB) total emissions were an order of magnitude lower than in the SoCAB; ROG emissions decreased, but estimates of NO<sub>x</sub>, SO<sub>x</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> emissions *increased* over this time period. The bulk of the emissions increase in this county was in the category “other-mobile-source” emissions, despite a drop in the “on-road motor vehicle” emissions category (NO<sub>x</sub> by 57% and PM<sub>2.5</sub> by 13%). The investigators attributed the increase in “other-mobile-source” emissions to oceangoing vessels at the ports of Los Angeles and Long Beach. At the ports, combined emissions of NO<sub>x</sub> and primary PM<sub>2.5</sub> increased approximately 160% during this time frame (data not shown).

Over the study period, the investigators reported that vehicle miles traveled in the SoCAB increased approximately 38% (IR Figure 6) and that the region's population increased.

In high-pollution (but not low-pollution) communities the decreasing trend in ambient concentrations of NO<sub>2</sub> and PM<sub>2.5</sub> across the CHS time period was generally consistent with the decreasing trend in emissions (IR Figure 7). This

was most evident for NO<sub>2</sub> — ambient levels of NO<sub>2</sub> and NO<sub>x</sub> emissions both decreased by approximately 50% over the course of the study. For O<sub>3</sub> and PM<sub>10</sub> the associations between the trend in ambient concentrations and trend in emissions were much weaker.

### ENFORCEMENT OF REGULATORY POLICIES

The investigators noted that national regulatory policies to limit emissions originated with the Federal Clean Air Act of 1970 and its subsequent amendments (1977 and 1980). In addition, following passage of the California Clean Air Act (1988), the CARB implemented policies to reduce emissions in the state from vehicles and other mobile sources.

Gilliland and colleagues listed nearly 20 major policies introduced in California at different times between 1985 and 2012 (IR Table 4). These policies were in four broad categories: (1) on-road emissions, which included policies regulating diesel emissions from heavy-duty trucks, reformulating gasoline, and reducing emissions from trucks used at ports (such as the Ports-Clean-Truck Program); (2) off-road emissions, which included policies regulating diesel fuel for oceangoing vessels and trains and diesel engines for agricultural use; (3) stationary point sources (power plants and factories), which included policies affecting NO<sub>x</sub> and SO<sub>x</sub>; and (4) area sources, which included measures to control paved and unpaved road dust and certificate programs for products and equipment. Some policies, such as those affecting fuel standards, were made more stringent by successive changes during this time frame.

### DIFFERENCES AMONG THE COHORT PARTICIPANTS

Overall, there were some differences in the characteristics of participants in Cohorts C, D, and E — especially between Cohort E on the one hand and Cohorts C and D on the other (IR Tables 6 and 14). In particular, in both substudies, Cohort E had a higher percentage of Hispanic participants (58% in the lung-function substudy) than Cohorts C or D (31% and 33%, respectively). Cohort E also had a *higher* prevalence of children with asthma at age 10 (21% versus 14% and 17%, respectively); children with health insurance; and children living in homes with gas stoves. Participants in Cohort E also had a *lower* prevalence of exposure to SHS or history of in-utero exposure to maternal smoking; and ownership of cats, dogs, or any other pets. In the respiratory symptoms substudy, but not the lung-function substudy, Cohort E had the lowest percentage of parents who completed a high-school education. Finally,

because recruitment was at ages 5 to 7, Cohort E also had a higher rate of dropout by age 10.

As discussed in the next section, the results of the study also showed that the cohorts differed in the proportion of children with normal lung function.

### GROWTH OF LUNG FUNCTION

In the lung-function substudy, the investigators found, as expected, that in both boys and girls FEV<sub>1</sub> and FVC estimated from their model were higher at age 15 than at age 11 (IR Table 8); that is, lung function grew over this critical 4-year period. The magnitude of lung-function growth was larger in boys. More important, the model-based estimated changes in lung function from age 11 to age 15 found the *increase* in children's 4-year lung growth was associated with *decreases* in the average levels — compared with the median of the five community-specific cross-cohort decreases in each pollutant — of NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>, but not O<sub>3</sub> (IR Table 9).

