IEc

Literature Review of Air Pollution-Related Health Endpoints and Concentration-Response Functions for Particulate Matter:

Results and Recommendations

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INTRODUCTION

Every four years, the South Coast Air Quality Management District (SCAQMD) updates the regional Air Quality Management Plan (AQMP) for Los Angeles, Orange, Riverside, and San Bernardino Counties in southern California. As part of the development of this Plan, SCAQMD considers the socioeconomic impacts of the AQMP. These estimated benefits and costs are detailed in a Socioeconomic Report that accompanies the AQMP.

A key analysis in the Socioeconomic Report is an assessment of the health benefits of the AQMP on residents of these four counties. This assessment of health impacts relies on data describing the baseline incidence of mortality and morbidity endpoints, the estimated change in air pollution concentrations, population data, and the relationship between exposure and health outcomes. SCAQMD draws this latter input from population-based epidemiological studies. These studies provide information on which health endpoints are associated with exposure to air pollutants, and the mathematical relationship between exposure and the outcome. This report presents our review of recent studies of the health impacts associated with exposure to particulate matter (PM) and provides recommendations to inform SCAQMD's decisions regarding which health endpoints to include in its benefits analysis of the 2016 AQMP and which mathematical functions should be used to evaluate each endpoint.

METHODS

Our approach consisted of three steps. First, we identified the endpoints and studies used in SCAQMD's 2012 Socioeconomic Analysis. Second, we reviewed the current evaluation of PM effects by the U.S. Environmental Protection Agency (U.S. EPA) in its most recent Integrated Science Assessment (ISA) document (U.S. EPA, 2009). Finally, we conducted a supplemental review of the health literature published since SCAQMD's 2012 Socioeconomic Report.

2012 SOCIOECONOMIC REPORT

IEc sought to identify the health endpoint categories and health studies used to evaluate the health benefits of the 2012 AQMP. IEc based its findings of the 2012 categories and inputs based on review of the 2012 Socioeconomic Report and appendices, additional background documentation provided by SCAQMD, and our knowledge of the standard BenMAP functions typically used at the time of the last assessment.

U.S. EPA INTEGRATED SCIENCE ASSESSMENT

In addition to our literature review, we also reviewed the most recent Integrated Science Assessment for PM published by the U.S. EPA in 2009. The comprehensive assessment of the health literature presented in the ISA provides U.S. EPA's current assessment of the strength of the evidence linking PM exposures with an array of health endpoint categories and thus serves as a suitable baseline against which we can compare the findings of recent research.

SUPPLEMENTAL LITERATURE REVIEW

In order to ensure SCAQMD uses the most current science when evaluating the health impacts of air pollution control, we conducted a literature review of mortality and morbidity impacts of exposure to particles less than 2.5 micrometers in diameter ($PM_{2.5}$). (Similar searches were also conducted for ozone (O_3), nitrogen oxides (NO_X), and sulfur dioxide (SO_2); results for these pollutants will be reported in a separate document.). We searched PubMed and Google Scholar for peer-reviewed articles on PM from 2012 onward, using search terms "$PM_{2.5}$ AND mortality" and "$PM_{2.5}$ AND morbidity."[1] We also included several studies that did not appear in our search, but were recommended by our scientific advisor, Dr. George Thurston. We prioritized studies to evaluate for inclusion in the 2016 Socioeconomic Report by evaluating them using the criteria described in our Evaluation Criteria Memo to SCAQMD dated August 20, 2015; these criteria are summarized in Exhibit 1. Our criteria serve as guidance for evaluating studies and weighing their strengths and limitations. No one study is likely to meet all criteria listed.

[1] The cutoff date for studies included in the 2012 Socioeconomic Assessment is not known, but may have preceded 2012. As a result, IEc also conducted a brief search for studies conducted in 2011. A review of the titles and abstracts from that search yielded no information likely to alter the conclusions of our review.

EXHIBIT 1. CRITERIA FOR EVALUATING EPIDEMIOLOGICAL STUDIES

CRITERIA
GENERAL:
1. Study is peer-reviewed. 2. Study is written in English. 3. Study measures exposure to at least one of the following pollutants: O_3, $PM_{2.5}$, PM_{10}, NO_x, SO_2, 4. Preference given to studies or groups of studies that significantly advance our understanding of the relationship between air pollution exposures and mortality and morbidity endpoints, including those endpoints previously quantified by the SCAQMD in its Air Quality Management Plans as well as new endpoints. 5. Study was published within the following timeframes: a. $PM_{2.5}/PM_{10}$: 2012 – present b. NO_2: 2012 – present c. O_3: 2007 – present d. SO_2: 2003 - present
GEOGRAPHY AND STUDY POPULATION:
6. Study measures exposures at or near ambient levels found in the South Coast Air Basin. Order of preference of study location: a. South Coast Air Basin (Los Angeles, Orange, Riverside, and San Bernardino Counties) b. Within State of California c. Within Western United States d. Within United States or Canada 7. Study uses study population with similar characteristics as found in Los Angeles, Orange, Riverside, and San Bernardino counties.
STUDY DESIGN:
8. Study is population-based, preferably using cohort or case-control epidemiological study designs. Controlled human exposure studies may be evaluated for supporting evidence, or in the absence of relevant epidemiology. Animal and in-vitro studies excluded. 9. Study controls for factors that may obscure the true concentration-response relationship, including selection bias, misclassification, recall bias, confounding (including by other pollutants), effect modification, mortality displacement, loss to follow-up, etc. 10. Study appropriately assesses any potential lag between exposure and outcomes. 11. Study appropriately assesses any potential exposure thresholds for health outcomes. 12. Study clearly presents information about uncertainty in results to facilitate evaluation and comparison with other studies. 13. Prefer studies that assess changes in the risk of incidence of disease, rather than exacerbation of existing cases or changes in symptoms.

RESULTS

In this section, we present the results of our research, first presenting baseline information on endpoints and functions used previously and current weight of evidence determinations about causality by U.S. EPA, and then presenting the results of our supplemental literature review.

ENDPOINTS AND FUNCTIONS USED IN 2012 SOCIOECONOMIC REPORT

PM MORTALITY ENDPOINTS AND STUDIES

Adult Mortality

The prior Socioeconomic Report estimated the reductions in premature mortality expected to result from reductions in long-term (i.e., annual average) $PM_{2.5}$ concentrations.[2] SCAQMD evaluated a number of mortality concentration-response functions, including several specific to the Los Angeles area, ultimately basing their estimates on the Los Angeles-specific estimates from the Krewski et al. 2009 ACS reanalysis.

- **Krewski et al. (2009)** conducted an extended analysis of the American Cancer Society cohort (followed for 18 years, 1982-2000). This study produced national mortality estimates as well as specific estimates for the Los Angeles metropolitan area, covering Los Angeles, San Bernardino, Ventura, Riverside, and Orange counties. Authors estimated exposure concentrations in three ways: a random effects model, a land-use regression (LUR) model, and kriging. The two latter techniques allowed authors to interpolate missing exposure values based on monitored data. The exposure models incorporated data from 23 $PM_{2.5}$ monitors and 42 O_3 monitors in the Los Angeles metropolitan area. Forty-four covariates were assessed, including information on smoking and neighborhood factors such as income, race, education, and unemployment. The 2012 Socioeconomic Report used the relative risk of 1.17 (95% CI: 1.05, 1.30) for all-cause mortality per each 10 $\mu g/m^3$ change in $PM_{2.5}$ based on exposures estimated using the kriging model for the Los Angeles area and the RR of 1.14 (95% CI: 1.03, 1.27), employing exposures estimated using the land use regression (LUR) model. This paper also

[2] While evidence linking short-term (i.e., daily) $PM_{2.5}$ exposures with premature mortality is also strong, estimating both impacts in the same analysis would likely lead to double-counting of the mortality, as the short-term effects are at least partially captured in the long-term mortality signal observed in the literature.

calculated the concentration-response function for ischemic heart disease (IHD), cardiopulmonary disease (CPD), lung cancer, digestive cancer, other cancers, endocrine disorders, diabetes, digestive disorders, male accidents, female accidents, and all other causes.

- **Jerrett et al. (2005)** analyzed the same dataset, focusing only on the ACS cohort in Los Angeles, California. This cohort study included nearly 23,000 subjects in the Los Angeles metropolitan area from 1982-2000 (with nearly 6,000 deaths) and used the same 44 individual confounders as in Krewski et al. (2009). The primary difference between Krewski et al. was the specifics of the exposure modeling. Authors developed a combined kriging and multiquadric model, based on 2000 data from 23 state and local $PM_{2.5}$ monitoring stations. This model provided concentration data for each 25m grid cell, and authors assessed $PM_{2.5}$ exposure at the ZIP code level. Authors also developed a similar O_3 model based on 42 monitoring stations and assessed distance to freeways. This study estimated the same relative risk (1.17) per 10 $\mu g/m^3$ change in $PM_{2.5}$ as found using the kriging model in Krewski et al. This study also considered the same 44 covariates as in Krewski et al. (2009). The same mortality endpoints as in Krewski et al. were analyzed.
- **Laden et al. (2006)** conducted an extended follow-up to the Harvard Six Cities cohort study. $PM_{2.5}$ exposure was assessed from 1979-1988. For each 10 $\mu g/m^3$ increase in $PM_{2.5}$, the study found rate ratios for:
    - Overall mean exposure: 1.16; 95% confidence interval [CI], 1.07–1.26
    - Exposure in the year of death: 1.14; 95% CI, 1.06–1.22
    - Lung cancer mortality: 1.27; 95% CI, 0.96–1.69
    - Cardiovascular mortality: 1.28; 95% CI, 1.13–1.44.

PM MORBIDITY ENDPOINTS AND STUDIES

The previous Socioeconomic Report quantified the morbidity endpoints for PM exposure listed in Exhibit 2 (derived from Figure 3-4 in the 2012 Socioeconomic Report). We were able to confirm the function used by SCAQMD in 2012 for acute myocardial infarction. For the remainder of the categories, the U.S. EPA default sources for the health impact functions for these endpoints are listed in Exhibit 2; because BenMAP was used to conduct the prior analysis, we assume that at least one of the listed studies was used in the previous Socioeconomic Report for each endpoint or that results from all the default studies were pooled to derive estimates in each category.

EXHIBIT 2. HEALTH ENDPOINTS FROM 2012 SOCIOECONOMIC REPORT

ENDPOINT GROUP	ENDPOINT	AUTHOR	LOCATION
Acute Bronchitis		Dockery et al., 1996	
Asthma Exacerbation	Cough, shortness of breath, wheeze	Ostro et al, 2001	Los Angeles, CA
	Cough, Shortness of breath	Mar et al., 2004	Spokane, WA
Acute Myocardial Infarction	Acute Myocardial Infarction, nonfatal	Peters et al., 2001	Boston, MA
		Pope et al., 2006	Greater Salt Lake City, UT
		Sullivan et al., 2005	King County, WA
		Zanobetti and Schwartz, 2006	Greater Boston Area
		Zanobetti et al., 2009	
Hospital Admissions, Cardiovascular	All CVD (except MI)	Moolgavkar 2000 and 2003 are from LA	Los Angeles, CA
		Bell et al., 2008	202 U.S. Counties
		Peng et al., 2008	108 U.S. Counties
		Peng et al., 200	119 U.S. Communities
		Zanobetti et al., 2009	26 U.S. Communities
Hospital Admissions, Respiratory	All Respiratory	Zanobetti et al., 2009	26 U.S. Communities
ER Visits, Respiratory	Asthma	Mar et al., 2010	Tacoma, WA
		Norris, 1999	Seattle, WA
		Slaughter et al., 2005	Spokane, WA
Lower Respiratory Symptoms		Schwartz and Neas, 2000	6 U.S. Cities
Upper Respiratory Symptoms		Pope et al., 1991	Utah Valley
Minor Restricted Activity Days		Ostro and Rothschild, 1989	
Work Loss Days		Ostro, 1987	Nationwide

U.S. EPA CAUSALITY DETERMINATIONS FROM 2009 INTEGRATED SCIENCE ASSESSMENT FOR PM

U.S. EPA's Integrated Science Assessment (ISA) for PM, last published in 2009, discusses the weight of evidence of PM's role in causing the mortality and morbidity endpoints. U.S. EPA uses the definitions in Exhibit 3 for its causality determinations.

EXHIBIT 3. U.S. EPA PM ISA SUMMARY

Table 1-3. Weight of evidence for causal determination.