In sensitivity analyses of the effects of NO<sub>2</sub> decline on 4-year lung growth (IR Table 10), the effects of a decline in NO<sub>2</sub> were larger in boys than girls and of the same magnitude in both those with and without diagnosed asthma, as well as in Hispanics and non-Hispanic whites. The effects of a decline in NO<sub>2</sub> were not modified by such factors as exposure to in-utero tobacco smoke or SHS or several indoor factors (including the presence of dogs, cats, or mildew). The estimated effects for the subset of children with complete data at ages 11 and 15 (IR Table 10) were also similar to those estimated for all children between ages 10 and 18 included in the primary analyses. The investigators indicated that sensitivity analyses of the effects of the other pollutants evaluated — presumably PM<sub>2.5</sub> and PM<sub>10</sub> — showed a pattern similar to that found in the sensitivity analyses of the effects of NO<sub>2</sub>, but they did not show these data in the report.

Cross-sectional analyses of lung function at age 15 showed that Cohort E had the smallest proportion of children with low lung function — that is, with observed/predicted FEV<sub>1</sub> and FVC of <90%, <85%, and <80% (IR Figure 11). For example, at an observed/predicted cutoff of 80%, only 3.6% of Cohort E had an FEV<sub>1</sub> below the cutoff, compared with 7.9% in Cohort C and 6.3% in Cohort D.

### RESPIRATORY SYMPTOMS

Gilliland and colleagues reported that cross-cohort decreases in levels of ambient air pollutants NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> were associated with reductions in children's bronchitic symptoms at ages 10 and 15 (IR Table 16). This association was found in children with and without asthma

at both ages, but reductions in bronchitic symptoms were greater in children with asthma — at age 10, bronchitic symptoms decreased by 21% for NO<sub>2</sub>, 34% for O<sub>3</sub>, 39% for PM<sub>10</sub>, and 32% for PM<sub>2.5</sub> in those children with asthma and by 16% for NO<sub>2</sub>, 15% for O<sub>3</sub>, 20% for PM<sub>10</sub>, and 21% for PM<sub>2.5</sub> in those children without asthma. As expected, the overall prevalence of bronchitic symptoms was higher in children with asthma (IR Figure 15).

Sensitivity analyses found no effect on these associations for factors including exposure to SHS and in-utero tobacco smoke, pets, asthma medication use, or restriction of the analyses to subjects with complete data during the target age range of 10 to 15 (IR Table 17). In the asthma group and for both ages 10 and 15, the effects of NO<sub>2</sub> and PM<sub>2.5</sub> were larger in boys and among children with family dog ownership (IR Table 18 and 19), but no other interaction tests were found to be significant.

In the analysis by individual community (IR Figure 15), the prevalence of symptoms in children with asthma decreased linearly with cross-cohort decreases in levels of NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> in five of the eight communities. The communities with the largest decreases in air pollutant levels showed the largest reductions in prevalence of bronchitic symptoms in children with asthma (IR Figure 16). For example, in the asthma group, a 12- $\mu\text{g}/\text{m}^3$  decline in PM<sub>2.5</sub> in Riverside was associated with a 20% reduction in prevalence of bronchitic symptoms. However, in three of the eight communities, Lake Elsinore, Santa Maria, and Alpine, which had small or no declines in pollutant levels, there were no changes in prevalence of symptoms in children with asthma with change in pollutant levels. Indeed, the small declines in PM<sub>2.5</sub> in Alpine (0.5  $\mu\text{g}/\text{m}^3$ ) and in NO<sub>2</sub> in Santa Maria (1 ppb) were associated with small *increases* in the prevalence of bronchitic symptoms.