Determination	Health Effects	Ecological and Welfare Effects
CAUSAL RELATIONSHIP	Evidence is sufficient to conclude that there is a causal relationship with relevant pollutant exposures. That is, the pollutant has been shown to result in health effects in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. For example: a) controlled human exposure studies that demonstrate consistent effects; or b) observational studies that cannot be explained by plausible alternatives or are supported by other lines of evidence (e.g., animal studies or mode of action information). Evidence includes replicated and consistent high-quality studies by multiple investigators.	Evidence is sufficient to conclude that there is a causal relationship with relevant pollutant exposures. That is, the pollutant has been shown to result in effects in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. Controlled exposure studies (laboratory or small- to medium-scale field studies) provide the strongest evidence for causality, but the scope of inference may be limited. Generally, determination is based on multiple studies conducted by multiple research groups, and evidence that is considered sufficient to infer a causal relationship is usually obtained from the joint consideration of many lines of evidence that reinforce each other.
LIKELY TO BE A CAUSAL RELATIONSHIP	Evidence is sufficient to conclude that a causal relationship is likely to exist with relevant pollutant exposures, but important uncertainties remain. That is, the pollutant has been shown to result in health effects in studies in which chance and bias can be ruled out with reasonable confidence but potential issues remain. For example: a) observational studies show an association, but copollutant exposures are difficult to address and/or other lines of evidence (controlled human exposure, animal, or mode of action information) are limited or inconsistent; or b) animal toxicological evidence from multiple studies from different laboratories that demonstrate effects, but limited or no human data are available. Evidence generally includes replicated and high-quality studies by multiple investigators.	Evidence is sufficient to conclude that there is a likely causal association with relevant pollutant exposures. That is, an association has been observed between the pollutant and the outcome in studies in which chance, bias and confounding are minimized, but uncertainties remain. For example, field studies show a relationship, but suspected interacting factors cannot be controlled, and other lines of evidence are limited or inconsistent. Generally, determination is based on multiple studies in multiple research groups.
SUGGESTIVE OF A CAUSAL RELATIONSHIP	Evidence is suggestive of a causal relationship with relevant pollutant exposures, but is limited because chance, bias and confounding cannot be ruled out. For example, at least one high-quality epidemiologic study shows an association with a given health outcome but the results of other studies are inconsistent.	Evidence is suggestive of a causal relationship with relevant pollutant exposures, but chance, bias and confounding cannot be ruled out. For example, at least one high-quality study shows an effect, but the results of other studies are inconsistent.
INADEQUATE TO INFER A CAUSAL RELATIONSHIP	Evidence is inadequate to determine that a causal relationship exists with relevant pollutant exposures. The available studies are of insufficient quantity, quality, consistency or statistical power to permit a conclusion regarding the presence or absence of an effect.	The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of an effect.
NOT LIKELY TO BE A CAUSAL RELATIONSHIP	Evidence is suggestive of no causal relationship with relevant pollutant exposures. Several adequate studies, covering the full range of levels of exposure that human beings are known to encounter and considering susceptible populations, are mutually consistent in not showing an effect at any level of exposure.	Several adequate studies, examining relationships with relevant exposures, are consistent in failing to show an effect at any level of exposure.

EXHIBIT 4. U.S. EPA'S DEFINITIONS FOR CAUSAL DETERMINATIONS FOR PM-RELATED HEALTH ENDPOINTS

Table 2-6. Summary of PM causal determinations by exposure duration and health outcome.

Size Fraction	Exposure	Outcome	Causality Determination
$PM_{2.5}$	Short-term	Cardiovascular Effects	Causal
		Respiratory Effects	Likely to be causal
		Central Nervous System	Inadequate
		Mortality	Causal
	Long-term	Cardiovascular Effects	Causal
		Respiratory Effects	Likely to be Causal
		Mortality	Causal
		Reproductive and Developmental	Suggestive
		Cancer, Mutagenicity, Genotoxicity	Suggestive
$PM_{10-2.5}$	Short-term	Cardiovascular Effects	Suggestive
		Respiratory Effects	Suggestive
		Central Nervous System	Inadequate
		Mortality	Suggestive
	Long-term	Cardiovascular Effects	Inadequate
		Respiratory Effects	Inadequate
		Mortality	Inadequate
		Reproductive and Developmental	Inadequate
		Cancer, Mutagenicity, Genotoxicity	Inadequate

Exhibit 4 reproduces the table from the U.S. EPA 2009 PM ISA that summarizes U.S. EPA's findings of causality for each PM health endpoint evaluated. It shows that both short- and long-term PM exposure causes effects to the cardiovascular system, increases mortality, and likely affects the respiratory system. It may also impact pregnancy and development, and may be linked to cancer risk. We will recommend health endpoints to include in the 2016 socioeconomic assessment based on consideration of U.S. EPA's assessment of causality in its most recent ISA documents combined with the additional evidence we identified in our literature review.

PM LITERATURE REVIEW FINDINGS

We discuss, in the following two sections, the results of our supplemental literature review for health effects of $PM_{2.5}$ published since 2012. We first discuss studies linking $PM_{2.5}$ and mortality, and then the studies linking $PM_{2.5}$ with various morbidity endpoints. A summary table listing details on all studies found in our review can be found in Appendix A.

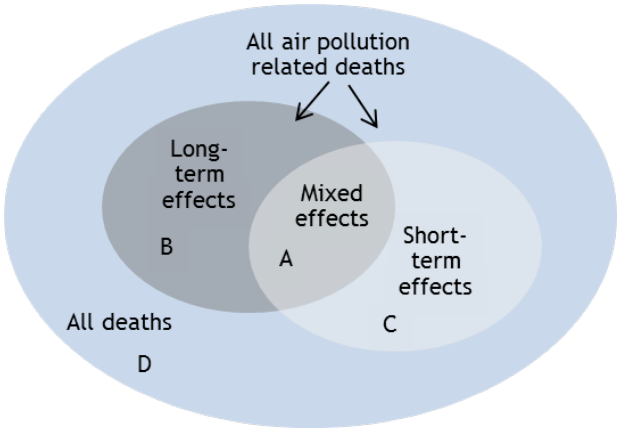
LITERATURE REVIEW FINDINGS: $PM_{2.5}$ AND MORTALITY

We found 27 studies published since 2012 that assessed the relationship between mortality and $PM_{2.5}$ exposure, and that were conducted in the U.S. or Canada. Eleven of the 27 studies focused on changes in daily mortality associated with short-term exposures to PM; 14 focused on mortality impacts of long-term PM exposures, and two (Kloog et al, 2013 and Shi et al. 2015) addressed both. Collectively, these studies support the existing weight of evidence determination by U.S. EPA regarding a causal association between $PM_{2.5}$ exposure and mortality due to both short- and long-term exposure.

We discuss findings of the review of both long-term and short-term studies below; however, we recommend that SCAQMD continue to base its primary estimate of PM-related mortality impacts on the long-term studies. We recommend focusing on one category of mortality impacts because summing the estimated benefits for both short- and long-term endpoints is likely to double count avoided mortality benefits. As shown in Exhibit 5 from Kunzli et al., 2001, long-term studies would be expected to capture both PM-related mortality resulting from development of PM-related chronic disease and frailty, as well as at least some of the mortality increases due to short term PM fluctuations. Thus, selection of the long-term exposure studies should provide a better, though still incomplete, estimate of the overall mortality impact.

We think it would be reasonable for SCAQMD to conduct a supplemental analysis of avoided PM-related mortality using a short-term function that would be presented separately from the primary mortality estimate. This calculation would provide the reader of the 2016 Socioeconomic Analysis a sense of the potential magnitude of additional avoided mortality benefits due to reduced short-term $PM_{2.5}$ fluctuations, reductions that may not be captured in the long-term estimate.

EXHIBIT 5. DIAGRAM ILLUSTRATING DEATHS CAPTURED BY LONG-TERM AND SHORT-TERM EPIDEMIOLOGICAL STUDIES



CATEGORY OF CASES	IMPACT OF AIR POLLUTION	
	UNDERLYING FRAILTY DUE TO AIR POLLUTION	OCCURRENCE OF DEATH (EVENT) TRIGGERED BY AIR POLLUTION
A	Yes	Yes
B	Yes	No
C	No	Yes
D	No	No

Graphic illustration of deaths due to ambient air pollution in a population, including cases related to both long-term and short-term air pollution. Exposure may affect the occurrence (event) of death ("short-term effects") and/or increase the underlying frailty in the population ("long-term effects"), leading to a shortening of lifetime. Circle sizes do not reflect relative effects. (Adapted from Kunzli et al., 2001).

Long-term Studies

We proceeded to narrow down the 16 studies that addressed long-term PM mortality, based on the types of results they presented. Three were excluded from further consideration because they focused exclusively on specific causes of death: Brook et al, 2013 (diabetes mortality); Gan et al, 2013 (COPD-related mortality); and Kravchenko et al, 2014 (respiratory mortality). Two other studies were excluded because they were designed primarily to study effect modification of the PM-mortality association: Kiomourtzouglou et al, 2015 (effect modification by particle composition); Pope et al, 2015 (modification by cardiometabolic disorders).

The geographic scope of the remaining 11 studies shown in Exhibit 6 ranged from effects estimated in single cities to national-level estimates in the US and Canada. From this list, we prioritized studies conducted in the U.S. that reported either Los Angeles-specific estimates, California-specific estimates, or national-level estimates of mortality impacts based on multi-city studies that included cities from the Western U.S., considering data from over one hundred cities across the United States. Seven studies reported results from national-level analyses; most of these studies looked at dozens of U.S. cities. Four studies focused on effects of $PM_{2.5}$ exposures on populations within California and/or within LA specifically and are summarized below.

In a study funded by the California Air Resources Board, **Garcia et al. (2015)** looked at the relationship between mortality and long-term $PM_{2.5}$ exposures in both rural and urban locations in California. This cross-sectional study focused on all Californian adults who died in 2006, and who were at least 65 years of age. Mortality endpoints included cardiovascular disease, ischemic heart disease, cardiopulmonary disease, and all-cause (non-accident). Monthly averages of ambient $PM_{2.5}$ were calculated from 116 stations in California's National, State, and Local Air Monitoring Network and in Interagency Monitoring of Protected Visual Environments network from 2000-2006. ZIP code –level averages were calculated via three exposure models (closest monitor, inverse distance weighting, and kriging). The average $PM_{2.5}$ concentrations were just over 10 $\mu g/m^3$ in rural areas and just over 15 $\mu g/m^3$ in urban areas. The study showed that the relative risk of mortality was greater in rural areas, but that a relationship between long-term PM exposure and mortality exists in both rural and urban areas. However, authors state that other confounding factors may account for this discrepancy, including arrival times for emergency responders, health behaviors, and health knowledge. This study did not control for smoking behaviors. We do not recommend its use in the Socioeconomic Report because the study only evaluates outcomes for one year, only includes an elderly population, and does not control for possible confounding by tobacco use.

Jerrett et al. (2013) is a further extended follow-up of the American Cancer Society prospective cohort study, which is the same cohort used in Krewski et al. (2009) and Jerrett et al. (2005). As with the 2005 paper, this study focused solely on those participants who resided in California. However, while the 2009 analysis assigns exposure at the ZIP code level, the 2013 analysis assigns exposure based on home residence using land-use regression models considering 112 stations measuring $PM_{2.5}$ from 1998 to 2002, 138 stations measuring NO_2, and 262 stations measuring O_3. This approach provides finer-scale exposure modeling than the previous paper. The mean $PM_{2.5}$ exposure reported was 14.09 $\mu g/m^3$, and the maximum was 25.09 $\mu g/m^3$. Because mortality is higher outside of metropolitan areas (but air pollution generally lower), Jerrett controlled for this potentially confounding factor, in addition to a similar suite of factors previously controlled for in 2005. The authors analyzed exposures to $PM_{2.5}$, NO_2, and O_3 for several causes of death, including CVD, IHD, stroke, respiratory disease, lung cancer, as well as all-cause mortality. $PM_{2.5}$ exposure was positively associated with all-cause mortality, and with CVD, and IHD-related deaths. The authors report an all-cause relative risk estimate for the state of California of 1.060 (1.003 – 1.120), which is similar to the national level ACS estimate of 1.065 (1.035 – 1.096), and they report an updated LA specific estimate for 1.104 (0.968 – 1.260). This point estimate, while lower than that of Krewski et al., 2009 and Jerrett et al, 2005, continues to indicate higher impacts in the LA area than in California overall, or in the nation as a whole.

Thurston et al. (2015) analyzed data from over half a million individuals from six U.S. states plus Atlanta and Detroit, including about 160,000 in California who were part of the National Institutes of Health/AARP Diet and Health cohort. Subjects were 50-71 years old. The study collects information on numerous covariates, including diet, exercise, smoking, education, and race. Contextual socioeconomic variables are also available at the census tract level from the NIH-AARP study (NIH-AARP, 2006).

Exposure data was estimated using a land-use regression model based on U.S. EPA's Air Quality System for each census tract. Authors calculated hazard ratios for all-cause, respiratory, and CVD mortality for the U.S. and for California. Average mean $PM_{2.5}$ levels were 12.2 $\mu g/m^3$ nationally and 10.4 $\mu g/m^3$ in California. Results are similar to Jerrett et al. 2013 and Krewski et al, 2009 overall, though slightly lower than Jerrett et al. 2013 for California. For the U.S., results are reported by smoking status, age, gender, and educational attainment. Results appear robust to alternative model specifications allowing for time varying exposure estimates. The list below contains the California-specific results.

- CVD: 1.10; 95% CI, 1.05, 1.16 for each 10 $\mu g/m^3$ increase in $PM_{2.5}$.
- All-cause: 1.02; 95% CI (0.99, 1.04)
- Respiratory: 1.01; 95% CI (0.93, 1.10)

Ostro et al. (2015) analyzed constituents of $PM_{2.5}$ on health outcomes from the California Teachers Study (CTS), a prospective cohort of over 130,000 active and retired female teachers. This study assessed the effects of $PM_{2.5}$ exposures to CTS participants ages 30 and over between 2001-2006. It controlled for smoking, second-hand smoke exposure, alcohol use, physical activity, fiber and calorie intake, menopausal status and use of hormones, family health history, and aspirin use. This paper used modeled exposure data from the University of California Davis/California Institute of Technology Source Oriented Chemical Transport model. The authors fitted Cox proportional hazards models; as a sensitivity analysis, they reran them to include variables to control for potential residential confounding, including Census data on poverty, educational attainment, income, percent unemployed, and racial make-up of neighborhood. These variables are all group-level indicators of socioeconomic and environmental factors that could also be associated with individual-level health outcomes. Authors ran a series of two pollutant models for IHD. Their findings indicate that several constituents of $PM_{2.5}$ and ultrafine PM are significantly associated with cardiovascular (CVD), ischemic heart disease (IHD), and all-cause mortalities. High sulfur and nitrate content of $PM_{2.5}$ was associated with CVD and IHD mortality and sulfur was additionally associated with all-cause mortality. IHD mortality was also associated with $PM_{2.5}$ mass, copper, elemental carbon, secondary organic aerosols, gas- and diesel-fueled vehicles, meat cooking, and high-sulfur fuel combustion. Because results are given only for constituents of PM, and not for overall PM, and because of the fact that cohort was limited to a specific subgroup, female teachers, we do not recommend using this study to the develop concentration response function for the 2016 Socioeconomic Report.

EXHIBIT 6. SUMMARY OF LONG-TERM $PM_{2.5}$-ASSOCIATED MORTALITY STUDIES.

CITATION	TITLE	JOURNAL	POLLUTANT(S)	MORTALITY CAUSE	GEOGRAPHIC SCOPE	POPULATION
Crouse et al., 2012	Risk of Nonaccidental and Cardiovascular Mortality in Relation to Long-term Exposure to Low Concentrations of Fine Particulate Matter: A Canadian National-Level Cohort Study	Environmental Health Perspectives	$PM_{2.5}$	All-cause/non-accidental; CVD; IHD	Canada	National sample of 2.1 million Canadian adults ≥25 years
Garcia et al., 2015	Association of Long-Term $PM_{2.5}$ Exposure with Mortality Using Different Air Pollution Exposure Models: Impacts in Rural and Urban California	International Journal of Environmental Health Research	$PM_{2.5}$	All-cause/non-accidental; CVD; CPD; IHD	Compares rural and urban locations in California	Individuals ≥ 65 years who died in 2006
Hart et al., 2015	The Association of Long-Term Exposure to $PM_{2.5}$ on All-Cause Mortality in the Nurses' Health Study and the Impact of Measurement-Error Correction	Environmental Health	$PM_{2.5}$	All-cause/non-accidental	United States	Participants in Nurses' Health Study, still alive in 2000
Jerrett et al., 2013	Spatial Analysis of Air Pollution and Mortality in California	Respiratory and Critical Care Medicine	$PM_{2.5}$, O_3, NO_2	All-cause; CVD; IHD; Stroke, Respiratory; Lung cancer;	Extended follow-up of American Cancer Society cohort in California/Los Angeles	California adults from American Cancer Society Cancer Prevention II Study
Kloog et al. 2013	Long- and Short-Term Exposure to $PM_{2.5}$ and Mortality: Using Novel Exposure Models	Epidemiology	$PM_{2.5}$	All-cause; CVD; Respiratory	State of Massachusetts	State of Massachusetts

CITATION	TITLE	JOURNAL	POLLUTANT(S)	MORTALITY CAUSE	GEOGRAPHIC SCOPE	POPULATION
LePeule et al., 2012	Chronic Exposure to Fine Particles and Mortality: An Extended Follow-up of the Harvard Six Cities Study From 1974 to 2009	Environmental Health Perspectives	$PM_{2.5}$	All-cause;CVD; Lung cancer;COPD	Six cities in eastern and Midwestern U.S. (Watertown, MA, Kingston and Harriman, TE, parts of St. Louis, MI, Steubenville, OH, Portage, Wyocena, and Pardeeville, WI, Topeka, KA)	Extended follow-up of U.S., Harvard Six Cities cohort
Ostro et al., 2015	Associations of Mortality with Long-Term Exposures to Fine and Ultrafine Particles, Species and Sources: Results from the California Teachers Study Cohort	Environmental Health Perspectives	PM, UF	All-cause; CVD; IHD; Respiratory	California	California Teachers Study Cohort; women >30 years
Shi et al, 2015	Low-Concentration $PM_{2.5}$ and Mortality: Estimating Acute and Chronic Effects in a Population-Based Study	Environmental Health Perspectives	$PM_{2.5}$	All-cause	New England	Medicare population aged ≥ 65 in New England
Thurston et al., 2015	Ambient Particulate Matter Air Pollution Exposure and Mortality in the NIH-AARP Diet and Health Cohort	Environmental Health Perspectives	$PM_{2.5}$	All-cause; CVD; Respiratory	Six states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and two metropolitan areas (Detroit, MI and Atlanta, GA)	National Institutes of Health-AARP cohort; ages 50-71 years; includes California specific estimates

CITATION	TITLE	JOURNAL	POLLUTANT(S)	MORTALITY CAUSE	GEOGRAPHIC SCOPE	POPULATION
Villeneuve et al., 2015	Long-term Exposure to Fine Particulate Matter Air Pollution and Mortality Among Canadian Women	Epidemiology	$PM_{2.5}$	All-cause non-accidental; Coronary heart disease, cerebrovascular disease, CVD; nonmalignant respiratory disease; cancer; lung cancer	Canada	Participants in the Canadian National Breast Screening Study between 1980 and 1985
Weichenthal et al., 2014	Long-Term Exposure to Fine Particular Matter: Association with Nonaccidental and Cardiovascular Mortality in the Agricultural Health Study Cohort	Environmental Health Perspectives	$PM_{2.5}$	All-cause/non-accidental; CVD; IHD; Cerebrovascular disease; Lung cancer	Iowa and North Carolina	Agricultural Health Study Cohort; rural populations

CVD=cardiovascular disease, CPD=cardiopulmonary disease, COPD= chronic obstructive pulmonary disease, IHD=ischemic heart disease

Short-term Studies

We reviewed the 13 studies that addressed short-term PM mortality to assess their applicability for the SCAQMD analysis. Three were excluded from further consideration because they focused exclusively on non-U.S. locations (Farhat et al., 2013; Goldberg et al., 2013; and Vanos et al., 2015). One (Hao et al., 2015) was excluded because it focused on a specific cause of death (chronic lower respiratory disease mortality). Three (Dai et al., 2014; Krall et al., 2013; and Zanobetti et al., 2014) were excluded because they were designed primarily to study relative toxicity of PM particles and effect modification by particle composition, and another (Cox et al., 2013) because it focused on joint impacts of PM and temperature. Moolgavkar et al., 2013 only studied PM_{10}, not $PM_{2.5}$ and thus was excluded, as were studies by Kloog et al., 2013; Sacks et al., 2012; and Shi et al., 2015, which were conducted exclusively on east coast populations. Additional details about the excluded studies can be found in Appendix A.

The remaining study of the mortality impacts of short-term exposures to $PM_{2.5}$ on daily mortality is a systematic review and meta-analysis of 68 peer-reviewed time-series studies by Atkinson et al. (2014). The studies, which were published through May 2011, include results from three California counties, but also include results from outside the United States. The authors provide region-specific meta-analysis estimates for World Health Organization regions, including American Region A (the U.S., Canada, and Cuba). Within each region, the authors conducted a two-stage meta-analysis using random-effects models, first pooling estimates from single-city studies, and then pooling this result with available multi-city results for that region. Studies were chosen for the meta-analysis based on a detailed evaluation of eligibility criteria related to study design, control for common confounders (e.g., temporal trends, weather), statistical methods, and the quantitative presentation of results. Worldwide, the authors found a 1.04% (0.52%, 1.56%) increase in the risk of death associated with a 10 $\mu g/m^3$ increase in daily $PM_{2.5}$. For the same incremental increase in American Region A, the authors found an increase in daily mortality rates of 0.94% (0.73%, 1.16%), based on a meta-analysis of five single-city and 2 multi-city studies selected from a review of 13 single-city and 12 multi-city studies conducted in the U.S. and Canada. Of the five selected single-city studies, two were conducted in California, and several California cities, including Los Angeles contributed data to one of the two multi-city studies included (Zanobetti et al., 2009).

LITERATURE REVIEW FINDINGS - $PM_{2.5}$ MORBIDITY

In this section, we discuss the findings of our literature review for both the health endpoints previously evaluated in the 2012 Socioeconomic Report, as well as for potential new health endpoints to quantify in the 2016 analysis.

We identified 85 relevant studies on PM and morbidity outcomes conducted in the United States or Canada since 2012. The geographic scope of these studies ranged from single-city to county-wide analyses. Thirteen studies were conducted within the state of

California, with eight of those studies specifically focusing on areas in southern California. Twenty-three studies included data either from multiple states and cities across the United States or focused on areas in the western part of the country. Details on all morbidity studies identified can be found in Appendix A.

Existing Health Endpoints

In general, we found the literature we reviewed to be consistent with existing U.S. EPA opinions concerning causality published in the 2009 ISA. As a result, we continue to recommend quantification of the health endpoints evaluated for PM in the 2012 analysis, though not necessarily using the same studies.

The previous Socioeconomic Report included the morbidity endpoints for PM exposure listed in Exhibit 2. We discuss below the endpoints where we identified additional studies conducted since 2012 in California, western U.S., or nationwide.

Acute Nonfatal Myocardial Infarction (MI)

Our literature review found one study of PM-related acute MIs published since 2012 within our geographic area of interest.

Ensor et al. (2013) conducted a case-crossover analysis of air pollution and out-of-hospital cardiac arrests based on EMS data from 2004 and 2011 in Houston, Texas and found that an increase of 6 µg/m^3 of $PM_{2.5}$ two days prior was associated with a relative risk of cardiac arrest of 1.046 (1.012 – 1.082). Limitations of this study include the use of citywide-averaged PM data, as well as a lack of control for pre-existing conditions and risk factors. In addition, this study did not ascertain whether the cardiac arrest was fatal; therefore the outcome measure may be capturing some of the mortality impacts addressed elsewhere.

Asthma Exacerbation

Our literature review found two studies of PM-related asthma exacerbation published since 2012:

Loftus et al. (2015) studied associations between $PM_{2.5}$ and asthma exacerbations among children in a rural agricultural community in Washington State. The authors found that an interquartile increase in weekly $PM_{2.5}$ of 6.7 µg/m^3 was associated with an increase in reported asthma symptoms, in particular wheezing, limitation of activities, and nighttime waking.

Nachman and Parker (2012) assessed the effect of a 10 µg/m3 increase in annual average $PM_{2.5}$ on asthma prevalence and asthma exacerbation (asthma attack). The population was the 110,000 adult (≥18 years) respondents to the National Health Interview Survey (NHIS); 4,000 of these participants reported an asthma attack in the previous year. Kriged $PM_{2.5}$ concentrations at the Census block group level, based on data from U.S. EPA's AirData System, were used to measure exposure. This study controlled for age, sex, body mass index, smoking, race-ethnicity, education, and urban status. The overall OR did not indicate an association between annual average $PM_{2.5}$

exposure and recent asthma attacks (OR of 0.90 (95% CI: 0.78, 1.03) per 10 µg/m^3 increase). However, when the authors stratified results by race-ethnicity (Hispanic, non-Hispanic white, non-Hispanic black), a strong positive association was seen for non-Hispanic blacks (OR of 1.76, (95% CI:1.07, 2.91)).

Young et al. (2014) investigated the association between $PM_{2.5}$ exposure and the incidence of new asthma, wheeze, or chronic cough in adult women (≥ 35 years) without symptoms or asthma diagnoses at the start of the study. Study participants were from the nationwide, 50,884 subject Sister Study, a cohort of women with one sister diagnosed with breast cancer, but who do not have the disease themselves. $PM_{2.5}$ exposure estimates were based on a national kriging and land-use regression model for the year 2006. Authors controlled for age, body mass index, race, education, occupational exposures, smoking, health insurance, and fiber consumption. For each interquartile range of $PM_{2.5}$ (3.6 µg/m3), the odds of developing asthma were 1.20 (95% CI: 0.99, 1.46). For developing wheeze, the OR was 1.14 (95% CI: 1.04, 1.26).

Cardiovascular Hospital Admissions

Our literature review found two studies of PM-related cardiovascular hospital admissions published since 2012:

Bell et al. (2015). Studied cardiovascular and respiratory hospital admissions in among Medicare beneficiaries 65 years and older across 213 U.S. cities to evaluate whether the effect of short-term $PM_{2.5}$ exposures on hospital admissions in the U.S. varied by gender. Cause-specific respiratory and cardiovascular hospital admissions for 12.6 million individuals were evaluated using Bayesian hierarchical modeling for associations with daily county-level $PM_{2.5}$ from U.S. EPA AQS monitors. PM data came from monitoring sources and was adjusted for weather, day of the week, and temporal trends. This study controlled for gender, location, and season. The study was designed primarily to assess differences in risk by gender, but did report some total risk estimates. While hospital admissions overall increased by 0.25 percent (respiratory) and 0.65 percent (cardiovascular) per 10 µg/m^3 increase in $PM_{2.5}$ (same day exposure, lag 0), results stratified by region showed non-significant results in the West (33 counties).