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## HEI REVIEW COMMITTEE EVALUATION

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### OVERVIEW

The current study was an important addition to the CHS, which has been collecting data on outdoor pollutant levels and children's respiratory health for more than 20 years in several Southern California communities that differ in their pollutant sources and initial levels of outdoor pollutants. The uniqueness of the current study was its goal of identifying air pollutant regulations introduced at both a national, statewide, and regional levels over the course of several years and exploring whether these regulations were associated with reductions in both emissions and air pollutant levels in the CHS communities. Were the

reductions in pollutant levels then associated with improvements in children's respiratory health?

Overall, the Committee agreed with the investigators' conclusions of decreases in emissions and outdoor levels of major pollutants — particularly in NO<sub>2</sub> and PM<sub>2.5</sub> and in communities with high starting levels of these pollutants — and that children's respiratory health improved across the study period. However, the Committee considered that further analysis and different types of analysis were needed in future studies to make convincing linkages between the introduction of specific regulations and decreases in emissions and between decreases in emissions, improvements in air quality, and improvements in health.

#### LINKING AIR QUALITY REGULATIONS TO CHANGES IN EMISSIONS AND POLLUTANT LEVELS

Using information from the U.S. Environmental Protection Agency and California state agencies, Gilliland and colleagues fulfilled the first Specific Aim — they developed a list of nearly 20 major policies introduced in California at various times between 1985 and 2012 for mobile, stationary, and area source emissions in Southern California (IR Table 4). In addition, using data from regional and national agencies, the investigators documented that total emissions of air pollutants and several categories of air pollutants — in particular, on-road emissions — decreased substantially over the study period. This finding was consistent with the findings of McDonald and colleagues (2012), who also reported substantial reductions in on-road vehicle NO<sub>x</sub> emissions in a geographical area and time frame (approximately 1990–2010) that overlapped with that of the current study. Furthermore, the current study's overall findings of decreases in several categories of air pollutants are consistent with the series of measurements of air pollutants, particularly air toxics, made over several years in the same region of Southern California (albeit in different cities and of many different pollutants) by SCAQMD in a series of Multiple Air Toxics Studies (MATES); the most recent, MATES IV, extended to 2012 (SCAQMD 2015). Similar decreases in mobile source emissions in California have been reported by other investigators, for example, Bishop and Stedman (2008) and Bishop and colleagues (2015).

The investigators pointed out that the decreases in emissions were all the more noteworthy because they occurred during a period of vigorous growth: a statewide increase in population of 30–50%, and an increase of about 38% in vehicle miles driven in the SoCAB. Given this, it seems plausible that the regulations would have contributed to the reductions in emissions. However, a more detailed

statistical analysis examining, for example, counterfactuals (described in more detail below), would have provided a more rigorous test. Such analyses would include the potential impact of other factors that may have contributed to the changes in emission levels reported in the current study. One such factor is the impact of the 2007–2008 economic recession, which reduced work-related travel, substantially reduced construction activity (including operation of on-road and nonroad diesel engines), but also resulted in increases in emissions from light-duty diesel vehicles, attributable to a reduced turnover of the fleet (Bishop and Stedman 2014).

Gilliland and colleagues also reported reductions in several CHS communities of levels of outdoor pollutants, particularly of NO<sub>2</sub> and PM<sub>2.5</sub> and particularly in communities with high starting levels of these pollutants, over the almost 20 years of the study. Reductions in average PM<sub>10</sub> and O<sub>3</sub> levels were smaller and more variable than those of NO<sub>2</sub> and PM<sub>2.5</sub>; indeed in some communities, O<sub>3</sub> levels increased over the time period.