Talbott et al. (2014) conducted a time-stratified case-crossover analysis with logistic regression to evaluate the association of daily $PM_{2.5}$ levels on cardiovascular disease hospital admissions (ICD-9 350-359). Outcome information for 2001-2008 was obtained from the CDC Environmental Public Health Tracking (EPHT) network for seven states (Florida, Massachusetts, New Hampshire, New Jersey, New Mexico, New York, and Washington) and regressed against modeled daily $PM_{2.5}$ estimated at zip code centroids and linked to the zip code of patient residence. Overall results from this study are likely weighted too heavily towards eastern U.S. locations to be appropriate for use in Los Angeles. While this study does report results for Washington State; we do not believe that these results should replace or supplement local Los Angeles data in the current studies (Moolgavkar, 2000, 2003) informing BenMAP-CE concentration-response functions for cardiovascular hospital admissions.

Chronic Bronchitis

Our literature search found one study (Nachman and Parker, 2012) that analyzed the relation of PM with this endpoint based on self-reported prevalence in the National Health Interview Study; the authors found no association of PM with chronic bronchitis.

Respiratory Emergency Room Visits

Our literature search found one study (Rodopoulou et al., 2014) that analyzed the relation of PM with this endpoint during severe air pollution events involving windblown dust and wildfires in New Mexico. This study does not appear to be relevant for the Socioeconomic Analysis of benefits because of its focus on extreme air events.

Respiratory Hospital Admissions

Our literature review found two studies of PM-related respiratory hospital admissions.

Delfino et al. (2014) assessed asthma-related hospital encounters (hospital admissions and emergency department visits) in a case-crossover study of over 11,000 children ages 0-18 years in Orange County, CA. This study measured $PM_{2.5}$, UFP, NO_2, and CO exposures. Mean $PM_{2.5}$ concentrations were 14.5 $\mu g/m^3$; however, one limitation of this study is that all $PM_{2.5}$ measurements came from a single monitor. Authors calculated effects from zero to seven day lags in exposure, and accounted for subjects that had more than one hospital encounter in a seven day stretch. Weather, age, sex, race, and insurance status were assessed. Both the warm and cool seasons showed positive associations with $PM_{2.5}$ exposures. We selected a lag of three days for the assessment of the effects of $PM_{2.5}$ exposure in this study. For a three day lag in the warm season, the interquartile range of $PM_{2.5}$ (15.4$\mu g/m^3$) lead to an 8.00% increase in asthma-related hospital encounters (95% CI 1.2%, 15.22%). In the cool season, the point estimate is 3.48% (95% CI -0.77%, 7.92).

Delamater et al. (2012) is an ecological study of asthma hospitalizations in Los Angeles County. Authors developed a kriging model based on monitor data in Los Angeles, CA to estimate exposures within 3 km x 3 km grid cells. They used data from OSHPD and interpolated annual state population data to calculate the average daily hospitalization rate by month. The study found that a one percent change in monthly average $PM_{2.5}$ was associated with a 0.11% (95% critical interval=0.01, 0.21) increase in hospitalizations.

LITERATURE REVIEW RESULTS: NEW ENDPOINTS

We identified studies addressing a wide array of health endpoints not previously evaluated by SCAQMD, including the following:

- Pregnancy outcomes
  - Birth weight
    - Low birth weight (generally <2500 g)
    - Very low birth weight (<1500 g)
    - Small for gestational age
    - Mean birth weight at term birth
  - Pre-term birth
  - Stillbirth
  - Birth defects
  - Gestational diabetes mellitus
  - Hypertensive disorders of pregnancy
- Asthma incidence
  - One each on asthma onset in children and in adult women
- Stroke and cerebrovascular disorders
- autism
- Other health outcomes including
  - appendicitis
  - anxiety and depression
  - breast cancer survival
  - diabetes
  - endometriosis
  - ED visits for non-specific abdominal pain
  - leukemia in adults
  - Parkinson's disease (one of these studies also reports time to first admission for dementia and Alzheimer's disease)
  - rheumatoid arthritis
  - uterine fibroids

Most of the endpoints in the "Other" category above consisted of only a single study; for endpoints where we found multiple studies (Parkinson's, rheumatoid arthritis, etc.) results either found no association or were mixed. Within the Pregnancy Outcomes, the most consistently studied outcome was Low Birth Weight, including several studies in the LA area. We focus below on that pregnancy endpoint, as well as stroke, asthma incidence, and autism.

Low Birth Weight

This review found five California-based studies, one nationwide-wide study, and one meta-analysis on PM2.5 exposure and low birth weight (LBW). These studies generally define LBW as <2,500g and full-term pregnancies as >37 weeks. These studies typically controlled for season of birth, gestational age, mother's age, race, and socioeconomic factors such as educational attainment and/or income. Overall, these studies provide evidence that exposure to $PM_{2.5}$ during pregnancy, especially higher exposures over an entire pregnancy, can increase the risk of low birth weight in the offspring. We include two pre-2012 studies, as they assess populations in Los Angeles and California. Below we summarize these seven studies.

- **Basu et al.** (2014) assessed ZIP code-level $PM_{2.5}$ exposure for nearly 650,000 term births in California. Results were adjusted for a number of socioeconomic status factors, gestational age, mother's age, sex, and month of birth. Birth weight decreased by 7g (95% CI 4, 9) per 7.6 $\mu g/m^3$ increase in $PM_{2.5}$ mass (interquartile range). This study breaks down results by PM constituent; however due to the difficulty in modeling those exposures, those results are not reported here.
- **Laurent et al.** (2014) studied over 960,000 births in Los Angeles County and assessed exposure to $PM_{2.5}$ via Bayesian kriging using $4km^2$ grid cells. Over the entire pregnancy, a 2.5% increase in the risk of LBW was associated with an interquartile range (5.82 $\mu g/m^3$ increase) in $PM_{2.5}$. This study controlled for many of the same factors as previously mentioned, although did not control for smoking.
- **Morello-Frosch et al**. (2010) found a decrease in birth weight of 12.8g (95% CI 11.3, 14.3) per 10 $\mu g/m^3$ $PM_{2.5}$ for full-term births (>37 weeks). This study looked at over 3.5 million births over 10 years in California. Air pollution was averaged by Census tract and ZIP code. Authors state a decrease of this magnitude is unlikely to adversely affect the health of an individual infant, but could have population-level impacts, due to the widespread exposure to air pollutants across California.[3]
- **Ritz et al.,** (2007) conducted a case-control study of about 58,000 births in Los Angeles County. About 2,500 mothers were interviewed to assess confounders. Air pollution exposure was based on ZIP code. For women exposed to average $PM_{2.5}$ over 21.36 $\mu g/m^3$, odds of a low birth weight baby increased 10% (95% CI 1.01, 1.20) (interviewed cohort) to 29% (95% CI 1.00, 1.67) (overall cohort). This study adjusted for mother's age, race, education, season, and for the interviewed cohort, smoking, alcohol use, and marital status.
- **Trasande et al. (2013)** assessed the impact of air pollutants on low birth weight across the U.S. This study used the Kids Inpatient Database (KID), which records

[3] For a discussion of the adverse impacts of shifts in population risk distributions, see American Thoracic Society. What constitutes an adverse health effect of air pollution? Official statement of the American Thoracic Society. Am J Respir Crit Care Med. 2000 Feb;161(2 Pt 1):665-73.

in-hospital births from up to 38 states (depending on year). Authors used pollutant concentrations from the U.S. EPA Aerometric Information Retrieval System (AIRS) coupled with random subsampling of over 2.6 million births in KID for 2000, 2003, and 2006. Authors controlled for gestational age, birth month, gender, race, socioeconomic variables. They were able to link one third of births in KID to AIRS data. Single pollutant models of $PM_{2.5}$ per ppm increase in the month of birth showed an association with odds of LBW (OR of 1.10 (95% CI of 1.06, 1.14)), very LBW (OR of 1.08 (95% CI of 1.05, 1.11)), pre-term LBW (OR of 1.09 (95% CI of 1.04, 1.14)), and LBW for term births (OR of 1.12 (95% CI of 1.08, 1.16)) per $\mu g/m^3$ mean $PM_{2.5}$. In the multi-pollutant models, the 62,906 births with birth weight as a continuous variable showed no significant association with air pollutants. However, for the 82,379 births with categorical data (i.e., <2,500g and <1,500g), the multi-pollutant models showed that each $\mu g/m^3$ of $PM_{2.5}$ led to a 9.3% and 7.2% increase in the odds of LBW and VLBW, respectively, per $\mu g/m^3$ mean $PM_{2.5}$.

- **Wilhelm et al.** (2012) studied nearly a quarter million births in Los Angeles County using data from the South Coast Air Quality Management District's Multiple Air Toxics Exposure Study (MATES III). Exposure was assessed using monitors within five miles of a woman's home address and also from a land-use regression model. Authors found a 5% increase in LBW for each 2.4 $\mu g/m^3$ $PM_{2.5}$ (from diesel and gasoline combustion-related $PM_{2.5}$) increase over the entire pregnancy. Point estimates for each trimester were similar. This study controlled for gestational age, mother's age, race, socioeconomic factors, and prenatal care, but not for smoking. Authors did not report an overall $PM_{2.5}$ estimate; the adjusted odds ratios by PM type are:
    - Elemental carbon $PM_{2.5}$: 1.05 (0.97, 1.14)
    - Diesel $PM_{2.5}$: 1.06 (0.99, 1.14)
    - Gasoline $PM_{2.5}$: 1.07 (0.97, 1.18)
    - Geological $PM_{2.5}$ (i.e., road dust): 1.05 (0.97, 1.14)
- In 2015, **Zhu et al.** conducted a meta-analysis of 25 epidemiological studies on the risk of low birth weight (LBW), pre-term birth (PTB), small for gestational age (SGA), and stillbirth from $PM_{2.5}$ exposure over the entire pregnancy. All outcomes except stillbirth were significantly associated with $PM_{2.5}$ exposure, with an average of 14.6g drop in expected birth weight. Results for each of the three trimesters showed no effect on PTB or stillbirth and no effect on weight for the first trimester. The odds ratios for average exposure across the entire pregnancy per 10 $\mu g/m^3$ increase in $PM_{2.5}$ were:
    - LBW: 1.05 (1.02,1.07)
    - PTB: 1.10 (1.03, 1.18)
    - SGA: 1.15 (1.10, 1.20)

Stroke

Our literature review found one study which assessed the risk of stroke in dozens of cities across the U.S. This meta-analysis by **Shin et al.** (2014) pooled 20 epidemiological studies which reported risk ratios (RR) for strokes following long and short-term $PM_{2.5}$ exposures. Authors used both frequentist and Bayesian methods to pool studies. Four studies (four RRs) involved long-term exposure and 16 studies (221 RRs) involved short-term exposures. Authors focused on single-pollutant models in each paper to more easily pool across a wider number of studies. The four long-term studies used cohorts involving Medicare recipients, the Women's Health Initiative (Miller et al., 2007), the California Teacher's Cohort (current and former female public school teachers), and patients at primary care centers in England. The pooled risk estimate from the long-term studies was 1.05 (95% CI= 1.00, 1.13). Of the 16 short-term studies, 15 focused on one city each and one (Dominici et al., 2006) reported 202 single-city RR across its U.S. multi-city assessment. Authors arrived at a pooled estimate of 1.05 (95% CI = 1.01, 1.09) for each 10 $\mu g/m^3$ increase in short-term $PM_{2.5}$ exposure. Results were similar regardless of the specific pooling method used.

Asthma incidence

We identified two studies addressing asthma incidence, one addressing onset in adults and the other addressing onset in children.

Young et al. (2014) studied onset of asthma in a cohort from The Sister Study, a U.S. cohort study of risk factors for breast cancer and other health outcomes (n = 50,884) in sisters of women with breast cancer enrolled between 2003 and 2009. The authors investigated the association between ambient air pollution exposures ($PM_{2.5}$ and nitrogen dioxide, NO_2) and the incidence of new-onset asthma in adult women ($\geq$ 35 years). Specific health endpoints examined included incident self-reported wheeze, chronic cough, and doctor-diagnosed asthma in women without baseline symptoms. Authors controlled for age, body mass index, race, education, occupational exposures, smoking, health insurance, and fiber consumption.

Annual average (2006) ambient $PM_{2.5}$ and NO_2 concentrations were estimated at participants' addresses, using a national land-use/kriging model incorporating roadway information. The medians (and interquartile ranges) for estimated exposures at participant locations were 10.8 $\mu g/m^3$ (3.6 $\mu g/m^3$) for $PM_{2.5}$ and 9.3 ppb (5.8 ppb) for NO_2.

The results of this large nationwide cohort study suggest that ambient $PM_{2.5}$ exposure or other related exposures may be involved in the development of respiratory symptoms, particularly wheeze, and incident asthma in women. Adjusted analyses included 254 incident cases of asthma, 1,023 of wheeze, and 1,559 of chronic cough. For an interquartile range (IQR) increase (3.6 $\mu g/m^3$) in estimated $PM_{2.5}$ exposure, the adjusted odds ratios (OR's) were:

- 1.20 (95% confidence interval [CI] = 0.99–1.46, P = 0.063) for incident asthma
- 1.14 (95% CI = 1.04–1.26, P = 0.008) for incident wheeze.

- For NO_2, there was evidence for an association with incident wheeze (OR = 1.08, 95% CI = 1.00–1.17, P = 0.048 per IQR of 5.8 ppb).
- Neither pollutant was significantly associated with incident cough.

Wendt et al., 2014 studied the impact of changes in ambient $PM_{2.5}$, ozone, and NO_2 on new-onset asthma in Medicaid-enrolled children in Harris County, Texas between 2005 and 2007 using a case-crossover design and conditional logistic regression. They found that new-onset asthma was more likely to occur following periods of higher exposures to all three pollutants in single-pollutant models; however, only the ORs for ozone and NO_2 remained significant in multi-pollutant models.

Autism

This literature review found three studies on $PM_{2.5}$ and autism in either California or nationwide. All three studies found positive associations with $PM_{2.5}$. Authors note that $PM_{2.5}$ exposures may initiate changes in immune system function leading to the development of autism, but that the mechanism is still largely unknown.

Becerra et al. (2013) assessed the impact of $PM_{2.5}$ exposure on the odds of developing autism among children living in Los Angeles. This study included 7,603 cases that were matched with 10 controls per case by sex, birth year, and gestational age. Exposure was measured via both the nearest monitoring station and by a land-use regression model. Results were adjusted by maternal age, education, race, maternal place of birth, type of birth, parity, insurance, and gestational age. For each interquartile range increase (4.68 $\mu g/m^3$) in $PM_{2.5}$, authors found a 7% increase in autism in a single pollutant model (95% CI of 1.00, 1.15); this estimate increased to 15% in a two pollutant model with O_3 (95% CI of 1.06, 1.24).

Raz et al. (2015) is a nested case-control study of births of participants in the Nurses' Health Study II. The study assessed air pollution exposure for 245 children with and 1,522 children without autism across the U.S. $PM_{2.5}$ concentrations were based on previously developed spatiotemporal models based on U.S. EPA's Air Quality System (AQS). For each interquartile range increase in monthly average $PM_{2.5}$ (4.42 $\mu g/m^3$) during pregnancy, the odds ratio of having a baby diagnosed with autism during follow-up after recruitment in 1995 (mean date of diagnosis was 1999 +-3.3) was 1.57 (95% CI: 1.22, 2.03), but $PM_{2.5}$ exposures nine months prior to or after pregnancy were either weakly associated or null.

Volk et al. (2013) conducted a case-control study on children enrolled in the Childhood Autism Risks from Genetics and the Environment (CHARGE) study in California. The study included 279 autistic children and 245 without autism. $PM_{2.5}$ exposures were assessed from interpolating all monitor data within 50 km of residence, with data from U.S. AQS and University of Southern California Children's Health Study. For every 8.7 $\mu g/m^3$ increase in $PM_{2.5}$, the odds of having autism increased. For gestational exposures, the OR was 2.08 (95% CI: 1.93, 2.25), and for exposures during the first year of life the

OR was 2.12 (95% CI: 1.45, 3.12) after adjusting for sex, ethnicity, parental education, maternal age, and prenatal smoking.

RECOMMENDATIONS

Exhibit 7 summarizes our recommended PM-related health endpoints for the 2016 Socioeconomic Analysis. In summary, we propose evaluation of the same endpoints evaluated in 2012, plus avoided incidence of hospital admissions for stroke in adults 65 and older. We also are expanding certain endpoint categories to include additional age groups or subpopulations from the studies we identified. Gray-highlighted rows indicate changes in recommended studies from the 2012 Socioeconomic Report.

Note that all C-R functions and related parameters were developed in accordance with the EPA's BenMAP-CE User's Manual Appendix C (U.S. EPA, 2015). Specific functional forms and input parameters were delivered to the SCAQMD and are consistent with the recommendations of studies and risk models specified in this report.

EXHIBIT 7. RECOMMENDED $PM_{2.5}$-RELATED HEALTH ENDPOINTS

ENDPOINT	POLLUTANT	STUDY	STUDY POPULATION
Premature Mortality			
Premature mortality—all-cause, long-term	$PM_{2.5}$ (annual avg)	Pooled estimate of Jerrett et al. (2013) LA Jerrett et al. (2005) LA Krewski et al. (2009) LA	>30 years
Premature mortality—all-cause, short-term SUPPLEMENTAL ANALYSIS	$PM_{2.5}$ (24-hour avg)	Atkinson et al. (2014)	
Chronic Illness			
Nonfatal myocardial infarction	$PM_{2.5}$ (24-hour avg)	Pope et al., 2006; Sullivan et al., 2005; Zanobetti et al., 2009; Zanobetti & Schwartz, 2006	Adults (>18 years)
Hospital Admissions			
Stroke, Ischemic	$PM_{2.5}$ (24-hour avg)	Shin et al., 2014	>65 years
Respiratory	$PM_{2.5}$ (24-hour avg)	Zanobetti et al, 2009, all respiratory	>65 years
Respiratory	$PM_{2.5}$ (24-hour avg)	Moolgavkar (2000)—ICD 490–492, 494-496 (COPD, less asthma)	18–64 years
Cardiovascular	$PM_{2.5}$ (24-hour avg)	Moolgavkar (2003)—ICD 390–429 (all cardiovascular)	>64 years
Cardiovascular	$PM_{2.5}$ (24-hour avg)	Moolgavkar (2000b)—ICD 390–429 (all cardiovascular)	20–64 years
Asthma-related ER visits and Hospital Admissions	$PM_{2.5}$ (24-hour avg)	Delfino et al. 2014.	<18 years
Other Health Endpoints			
Acute bronchitis	$PM_{2.5}$ (annual avg)	Dockery et al. (1996)	8–12 years
Lower respiratory symptoms	$PM_{2.5}$ (24-hour avg)	Schwartz and Neas (2000)	7–14 years
Upper respiratory symptoms	$PM_{2.5}$ (24-hour avg)	Pope et al. (1991)	9–11 years
Asthma exacerbation	$PM_{2.5}$ (24-hour avg)	Pooled estimate: Ostro et al. (2001) (cough, wheeze, shortness of breath) Mar et al., 2004 (cough, shortness of breath)	6–18 years
Asthma exacerbation	$PM_{2.5}$ (24-hour avg)	Young et al., 2014	>34 years
Minor restricted-activity days	$PM_{2.5}$ (24-hour avg)	Ostro and Rothschild (1989)	18–64 years
Work loss days	$PM_{2.5}$ (24-hour avg)	Ostro (1987)	18–64 years

PM MORTALITY - ADULTS

We recommend that SCAQMD use a pooled estimate of the Los Angeles-specific results from Krewski et al., 2009; Jerrett et al., 2005, and: Jerrett et al. 2013 to assess PM-associated adult mortality. All are high quality studies based on follow-up of the well-regarded ACS cohort that apply results from that study population to assess the mortality impacts at a finer spatial scale within the Los Angeles metropolitan area. Each successive study applies a finer resolution exposure assessment than the Jerrett et al., 2005 study. The Jerrett et al., 2013 study is an update of the Krewski analysis that estimates $PM_{2.5}$ exposures at finer resolution than the previous analyses, while otherwise maintaining the previous studies' methodological strengths.

All three studies illustrate a larger mortality effect estimate in Los Angeles than is observed nationally, with the 2013 study estimate finding a somewhat lower relative risk in LA than the 2005 and 2009 values. We also note that the latest Jerrett study also reports PM mortality estimates for the entire state of California that are consistent with both past work (Jerrett et al., 2005) and with the recently released study of PM mortality in the AARP cohort (Thurston et al., 2015). The Los Angeles all-cause mortality RR of 1.104 in the Jerrett et al., 2013 study is not statistically significant at the 0.05 level (95% CI, 0.968 – 1.260). However, the authors note that sample sizes for the two Jerrett et al. studies differed due to differences in approach related to the exposure assessment. It is possible this may a contributing factor to the lack of significance. Nonetheless, we believe that the quality of the 2013 study overall, the consistency of its results with past and current estimates at the state level, its consistent cause-specific results for LA, and its consistent results for spatial trends of the PM mortality relationship warrant inclusion in the 2016 analysis. We conclude that a pooling of four estimates would be a reasonable approach: two mortality estimates from the Krewski et al., 2009 study used in the 2012 Socioeconomic Analysis (the kriging-based estimate of 1.17 (95% CI, 1.05 - 1.30) and the LUR-based estimate of 1.14 (95% CI, 1.03 - 1.27); a function based on the 1.14 (95% CI, 1.03 – 1.29) all-cause mortality RR from Jerrett et al., 2005; and a function based on the 1.104 (95% CI, 0.968 – 1.26) all-cause mortality RR from Jerrett et al., 2013.[4] This approach makes optimal use of the most recent science for the Los Angeles area. We recommend using the Fixed or Random Effects Pooling mode for the BenMAP-CE runs conducted with these CR functions; while fixed effects pooling seems intuitively plausible for combining these functions, this approach will allow for the use of a random effects approach if the fixed effects approach is not statistically supported.[5]

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[4] All RR values from these studies are derived from risk models that control for confounding using the standard ACS set of individual-level covariates and contextual/ecological covariates.

[5] BenMAP-CE calculates a test statistic, Q_w, using the following equation: $Q_w = \Sigma_i[(1/v_i)*(\beta_{fe}-\beta_i)^2]$, where v_i is the variance of study i, β_{fe} is the weighted beta parameter from a fixed effects pooling and β_i is the beta parameter from study i. The test statistic has a chi-squared distribution with n-1 degrees of freedom, where n is the number of studies being pooled. If Q_w exceeds the critical value at the desired confidence level (BenMAP-CE uses 5 percent, one-tailed test), the null hypothesis that a fixed effects pooling is appropriate is rejected and a random effects pooling is performed (RTI, International, 2015b).

Regarding the issue of a threshold in the PM-mortality C-R function, previous U.S. EPA Science Advisory Board guidance has noted a lack of evidence in general to support a threshold for mortality effects of $PM_{2.5}$ in the U.S. population (U.S. EPA SAB, 2010). We found no evidence in our literature review to contradict this conclusion; in fact, the Lepeule et al., 2012 study found that the $PM_{2.5}$-mortality association is plausibly linear down to a concentration of 8 $\mu g/m^3$. Thurston et al. (2015), in their US study similarly found a relationship between long-term exposure $PM_{2.5}$ and CVD mortality that was consistent with linearity at even lower levels.

We recommend that SCAQMD follow the "lowest measured level" (LML) approach used by both U.S. EPA and CARB when estimating avoided PM-related long-term premature mortality impacts (U.S. EPA, 2012; CARB, 2010), where the LML is defined as the lowest measured concentration reported in the epidemiological studies on which SCAQMD is basing its benefits assessment. Specifically, we recommend that SCAQMD distinguish between benefits resulting from reducing $PM_{2.5}$ only down to the LML and results that include PM reductions down to the policy relevant levels of $PM_{2.5}$ that have been identified by SCAQMD (and which are likely in most cases to be lower than the LML). Among the studies we recommend above, we identified an LML of 9.5 $\mu g/m^3$ associated with the Krewski et al., 2009 urban-scale Los Angeles study; assessing changes in mortality risks associated with PM levels below this LML would require extrapolating the relevant risk models beyond the range of observed data in their respective studies, which would introduce additional uncertainty into the results.[6] Employing the LML approach will allow SCAQMD to emphasize the benefit results in which it has the greatest confidence.

We emphasize, however, that we are not recommending that SCAQMD apply a threshold when assessing the mortality impacts of $PM_{2.5}$. As USEPA notes in its most recent PM RIA, "the current body of scientific literature indicates that a no-threshold model provides the best estimate of PM-related long-term mortality," (2012) and as we stated above, we found no evidence in our supplemental literature search to change this conclusion. Therefore, it would be reasonable for SCAQMD to also report long-term PM-mortality results that may result from AQMP-related reductions that reach below the LML, even down to policy relevant levels, along with a caveat indicating that these results are associated with less confidence because of the required extrapolations. Doing so will provide valuable context on uncertainty and the potential magnitude of benefits.

[6] The LML for Jerrett et al., 2005 is not specified, but based on the exposure surface shown in Figure 1, whose lowest concentration bin starts at 9 ug/m3, it's LML appears to be similar to the Krewski et al. value. The LML from Jerrett et al 2013 is also not specified, therefore we recommend using the 9.5 ug/m3 value from the LA analysis in Krewski et al., 2009 for the LML.

We note that this value is considerably higher than the LML of 5.8 ug/m3 observed in the national Krewski et al. analysis and used by U.S. EPA and CARB in their analyses. It is not clear whether the LML for the LA analysis reflects generally higher PM concentrations in the LA basin or limitations in the particular years of data employed for this urban-scale analysis. Because the national study found long-term PM-mortality effects down to a much lower LML, if SCAQMD uses the 9.5 LML, they will be taking a conservative approach that likely means that they are underestimating these benefits. SCAQMD could consider employing 5.8 ug/m3 as the LML in its sensitivity analyses for comparison.