The investigators interpreted the reductions in pollution levels to be the result of the policies introduced by the regulatory agencies. As the investigators acknowledged, however, different regulations were introduced at different times during the study period, some of them overlapping, such that Gilliland and colleagues could not directly attribute the effect of any individual regulatory action to a reduction in pollutant levels. More important, the Committee considered that the linkage made in the study between specific regulatory initiatives and improved ambient air quality, though plausible, was largely descriptive and was not based on formal analysis. Consequently, the analysis performed could be described as only an *indirect* assessment of the impact of these regulatory initiatives on pollutant levels, showing that the reductions in emissions occurred in the same time period that various regulations were introduced. The regulations very likely did contribute to those reductions, but Gilliland and colleagues did not provide conclusive evidence that linked the introduction of *specific* regulations to a change or changes in *specific* pollutant and ambient levels. However, the rich data collected in the course of this work provide ample opportunities to explore such links in the future, and such analyses might provide additional insights into the findings reported here.

Additionally, the Committee considered that factors not extensively explored by the investigators might have provided or ruled out alternative explanations for the findings reported. These alternative explanations needed to be considered and eliminated before accepting that the introduction of regulatory policies had a direct impact on the

pollutant levels and health endpoints evaluated. The Review Committee agreed with the comments provided to the investigators by the Research Committee after the study had started and considered that evaluation of alternative hypotheses and explanations for the findings is critical in accountability studies of this type and importance.

The Review Committee acknowledges that the challenges in considering detailed and alternative explanations are not unique to the current study but have been encountered by many other investigators in accountability studies who have sought to assess both changes in pollutant levels and the possible health effects of a change in air pollution regulations. In some previous accountability studies, initial reports that the implementation of a particular policy led to improvements in health have had to be reinterpreted as the result of subsequent studies that undertook more in-depth analyses. This occurred, for example, in evaluating the effects of policies to reduce traffic in Atlanta during the 1996 Olympics (Peel et al. 2010; extending the original analysis by Friedman et al. 2001) and in the introduction of a ban on the use of coal in Dublin and other cities in Ireland (Dockery et al. 2013; extending the original analysis by Clancy et al. 2002). The results of these previous accountability studies emphasize both the importance and the challenges of trying to disentangle the effects of policy implementation from social and economic factors and other concurrent changes that influence trends in air quality and health.

A recently published study, funded by HEI under this RFA at the same time as the Gilliland study, provides a possible analytical approach as to how such analyses may be performed in the future. Zigler and colleagues (2016; see both the IR and the accompanying Commentary) extended air pollution outcomes assessment by providing an explicit causal effects modeling approach to evaluating relationships between an action and its associated outcomes that specifically considered what outcomes might have occurred in the absence of the action. Such new analytical techniques, along with the extensive CHS data, offer unique opportunities for future explorations of important accountability issues.

#### ASSOCIATIONS BETWEEN CHANGES IN POLLUTANT LEVELS AND HEALTH EFFECTS

Overall, the investigators concluded that the results of their two health substudies show that the decreases observed in multiyear averages of the levels of  $PM_{2.5}$  and  $NO_2$  in the CHS communities — particularly in communities with high starting levels of these pollutants — were associated with both a cross-cohort improvement in children's lung-function growth and with a cross-cohort

decrease in children's respiratory symptoms, particularly in children with asthma.

The Committee thought that the use of multilevel statistical models Gilliland and colleagues developed for the CHS was a strong feature of the current study. The investigators also incorporated several factors (such as ethnicity and BMI) into their models that might have had a confounder or effect modification role.

Nonetheless, the Committee considered that other factors not explored by the investigators' analysis might also have contributed to the improvements in lung-function growth and symptoms over the 20 years of the CHS. All exposure estimates were based on community-level long-term averages (4 years in the lung-function substudy, 9 or 10 years in the respiratory symptoms substudy) for each cohort. The primary contrasts that were analyzed were those between distinct cohorts within a community. The lack of controls for other secular trends was an important limitation of the analysis. Demographic shifts — particularly affecting the most recently recruited Cohort E vis-à-vis the earlier Cohorts C and D — may have introduced bias; in particular, across both substudies, Cohort E had more children of Hispanic origin and more with asthma, and fewer children exposed to in-utero secondhand smoking. Additional factors that may have played a role include changes in access to healthcare (including management of asthma and use of medications), nutrition and other factors that might have affected lung growth and asthma symptoms over the course of the study, and differential dropout across cohorts (discussed below). In addition, although environmental tobacco smoke was included in the analysis at an individual level, it was not considered at the community level; several studies indicate that recent legislation introduced to make communities smoke free resulted in improvements in asthma (e.g., showing substantial reductions in children's hospitalizations for asthma [Mackay et al. 2010]).

As the investigators indicated, declines in  $NO_2$  and  $PM_{2.5}$  pollutant levels varied among the five communities in the lung-function substudy. However, it is apparent that the association between improvements in lung function and decreases in levels of various pollutants was not consistent from community to community. Riverside, in particular, was different from the four other communities analyzed: It had the *smallest* reduction in  $NO_2$  levels but one of the *largest* reductions in  $PM_{2.5}$  levels of any community (IR Figures 2, 3, 4, and 13) and the *smallest* increase in growth of  $FEV_1$  (IR Figure 11). In other words, despite the enormous decline in  $PM_{2.5}$  in Riverside, participants from this community showed the smallest improvement in lung-function growth.

What was unique about Riverside is not clear and could have been explored in more depth. Its uniqueness may have resulted from factors such as community-specific sources of pollution, the demographics of its inhabitants, or other unknown factors. Whatever the reasons for these differences, they weaken the generalizability of the associations reported between air pollution declines and improvements in lung function across the communities. A similar lack of consistency among communities was noted in the respiratory symptoms substudy — five communities showed a more or less linear association between the decrease in prevalence of bronchitis, cough, and phlegm and decreasing long-term pollutant levels, but no such relationship was found in the three remaining communities.

Given the richness of this data set, conducting additional community-level analyses in the future might shed some light on these issues. For example, community- and period-specific “leave-one-out” analyses may identify influential time windows, and directly comparing two communities with high NO<sub>2</sub>/low PM<sub>2.5</sub> and low NO<sub>2</sub>/high PM<sub>2.5</sub> may provide additional insights into the effects of individual pollutants.

Conducting further two-pollutant analyses may also be useful. The investigators indicated that the changes in levels of pollutants were highly correlated after adjusting for community (IR Tables 12 and 20), so extensive two-pollutant analyses were not performed. However, the Committee pointed out that the values shown in these two tables were correlations between the within-cohort and community pollutant average pairs (e.g., PM<sub>2.5</sub> versus NO<sub>2</sub>) after the community mean for each pollutant had been removed. Thus, the correlations reported did not provide information about the relationship between reductions in the pollutants. For this reason, the Committee considered that an in-depth analysis to explore the correlations among community-specific *changes* in pollutants would be informative.

The Committee also concluded that the report's focus on *cohort and community* averages of pollutant levels missed crucial *within-community and cohort* variations in air pollution levels and their impact. For the assessment of exposure to pollution in a particular community, the investigators used only the information provided by a multiyear average for a specific cohort from a single, central-site monitor; they recognized that this was a likely source of exposure misclassification. Prior publications from the CHS investigators have illustrated the importance of incorporating measures of within-community variations in air pollution (Gauderman et al. 2007; Urman et al. 2014); these studies have shown that participants who lived within 500 meters of a

freeway experienced greater declines in lung function associated with exposure to specific air pollutants than did those who lived farther away (Gauderman et al. 2007; Urman et al. 2014). In addition, other CHS publications have shown that exposure at school versus at home is a major source of variation in exposures to pollution (McConnell et al. 2010); this difference could also be explored in future analyses. Furthermore, in earlier CHS analyses, O<sub>3</sub> effects were limited only to the subset of children playing sports outdoors (McConnell et al. 1999, 2002, 2003).