Given the variation in the magnitude and statistical significance of all-cause mortality RR estimates between the first two LA studies and the 2013 study, uncertainty remains as to the true difference between the PM all-cause mortality impact in LA and elsewhere. Therefore, we recommend that SCAQMD consider conducting additional sensitivity analyses to address this uncertainty. Exhibit 8 presents the studies we propose for the sensitivity analyses. The first two sensitivity analyses would use the results from studies conducted at progressively larger geographic scales. That is, SCAQMD could apply a sensitivity analysis using a state-level PM mortality estimate and also an estimate using a national-scale PM-mortality estimate. The third analysis would use results from studies of populations from LA and California, but that focus specifically on the impact of $PM_{2.5}$ exposures on cardiovascular mortality (ICD10; I00-I99).

The studies we recommend pooling to calculate the California all-cause mortality risk estimates are the Jerrett et al., 2013 analysis (1.060, 95% CI, 1.003 – 1.120) and the 2015 AARP cohort study conducted by Thurston et al. (1.02, 95% CI, 0.99 – 1.04). Both are large, well-conducted long-term cohort studies with extensive control for potential individual and contextual confounding factors; both employ refined assessments of exposure; and both estimate relative risks to populations from the state of California. We recommend a Fixed or Random Effects pooling of these two studies; we do not recommend including the Ostro et al., 2015 study of $PM_{2.5}$ mortality impacts because that study population was restricted to women only. We note that the ages of the Thurston et al. and Jerrett et al. California study populations differ, with the former studying individuals aged 50 and older and the latter studying individuals aged 30 and older; however, we conclude that pooling of these studies is appropriate because the majority of deaths in the ACS study population occurs in individuals aged 50 and older. Therefore, the Thurston et al. estimate represents a reasonable additional RR value estimate for the larger population and is unlikely to significantly bias the results.

For the national-level sensitivity analysis, we recommend a Fixed or Random Effects pooling of the two studies applied by U.S. EPA in the 2015 ozone NAAQS RIA: Krewski et al., 2009 and Lepeule et al., 2012. The Krewski et al., study was described in the section summarizing the studies used in the 2012 Socioeconomic Analysis. For the national-level sensitivity analysis, we recommend using the RR for a 10 $\mu g/m^3$ change from the random effects risk model for all-cause mortality that controls for the 44 individual covariates and seven contextual covariates (1.06, 95% CI, 1.04 – 1.08). The study by Lepeule et al. is the latest follow-up to the Six Cities cohort studies. This study added 11 additional years of follow-up, assessing exposures from 1974 to 2009, and tested the sensitivity of the Six Cities results to alternative model specifications, lower concentrations of PM exposure, and lag times. The authors found results consistent with past Six Cities analyses, even under alternative model assumptions such as allowing the effects of age, smoking, and sex to vary over time, and including more recent exposure data characterized by lower levels of $PM_{2.5}$. The authors found the concentration response relationship to be linear down to the lowest measured levels of 8 $\mu g/m^3$ and found no clear association between changes in the PM-mortality RR and the drop in the

sulfate fraction of $PM_{2.5}$ over time. We recommend that SCAQMD use the RR for a 10 $\mu g/m^3$ of 1.14 (95% CI, 1.07 – 1.22) based on the Cox proportional hazard model with three individual covariates, consistent with U.S. EPA's application.

For the final PM mortality sensitivity analysis, we recommend re-estimating mortality-related benefits in the South Coast Air Basin using a Fixed or Random Effects pooling of three RRs from two studies: the cardiovascular mortality RRs from the Jerrett et al., 2013 ACS reanalysis for Los Angeles (1.124, 95% CI 0.918 – 1.375) and California (1.122, 95% CI 1.030 – 1.223), and the cardiovascular mortality RR for California from the Thurston et al., 2015 AARP cohort study (1.10, 95% CI 1.05 – 1.60). This last uncertainty analysis will assess the sensitivity of SCAQMD's findings if mortality impacts were restricted to one of the cause-specific mortality types consistently associated with mortality in California and elsewhere. Restricting the results in this manner is very likely to produce an underestimate of the true magnitude of mortality benefits associated with decreases in $PM_{2.5}$ in the South Coast Air Basin, however, and the results should be considered a minimum estimate.

As noted above, we also recommend that SCAQMD conduct a supplemental analysis of avoided premature mortality associated with reduced short-term exposures to $PM_{2.5}$, based on the American Region A estimate from the Atkinson et al., 2014 study. The Atkinson review and meta-analysis represents a rigorous, recent evaluation and integration of the time-series literature, and it provides a comprehensive estimate of the effect of PM on short-term mortality in the U.S. This estimate is based on studies conducted across a range of years and locations, including two California single-city studies and a multi-city study (Zanobetti et al., 2009) that included Los Angeles and several other California cities.

PM MORTALITY - INFANTS

We identified no additional research on this endpoint conducted since 2012; as a result we do not recommend any changes to SCAQMD's approach to this endpoint in 2016.

EXHIBIT 8. RECOMMENDED $PM_{2.5}$-RELATED MORTALITY STUDIES FOR SENSITIVITY ANALYSIS

ENDPOINT	POLLUTANT	STUDY	STUDY POPULATION
National Level Estimates			
Premature mortality—all-cause[a]	$PM_{2.5}$ (annual avg)	Pooled estimate of Krewski et al. (2009) Lepeule et al., (2012)	>30 years (Krewski) >25 years (Lepeule)
State of California			

ENDPOINT	POLLUTANT	STUDY	STUDY POPULATION
Premature mortality—all-cause	$PM_{2.5}$ (annual avg)	Pooled estimate of Jerrett et al. (2013) CA Thurston et al. (2015) CA	>30 years (Jerrett) >50 years (Thurston)
Cardiovascular Mortality			
Premature mortality—cardiovascular (ICD10 I00-I99)	$PM_{2.5}$ (annual avg)	Pooled estimate of Jerrett et al. (2013) LA Jerrett et al. (2013) CA Thurston et al. (2015) CA	>30 years (Jerrett) >50 years (Thurston)

PM MORBIDITY

For existing morbidity endpoints, we recommend using existing pre-2012 studies and BenMAP-CE C-R functions for most of them, because for most endpoints we either found no new studies for endpoints, or we do not find that the latest studies we identified present a compelling case to replace existing C-R functions in BenMAP-CE. We do, however, recommend that SCAQMD choose from among the default BenMAP-CE studies in a manner that emphasizes results that are as geographically specific as possible. Thus, the existing studies we recommend in the table above are either conducted in the Los Angeles area (e.g., the Moolgavkar hospital admission studies), or in California and/or other western states, or represent an average U.S. estimate across a broad range of locations.[7] We excluded from our recommendations table studies conducted in a single location outside of the western U.S., unless no other studies were available. Where multiple studies area listed in the recommendations table, we propose these studies be pooled with equal weights, in the absence of compelling evidence to include one over the other.

For children's ER visits for asthma, we assessed the available studies for appropriateness to this application. We do not recommend using the Delamater et al. results. We are uncertain about the strength of the association, given the paper's reliance on monthly mean hospitalization rates that are derived based on the authors' own assumptions about interpolating annual population growth. We instead recommend developing a function based on the work by Delfino et al. in Orange County for all hospital encounters (ER visits and admissions) for asthma in children using a seasonally pooled $PM_{2.5}$ estimate for

[7] For respiratory hospital admissions for populations 65 and older, we recommend using the Zanobetti et al., derived C-R function, which is based on a nationwide analysis of impacts on hospital admissions for all respiratory causes. While the Moolgavkar Los Angeles study from 2000 provides an LA-specific estimate, that estimate is specific to COPD admissions. Therefore, we recommend using the more complete nationwide estimate in this case.

all subjects. We find this to be a strong, well-documented, locally applicable study whose strengths outweigh the limitations associated with the use of PM exposure data from a single monitor. We propose to pool the results of two season specific C-R functions based on the 3-day lag estimates for $PM_{2.5}$.

We also propose augmenting the asthma exacerbation endpoint category with a new C-R function based on a new study of asthma exacerbation in adults. We propose to apply the fully-adjusted OR for incident wheeze in adult women from the Young et al. 2014 U.S. cohort study, which assessed changes in asthma exacerbation in that subpopulation.

For new endpoints, we propose to add a C-R function for hospital admissions for ischemic stroke based on the Shin et al. meta-analysis of long-term and short-term PM effects on stroke incidence. Although the Shin analysis was the only paper on PM and stroke we found published since 2012, the paper makes a compelling argument for including stroke as an endpoint. First, it cites a broad base of existing evidence to support a biological mechanism between PM and stroke, including the substantial evidence showing PM induces cardiovascular effects that contribute to stroke risk. Second, it presents robust meta-analysis results for both long-term and short-term exposures using both traditional frequentist and Bayesian approaches to combining study estimates. We recommend that a C-R function be developed for the short-term RR estimates for ischemic stroke. The short-term estimate is derived from a larger literature base than the long-term estimate, and ischemic stroke RR (1.05, 1.01 – 1.09 using the Gamma prior; 1.05, 0.99 – 1.14 using the normal prior) demonstrated the tightest confidence intervals across both frequentist and Bayesian approaches. We conclude that the use of the gamma-based estimate is justified given the likelihood of a causal relationship via the cardiovascular impacts of $PM_{2.5}$.

We are reserving judgment at this time regarding asthma incidence from PM exposure. We believe Young et al., 2014 is a strong study, and we particularly like its rigorous definition of asthma onset. However, given that there is very little other evidence linking PM with adult asthma onset, we are reluctant to recommend evaluating this endpoint for PM. We instead re-evaluate this endpoint as part of our assessment of NO_2, where this is a larger body of published literature evaluating associations.

We are not proposing to evaluate the Low Birth Weight endpoint at this time with respect to PM. While this continues to be a growing field of study and we discovered several studies conducted in the Los Angeles area specifically that reported positive associations, we do not believe the results are yet consistent enough to produce a reliable C-R function. For example, the Laurent study found positive associations with Low Birth Weight but did not control for the smoking; the Ritz study found effects only when exposure occurs over relative high PM threshold; and the Wilhelm study was not able to find a significant association, though results were consistently positive. In addition, many of the measured weight differences are of uncertain clinical significance, as noted in the Morello-Frosch paper. Taken collectively, we find this evidence continues to be strongly suggestive of a causal relationship, but does not sufficiently support inclusion of this endpoint in the 2016 Socioeconomic Analysis.

The new studies finding associations between PM and autism may warrant additional research, but we do not recommend including this endpoint at this time, due to the 1) acknowledged lack of understanding of a possible biological mechanism; 2) the lack of concordance between results based on spatial differences in exposure and those based on exposure during and following gestation in the Raz et al. study; and 3) the small sample size of the Volk et al. study.

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APPENDIX A:

RESULTS OF PM HEALTH EFFECTS LITERATURE REVIEW FOR SCAQMD SOCIOECONOMIC ANALYSIS OF 2016 AQMP

Table 1. Mortality

Table 1. Mortality

Authors	Title	Year Published	Journal Published	Pollutant(s) Studied	Causes of Mortality or Morbidity Considered	Geographic scope	Population studied	Study question	Statistically significant relationships?	Analysis method	Controls for factors that could obscure relationship?	Assesses potential lag between exposure and outcome?	Reports uncertainty?	Abstract
Anderson, G.B., Krall, J.R., Peng, R.D., Bell, M.L.	Is the Relation Between Ozone and Mortality Confounded by Chemical Components of Particulate Matter? Analysis of 7 Components in 57 US Communities	2012	American Journal of Epidemiology	O3, PM2.5	All-cause non-accidental	57 US communities	All deaths of residents, 2000-2005	Investigates whether the ozone-mortality relationship is confounded by the 7 main components of PM2.5	Fit community-specific generalized linear models, with mortality counts described by an overdispersed Poisson distribution. Tested each of the 7 PM2.5 components separately for confounding of the ozone-mortality relationship. Finally, combined community-level estimates to generate an overall estimate using 2-level normal independent sampling estimation.	Within each community-level model, controlled for potential time-varying confounders, including day of week, long-term and seasonal trends in community mortality rates, and weather (temperature, dew point temperature)	Calculates average of same day and previous day 24-hr O3 concentration	Yes	No	Epidemiologic studies have linked tropospheric ozone pollution and human mortality. Although research has shown that this relation is not confounded by particulate matter when measured by mass, little scientific evidence exists on whether confounding exists by chemical components of the particle mixture. Using mortality and particulate matter with aerodynamic diameter ≤2.5 μm (PM2.5) component data from 57 US communities (2000–2005), the authors investigate whether the ozone-mortality relation is confounded by 7 components of PM2.5: sulfate, nitrate, silicon, elemental carbon, organic carbon matter, sodium ion, and ammonium. Together, these components constitute most PM2.5 mass in the United States. Estimates of the effect of ozone on mortality were almost identical before and after controlling for the 7 components of PM2.5considered (mortality increase/10-ppb ozone increase, before and after controlling: ammonium, 0.34% vs. 0.35%; elemental carbon, 0.36% vs. 0.37%; nitrate, 0.27% vs. 0.26%; organic carbon matter, 0.34% vs. 0.31%; silicon, 0.36% vs. 0.37%; sodium ion, 0.21% vs. 0.18%; and sulfate, 0.35% vs. 0.38%). Additionally, correlations were weak between ozone and each particulate component across all communities. Previous research found that the ozone-mortality relation is not confounded by particulate matter measured by mass; this national study indicates that the relation is also robust to control for specific components of PM2.5.
Atkinson, R.W., Kang, S., Anderson, H.R., Mills, I.C., Walton, H.A.	Epidemiological Time Series Studies of PM2.5 and Daily Mortality and Hospital Admissions: a Systematic Review and Meta-Analysis	2014	Thorax	PM2.5	All-cause mortality, IHD mortality, stroke mortality, COPD (excl. asthma) mortality, hospital admissions for cardiovascular and respiratory diseases: all ages: cardiovascular, respiratory, 65+ years: cardiovascular, COPD incl astha, COPD excl asthma, lower resp infection, respiratory, IHD, heart failure, cardiac, stroke, dysrhythmia; 0-14: respiratory, asthma	Worldwide, but provides estimates specific to WHO American Region A (U.S., Canada, Cuba)	For different health endpoints, considers all ages, 65+ years, 0-14 years	Assesses the evidence for associations between PM2.5 and daily mortality and hospital admissions for a range of diseases and ages using a comprehensive review and meta-analysis	Yes	Did a systematic, comprehensive review of 110 peer-reviewed time series studies published through May 2011. Within each WHO region, did a two stage meta-analysis, first pooling single-city estimates and then pooling these summary estimates with the selected multicity study estimates to get a WHO region-specific summary estimates. In WHO American Region A, had 33 total mortality studies, 31 hospital admission studies.	They assessed small study bias in single-city estimates and selected multicity estimates. They choose studies that attempt to control for confounding factors like season, lont-term temporal trends and meteorological conditions	Studies vary in the time lag they study for short-term effects.	Yes	**Background:** Short-term exposure to outdoor fine particulate matter (particles with a median aerodynamic diameter <2.5 μm (PM2.5)) air pollution has been associated with adverse health effects. Existing literature reviews have been limited in size and scope. **Methods:** We conducted a comprehensive, systematic review and meta-analysis of 110 peer-reviewed time series studies indexed in medical databases to May 2011 to assess the evidence for associations between PM2.5 and daily mortality and hospital admissions for a range of diseases and ages. We stratified our analyses by geographical region to determine the consistency of the evidence worldwide and investigated small study bias. **Results:** Based upon 23 estimates for all-cause mortality, a 10 μg/m3 increment in PM2.5 was associated with a 1.04% (95% CI 0.52% to 1.56%) increase in the risk of death. Worldwide, there was substantial regional variation (0.25% to 2.08%). Associations for respiratory causes of death were larger than for cardiovascular causes, 1.51% (1.01% to 2.01%) vs 0.84% (0.41% to 1.28%). Positive associations with mortality for most other causes of death and for cardiovascular and respiratory hospital admissions were also observed. We found evidence for small study bias in single-city mortality studies and in multicity studies of cardiovascular disease. **Conclusions:** The consistency of the evidence for adverse health effects of short-term exposure to PM2.5 across a range of important health outcomes and diseases supports policy measures to control PM2.5 concentrations. However, reasons for heterogeneity in effect estimates in different regions of the world require further investigation. Small study bias should also be considered in assessing and quantifying health risks from PM2.5.

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Brook, R.D., Cakmak, S., Turner, M.C., Brook, J.R., Crouse, D.L., Peters, P.A., van Donkelaar, A., Villeneuve, P.J., Brion, O., Jerrett, M., Martin, R.V., Rajagopalan S., Goldberg, M.S., Pope, C.A., Burnett, R.T.	Long-Term Fine Particulate Matter Exposure and Mortality From Diabetes in Canada	2013	Diabetes Care	PM2.5	Diabetes-related (ICD-9: 250, ICD-10: E10-E14)	Canada	>=25 years Canadian residents, non-immigrant	Estimates the effect of long-term PM2.5 exposure on mortality from diabetes	Yes	Used Cox proportional hazards model, using long-term exposure defined as average of concentration from 2001-2006. Stratified analysis by single year age groups and sex.	Included controls for subjects' demographic and SE environment, population size of home community. Tested for effect modification by excluding subjects in different age groups and for modification by sex, education status, income level, and community size. Acknowledge possible misclassification in cause of death and possible confounding from regional differences.	Assessed long-term exposure by averaging concentrations for 2001-2006 from satellite remote sensing observations.	Yes	OBJECTIVE Recent studies suggest that chronic exposure to air pollution can promote the development of diabetes. However, whether this relationship actually translates into an increased risk of mortality attributable to diabetes is uncertain. RESEARCH DESIGN AND METHODS We evaluated the association between long-term exposure to ambient fine particulate matter (PM2.5) and diabetes-related mortality in a prospective cohort analysis of 2.1 million adults from the 1991 Canadian census mortality follow-up study. Mortality information, including ~5,200 deaths coded as diabetes being the underlying cause, was ascertained by linkage to the Canadian Mortality Database from 1991 to 2001. Subject-level estimates of long-term exposure to PM2.5 were derived from satellite observations. The hazard ratios (HRs) for diabetes-related mortality were related to PM2.5 and adjusted for individual-level and contextual variables using Cox proportional hazards survival models. RESULTS Mean PM2.5 exposure levels for the entire population were low (8.7 µg/m3; SD, 3.9 µg/m3; interquartile range, 6.2 µg/m3). In fully adjusted models, a 10-µg/m3 elevation in PM2.5 exposure was associated with an increase in risk for diabetes-related mortality (HR, 1.49; 95% CI, 1.37–1.62). The monotonic change in risk to the population persisted to PM2.5 concentration <5 µg/m3. CONCLUSIONS Long-term exposure to PM2.5, even at low levels, is related to an increased risk of mortality attributable to diabetes. These findings have considerable public health importance given the billions of people exposed to air pollution and the worldwide growing epidemic of diabetes.
Cox, L.A., Popken, D.A., Ricci, P.F.	Warmer is Healthier: Effects on Mortality Rates of Changes in Average Fine Particulate Matter (PM2.5) Concentrations and Temperatures in 100 U.S. Cities	2013	Regulatory Toxicology and Pharmacology	PM2.5	All-cause non-accidental (ICD-9: 0-799, ICD-10: A00-R99)	110 US cities	Primary analysis on >75 years, but do Bayesian model averaging and Granger-Sims causality for all ages	Examine the empirical correspondence between changes in average PM2.5 levels and temperatures from 1999 to 2000 and corresponding changes in average daily mortality rates--non-parametric; looking for relationships, but not quantifying their magnitude	No	Longitudinal panel, looking at city-month pairs between 1999 and 2000, producing Spearman correlation coefficients. Do a Granger test for causality between city-specific daily temp and PM2.5 concentration and mortality rates	Controls for city characteristics that stayed constant between 1999 and 2000.	Uses monthly data for mortality and air pollution	No	Recent studies have indicated that reducing particulate pollution would substantially reduce average daily mortality rates, prolonging lives, especially among the elderly (age ≥ 75). These benefits are projected by statistical models of significant positive associations between levels of fine particulate matter (PM2.5) levels and daily mortality rates. We examine the empirical correspondence between changes in average PM2.5 levels and temperatures from 1999 to 2000, and corresponding changes in average daily mortality rates, in each of 100 U.S. cities in the National Mortality and Morbidity Air Pollution Study (NMMAPS) data base, which has extensive PM2.5, temperature, and mortality data for those 2 years. Increases in average daily temperatures appear to significantly reduce average daily mortality rates, as expected from previous research. Unexpectedly, reductions in PM2.5 do not appear to cause any reductions in mortality rates. PM2.5 and mortality rates are both elevated on cold winter days, creating a significant positive statistical relation between their levels, but we find no evidence that reductions in PM2.5 concentrations cause reductions in mortality rates. For all concerned, it is crucial to use causal relations, rather than statistical associations, to project the changes in human health risks due to interventions such as reductions in particulate air pollution.

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Crouse, D.L., Peters, P.A., van Donkelaar, A., Goldberg, M.S., Villeneuve, P.J., Brion, O., Khan, S., Atari, D.O., Jerrett, M., Pope, C.A., Brauer, M., Brook, J.R., Martin, R.V., Stiev, D., Burnett, R.T.	Risk of Nonaccidental and Cardiovascular Mortality in Relation to Long-term Exposure to Low Concentrations of Fine Particulate Matter: A Canadian National-Level Cohort Study	2012	Environmental Health Perspectives	PM2.5	All-cause non-accident (ICD-9: <800, ICD-10: starting with A through R), ischemic heart disease (ICD-9: 410-414, ICD-10: I20-I25), cerebrovascular disease (ICD-9: 430-434, 436-438, ICD-10: I60-I69), cardiovascular disease (ICD-9:410-417, 420-438, 440-449, ICD-10: I20-I28, I30-I52, I60-I79), circulatory disease (ICD-9: 390-459, ICD-10: I00-I99)	Canada	>=25 years, Canadian residents, non-immigrant	Investigates the association between long-term exposure to ambient PM2.5 and non-accidental and cardiovascular mortality in nonimmigrant Canadian adults	Yes	Calculated hazard ratios, adjusting for individual-level and neighborhood covariates using both Cox proportional survival models and nested, spatial random-effect survival Cox models. Stratified analysis by single-year age groups and sex	Included controls for subjects' demographic and SE environment, population size of home community. Acknowledge issue of potential exposure misclassification due to mobility of subjects	Used long-term exposure defined as average of concentration from 2001 to 2006 for full cohort and then did sub-analysis of 11 cities using mean annual conc from 1987 to 2001.	Yes	Background: Few cohort studies have evaluated the risk of mortality associated with long-term exposure to fine particulate matter [≤ 2.5 µm in aerodynamic diameter (PM2.5)]. This is the first national-level cohort study to investigate these risks in Canada. Objective: We investigated the association between long-term exposure to ambient PM2.5 and cardiovascular mortality in nonimmigrant Canadian adults. Methods: We assigned estimates of exposure to ambient PM2.5 derived from satellite observations to a cohort of 2.1 million Canadian adults who in 1991 were among the 20% of the population mandated to provide detailed census data. We identified deaths occurring between 1991 and 2001 through record linkage. We calculated hazard ratios (HRs) and 95% confidence intervals (CIs) adjusted for available individual-level and contextual covariates using both standard Cox proportional survival models and nested, spatial random-effects survival models. Results: Using standard Cox models, we calculated HRs of 1.15 (95% CI: 1.13, 1.16) from nonaccidental causes and 1.31 (95% CI: 1.27, 1.35) from ischemic heart disease for each 10-µg/m3 increase in concentrations of PM2.5. Using spatial random-effects models controlling for the same variables, we calculated HRs of 1.10 (95% CI: 1.05, 1.15) and 1.30 (95% CI: 1.18, 1.43), respectively. We found similar associations between nonaccidental mortality and PM2.5 based on satellite-derived estimates and ground-based measurements in a subanalysis of subjects in 11 cities. Conclusions: In this large national cohort of nonimmigrant Canadians, mortality was associated with long-term exposure to PM2.5. Associations were observed with exposures to PM2.5 at concentrations that were predominantly lower (mean, 8.7 µg/m3; interquartile range, 6.2 µg/m3) than those reported previously.
Dai, L., Zanobetti, A., Koutrakis, P., Schwartz, J.D.	Associations of Fine Particulate Matter Species with Mortality in the United States: a Multicity Time-Series Analysis	2014	Environmental Health Perspectives	PM2.5	All-cause non-accidental (ICD-9: 0-799, ICD-10: A00-R99), cardiovascular diseases (ICD-9: 390-429, ICD-10:I01-I59), respiratory diseases (ICD-9: 460-519, ICD-10: J00-J99), myocardial infarction (ICD-9: 410, ICD-10: I21-I22), and stroke (ICD-9: 430-438, ICD-10: I60-I69) *ICD-10 codes are reported in the text; I made my best effort to convert to ICD-9 codes	75 US cities	All deaths	Estimates the effects of PM2.5 species on mortality, broken down by causes of death, and how infiltration rates may modify those associations.	Yes (all-cause mortality, CVD, MI, stroke, respiratory, with exacerbation by smoking and alcohol)	City-specific Poisson regression, estimating effect of PM2.5 on death rates for all causes, CVD, myocardial infarction, stroke, and respiratory diseases at daily level, broken down by PM2.5 species. Then used multivariate random effects meta-analysis to combine the 300 city-season effect estimates into overall estimate	Control for seasonal confounder doing city-season specific analysis, and control for city fixed effects. They look for effect modification by PM2.5 species.	Looks at short-term effects using average of same and previous day PM2.5	Yes	**Background**: Epidemiological studies have examined the association between PM2.5 and mortality, but uncertainty remains about the seasonal variations in PM2.5-related effects and the relative importance of species. **Objectives**: We estimated the effects of PM2.5 species on mortality and how infiltration rates may modify the association. **Methods**: Using city–season specific Poisson regression, we estimated PM2.5 effects on approximately 4.5 million deaths for all causes, cardiovascular disease (CVD), myocardial infarction (MI), stroke, and respiratory diseases in 75 U.S. cities for 2000–2006. We added interaction terms between PM2.5 and monthly average species-to-PM2.5 proportions of individual species to determine the relative toxicity of each species. We combined results across cities using multivariate meta-regression, and controlled for infiltration. **Results:** We estimated a 1.18% (95% CI: 0.93, 1.44%) increase in all-cause mortality, a 1.03% (95% CI: 0.65, 1.41%) increase in CVD, a 1.22% (95% CI: 0.62, 1.82%) increase in MI, a 1.76% (95% CI: 1.01, 2.52%) increase in stroke, and a 1.71% (95% CI: 1.06, 2.35%) increase in respiratory deaths in association with a 10-µg/m3 increase in 2-day averaged PM2.5 concentration. The associations were largest in the spring. Silicon, calcium, and sulfur were associated with more all-cause mortality, whereas sulfur was related to more respiratory deaths. County-level smoking and alcohol were associated with larger estimated PM2.5 effects.
Farhat, N., Ramsay, T., Jerrett, M., Krewski, D.	Short-Term Effects of Ozone and PM2.5 on Mortality in 12 Canadian Cities	2013	Journal of Environmental Protection	PM2.5, O3	All-cause non-accidental (ICD-9: <800), cardiovascular (ICD-9: 390-459), respiratory (ICD-9: 460-519)	12 Canadian cities	All deaths, 1981-2001	Quantitatively assesses the impact of fine particulate matter and ozone on mortality in Canada, and explores the sensitivity of these effects to different model specifications	Yes (with stronger associations among the elderly)	Estimated Poisson regression models allowing for overdispersion. Performed sensitivity analysis exploring the effect of degrees of freedom allowed for seasonality control and for lag period. Then combined city-specific estimates by applying fixed effects and random effects regression models.	Includes controls for seasonality with natural cubic splines and controls for temperature, holidays, day of the week. Looked at possible effect modification by various ecologic covariates, including area, unemployment among males, manufacturing, and stress levels. Considered confounding between PM2.5 and O3. Acknowledges possible misclassification of exposure to PM2.5	Considered a variety of lag structures, including lag1, lag0 (same day), lag2, and moving averages	Yes	Numerous recent epidemiological studies have linked health effects with short-term exposure to air pollution levels commonly found in North America. The association between two key pollutants—ozone and fine particulate matter— and mortality in 12 Canadian cities was explored in a time-series study. City-specific estimates were obtained using Poisson regression models, adjusting for the effects of seasonality and temperature. Estimates were then pooled across cities using the inverse variance method. For a 10 ppb increase in 1-hr daily maximum ozone levels, significant associations were in the range of 0.56% - 2.47% increase in mortality. For a 10 µg/m3increase in the 24-hr average PM2.5 concentration of, significant associations varied between 0.91% and 3.17% increase in mortality. Generally, stronger associations were found among the elderly. Effects estimates were robust to adjustment for seasonality, but were sensitive to lag structures. There was no evidence for effect modification of the mortality-exposure association by city-level ecologic covariates.

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Gan, W.Q., Fitzgerald, J.M., Carlsten, C., Sadatsafavi, M., Brauer, M.	Associations of Ambient Air Pollution with Chronic Obstructive Pulmonary Disease Hospitalization and Mortality	2013	American Journal of Respiratory and Critical Care Medicine	PM2.5, NO2, NO	Chronic obstructive pulmonary disease (ICD-9: 490-492, 496, ICD-10: J40-J44)	Vancouver metropolitan area, Canada	All residents who were registered with the provincial health insurance plan, lived in the study region during 5-year exposure period, 45-85 years, no previous diagnosis of COPD	Investigates the associations of long-term exposure to elevated traffic-related air pollution and woodsmoke pollution with the risk of COPD hospitalization and mortality.		First, used a chi-square test for categorical variables and t test for continuous variables to compare baseline characteristics between cases and others. Looked at correlations between air pollutants using Spearman rank correlation. Then used Cox proportional hazards regression model to determine associations. Calculated person-days of follow-up from baseline to date of first COPD hospitalization, COPD death, or end of follow-up. Furhter examined C-R trends using natural cubic spline functions.	Controlled for age, sex, preexisting comorbid conditions, and neighborhood socioeconomic status. Comorbid conditions included asthma, diabetes, and hypertensive heart disease. Also adjusted for copollutants to control for confounding. Performed stratified analyses to examine effect modification by age, sex, preexisting comorbid conditions, and neighborhood SES.	Used 5-year long-term exposure averages	Yes	Rationale: Ambient air pollution has been suggested as a risk factor for chronic obstructive pulmonary disease (COPD). However, there is a lack of longitudinal studies to support this assertion. Objectives: To investigate the associations of long-term exposure to elevated traffic-related air pollution and woodsmoke pollution with the risk of COPD hospitalization and mortality. Methods: This population-based cohort study included a 5-year exposure period and a 4-year follow-up period. All residents aged 45–85 years who resided in Metropolitan Vancouver, Canada, during the exposure period and did not have known COPD at baseline were included in this study (n = 467,994). Residential exposures to traffic-related air pollutants (black carbon, particulate matter <2.5 μm in aerodynamic diameter, nitrogen dioxide, and nitric oxide) and woodsmoke were estimated using land-use regression models and integrating changes in residences during the exposure period. COPD hospitalizations and deaths during the follow-up period were identified from provincial hospitalization and death registration databases. Measurements and Main Results: An interquartile range elevation in black carbon concentrations (0.97 × 10−5/m, equivalent to 0.78 μg/m3 elemental carbon) was associated with a 6% (95% confidence interval, 2–10%) increase in COPD hospitalizations and a 7% (0–13%) increase in COPD mortality after adjustment for covariates. Exposure to higher levels of woodsmoke pollution (tertile 3 vs. tertile 1) was associated with a 15% (2–29%) increase in COPD hospitalizations. There were positive exposure–response trends for these observed associations. Conclusions: Ambient air pollution, including traffic-related fine particulate pollution and woodsmoke pollution, is associated with an increased risk of COPD.
Garcia, C.A., Yap, O., Park, H., Weller, B.L.	Association of Long-Term PM2.5 Exposure with Mortality Using Different Air Pollution Exposure Models: Impacts in Rural and Urban California	2015	International Journal of Environmental Health Research	PM2.5	Cardiovascular disease (ICD-10: I00-I99), ischemic heart disease (ICD-10: I20-I25), cardiopulmonary disease (ICD-10: I00-I99 and J00-J98), all-cause non-accidental (ICD-10: A00-R99, excluding V01-V99)	California	>=65 in California who died in 2006	Investigates the impacts of long-term PM2.5 exposure in rural vs. urban areas in California on mortality from CVD, ischemic heart disease, cardiopulmonary disease, and all-cause non-accidental mortality in an elderly population. Also assess the effects of different methodologies used to estimate PM2.5 exposure	Yes (but for urban areas, only when using the most restrictive exposure model)	Calculated 2000-2006 average PM2.5 concentration using monthly averages. Summed total mortality and cause-specific mortality at each zip code, then did Poisson regression stratified rural vs. urban analysis. Performed all statewide analysis using indicator variable for urban vs. rural.	Controlled for unemployment and low-education variables at zipcode-level.	Looked at long-term exposure, average monthly PM2.5 values for 2000 to 2006	Yes	Most PM2.5-associated mortality studies are not conducted in rural areas where mortality rates may differ when population characteristics, health care access, and PM2.5 composition differ. PM2.5-associated mortality was investigated in the elderly residing in rural–urban zip codes. Exposure (2000–2006) was estimated using different models and Poisson regression was performed using 2006 mortality data. PM2.5 models estimated comparable exposures, although subtle differences were observed in rate ratios (RR) within areas by health outcomes. Cardiovascular disease (CVD), ischemic heart disease (IHD), and cardiopulmonary disease (CPD), mortality was significantly associated with rural, urban, and statewide chronic PM2.5 exposures. We observed larger effect sizes in RRs for CVD, CPD, and all-cause (AC) with similar sizes for IHD mortality in rural areas compared to urban areas. PM2.5 was significantly associated with AC mortality in rural areas and statewide; however, in urban areas, only the most restrictive exposure model showed an association. Given the results seen, future mortality studies should consider adjusting for differences with rural–urban variables.

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Goldberg, M.S., Burnett, R.T., Stieb, D.M., Brophy, J.M., Daskalopoulou, S.S., Valois, M., Brook, J.R.	Associations Between Ambient Air Pollution and Daily Mortality Among Elderly Persons in Montreal, Quebec	2013	Science of the Total Environment	NO2, O3, CO, SO2, PM2.5	Looks at general all-cause non-accident mortality, but within subgroups with underlying health conditions: all cardiovascular (ICD-9: 400-440, ICD-10: I10-I70), congestive heart failure (ICD-9: 428.0, ICD-10: I50.0), acute coronary artery disease (ICD-9:?, ICD-10: I25.4?), chronic coronary artery disease (ICD-9:?, ICD-10?), atrial fibrillation (ICD-9: 427.3, ICD-10: I48), hypertension(ICD-9: 401-405, ICD-10: I10-I15), cerebrovascular disease (ICD-9:430-438 , ICD-10: I60-I69), acute lower respiratory disease (ICD-9: 466, 480-488, ICD-10: J09-J18, J20-J22), airways disease (ICD-9: 504, ICD-10: J66), chronic lower respiratory disease (ICD-9: 490-494, ICD-10: J40-J47), cancer (ICD-9: 140-239, ICD-10: C00-D48), diabetes (ICD-9: 250, ICD-10: E10-E14), and combinations *The text does not report these ICD codes; I assigned them to the best of my ability.	Montreal, Quebec	>=65 years who died between 1990 and 2003, resident in Montreal during 1990-2003, registered with universal Quebec Health Insurance Plan	Associations between ambient air pollution (NO2, O3, CO, SO2, PM2.5) and daily mortality among elderly persons in Montreal, Quebec. In particular, looks at the effect of air pollution on mortality for people with different underlying heath conditions, including various respiratory conditions, cardiovascular disease, cancer, and diabetes mellitus	Yes (non-accidental mortality, among people with CVD, congestive heart failure, atrial fibrillation, diabetes, and diabetes+CVD, with other associations just in the warm season)	Used parametric log-linear Poisson models wtihin distributed lag non-linear models framework, which were adjusted for long-term temporal trends and daily maximum temperature. Performed this analysis for all deaths and then separately for deaths of people in certain high-risk categories (i.e. diagnosed with diabetes within the past year)	Removed seasonal and sub-seasonal cycles in the mortality time series using a natural cubic spline function and included a factor for day of week. Assess the influence of mortality displacement. Allows for effect modification by the presence of other high-risk diseases and by season of the year by running analysis separately for population subgroups and different seasons.	Use daily pollution and mortality data, but uses a distributed lag non-linear model to allow delayed dependences in the relationship between mortality and air pollution, which provides an estimate of the overall effect in the presence of "harvesting"	Yes	Background: Persons with underlying health conditions may be at higher risk for the short-term effects of air pollution. We have extended our original mortality time series study in Montreal, Quebec, among persons 65 years of age and older, for an additional 10 years (1990-2003) to assess whether these associations persisted and to investigate new health conditions. Methods and Results: We created subgroups of subjects diagnosed with major health conditions one year before death using billing and prescription data from the Quebec Health Insurance Plan. We used parametric log-linear Poisson models within the distributed lag non-linear models framework, that were adjusted for long-term temporal trends and daily maximum temperature, for which we assessed associations with NO2, O3, CO, SO2, and particles with aerodynamic diameters 2.5 μm in diameter or less (PM2.5). We found positive associations between daily non-accidental mortality and all air pollutants but O3 (e.g., for a cumulative effect over a 3-day lag, with a mean percent change (MPC) in daily mortality of 1.90% [95% confidence interval: 0.73, 3.08%] for an increase of the interquartile range (17.56 μg m(-3)) of NO2). Positive associations were found amongst persons having cardiovascular disease (cumulative MPC for an increase equal to the interquartile range of NO2=2.67%), congestive heart failure (MPC=3.46%), atrial fibrillation (MPC=4.21%), diabetes (MPC=3.45%), and diabetes and cardiovascular disease (MPC=3.50%). Associations in the warm season were also found for acute and chronic coronary artery disease, hypertension, and cancer. There was no persuasive evidence to conclude that there were seasonal associations for cerebrovascular disease, acute lower respiratory disease (defined within 2 months of death), airways disease, and diabetes and airways disease. Conclusions: These data indicate that individuals with certain health conditions, especially those with diabetes and cardiovascular disease, hypertension, atrial fibrillation, and cancer, may be susceptible to the short-term effects of air pollution.
Hao, Y., Balluz, L., Strosnider, H., Wen, X.J., Li, C., Qualters, J.R.	Ozone, Fine Particulate Matter and Chronic Lower Respiratory Disease Mortality in the United States	2015	American Journal of Respiratory and Critical Care Medicine	O3, PM2.5	Chronic lower respiratory disease (ICD-9:?, ICD-10: J40-J47) *I do not have access to the full text, so I have assigned this code to the best of my ability	Contiguous United States	2007-2008 CLRD deaths	Examines the effect of long-term exposure to O3 and PM2.5 on chronic lower respiratory disease mortality	No	Derived county-level average daily exposure levels for 2001-2008 and then fit