Indeed, in light of the investigators' not unreasonable interpretation of their emissions results — that the policies introduced affected vehicle emissions — the Committee considered that it would be informative to evaluate whether CHS participants with higher initial exposures to traffic pollution, such as those residing in proximity to freeways, may have benefited *more* from decreases in ambient pollutant levels over the duration of the study than did participants who lived farther away from traffic. Even without a full analysis of individual-level exposures, a simple analysis in which participants are stratified by those with high versus low proximity to traffic sources could provide confirmatory evidence for the hypothesis that the policies that focused on decreasing motor vehicle emission were associated with improvements in lung-function growth and bronchitis symptoms.

In addition, the Committee pointed out that there were different numbers of participants in different analyses; for example, Cohort E had the largest number of participants in both the lung-function (863) and respiratory symptoms (2,527) substudies but had a much higher proportion of total participants in the respiratory symptoms substudy than the lung-function substudy (55% compared with 41%). Similarly, some sensitivity analyses were conducted with a very low proportion of the whole group — for example, “subjects with complete data” were only 26% of the total bronchitic symptoms group. The impact of having so many participants in these analyses from Cohort E, which had many differences in characteristics from the earlier cohorts and was exposed to the lowest average levels of most outdoor pollutants, is unclear.

There was also relatively more dropout from Cohort E than from the other two cohorts — the total number of children recruited originally into Cohort E was approximately 5,000 (McConnell et al. 2006b), meaning that the 863 and 2,527 participants in the two substudies were likely more highly selected subpopulations of the original cohort. This dropout from Cohort E in comparison with the other cohorts is also understandable because children in Cohort E were initially recruited at ages 5 to 7 rather than age 10, as was done in Cohorts C and D; thus, there was more time

for dropout from Cohort E before the current study started. Dropout from Cohort E may also explain why Cohort E had the highest prevalence of children with health insurance — it is plausible that more of the children remaining after dropout since enrollment occurred were likely to be in families that carried health insurance.

## CONCLUSIONS

The HEI Review Committee considered that Gilliland and colleagues conducted an important study to evaluate the outcomes of long-term regulatory actions. The study assessed how air pollution regulations introduced during the study period may have affected emissions and ambient levels of air pollutants in Southern California and whether changes in pollutant levels were, in turn, associated with improvements in children's respiratory health.

A major strength of the study was that it brought together extensive pollutant monitoring data and health effects information collected over 20 years in this unique and well-studied data set from participants in the CHS. The investigators used data from a large number of children who lived in several communities in Southern California that differed in sources and levels of major pollutants (NO<sub>2</sub>, PM, and O<sub>3</sub>). They also collected detailed information about the children's health and relevant covariates in the cohort population.

The investigators found that emissions of pollutants and precursors decreased over the 20-year time frame of the study, as did most ambient pollutant levels, and particularly in communities with initially high levels of NO<sub>2</sub> and PM<sub>2.5</sub>. Gilliland and colleagues noted that the large number of pollution control policy measures taken, with a focus on reducing motor vehicle and other emissions, made it difficult to link any specific action closely to a specific improvement in air quality. The Committee agreed that the regulations likely did contribute to those reductions, although it also noted the absence of analyses for other factors that might have contributed to changes in pollutant emissions.

The major health findings of the study were that decreases in long-term community-level averages of pollutants (particularly NO<sub>2</sub> and PM<sub>2.5</sub>) across cohorts were associated with increased growth of children's lung function. In addition, in the cohort with the lowest overall levels of outdoor pollutants (Cohort E) there were fewer children with clinically relevant deficits in FEV<sub>1</sub> and FVC at age 15 than in the other two cohorts. Furthermore, decreases in levels of NO<sub>2</sub>, PM<sub>2.5</sub>, PM<sub>10</sub>, and O<sub>3</sub> were also associated with decreases in the prevalence of bronchitic symptoms across the cohorts, particularly in children with asthma.

The Committee agreed with these health findings. However, it noted that the changes in lung function and respiratory symptoms were not uniform with regard to decreases in pollutant levels across the communities. There was, however, variability in the relationship between pollution decreases and changes in lung-function and respiratory symptom measures among the communities. This variability in lung function and respiratory symptoms results across communities suggested that unexplored between-community and within-community factors could be important. In addition, for all analyses, the reliance on multiyear averages from a single central monitor in each community likely reduced the ability both to understand how exposure varied within a community and to assess the impact of regulations and emissions reductions.

In summary, the Committee concurred with the investigators that decreases in levels of major outdoor pollutants were associated with improvements in children's health. However, the Committee noted that the analyses did not fully consider some differences between successive cohorts over time that might also have contributed to improvements in children's health, making it more challenging to draw strong conclusions from the study unless alternative explanations for the health benefits can be ruled out.

Taken together, the findings of this important contribution to the accountability literature indicate that regulations directed toward reductions in emissions of mobile-source and other pollutants over the course of the study by national and California agencies were likely contributors to improvements in air quality that were linked to improvements in children's health, although the regulations themselves could not be definitively linked to the health improvements. Even so, the findings suggest the potential for important public health benefits resulting from levels of major outdoor pollutants that have been decreasing as a result of public policy measures.

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## ACKNOWLEDGMENTS

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The Review Committee thanks the ad hoc reviewers for their help in evaluating the scientific merit of the Investigators' Report. The Committee is also grateful to Annemoon van Erp, Aaron Cohen, and Hanna Boogaard for their oversight of the study, to Kate Adams for her assistance during the review process, to Geoffrey Sunshine and Rashid Shaikh for their assistance in preparing the Commentary, to Mary Brennan for science editing of this Report and its Commentary, and to Hope Green, Fred Howe, Hilary Selby Polk, and Ruth Shaw for their roles in preparing this Research Report for publication.

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## ABBREVIATIONS AND OTHER TERMS

AQMP	Air Quality Management Plan	MATES	Multiple Air Toxics Studies
ATS	American Thoracic Society	MMEF	maximal midexpiratory flow
BAM	Beta attenuation monitor	NAAQS	National Ambient Air Quality Standards
BMI	body mass index	NIEHS	National Institute of Environmental Health Sciences
CAA	Clean Air Act	NO <sub>2</sub>	nitrogen dioxide
CARB	California Air Resources Board	NO <sub>x</sub>	oxides of nitrogen
Carl Moyer Program	California-funded program providing incentive grants for emissions reductions on an accelerated or early schedule	O <sub>3</sub>	ozone
CEPAM	California Emissions Projection Analysis Model	OC	organic carbon
CHS	Children's Health Study	PM	particulate matter
EC	elemental carbon	PM <sub>10</sub>	particulate matter ≤10 μm in aerodynamic diameter
EMFAC	Emissions Factors Model (released by the California Air Resources Board)	PM <sub>2.5</sub>	particulate matter ≤2.5 μm in aerodynamic diameter
EPA	(U.S.) Environmental Protection Agency	QA	quality assurance
ERS	European Respiratory Society	QAPP	Quality Assurance Project Plan
FEF <sub>75</sub>	forced expiratory flow at 75% maximum expiration	RECLAIM	Regional, Clean Air Incentive Market
FEM	Federal Equivalent Method (i.e., equivalent to the FRM for air monitoring)	RFA	Request for applications
FEV <sub>1</sub>	forced expiratory volume in the first second of exhalation	ROG	reactive organic gases
FRM	Federal Reference Method	SCAQMD	South Coast Air Quality Management District
FVC	forced vital capacity	SHS	secondhand smoke
GDP	gross domestic product	SoCAB	South Coast Air Basin
IR	Investigators' Report	SIPs	State Implementation Plans
LEV	low-emission vehicles	SO <sub>x</sub>	oxides of sulfur
		STN	Speciation Trends Network
		TEOM	tapered element oscillating microbalance
		VMT	vehicle miles traveled



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RESEARCH  
REPORT

Number 190  
January 2017

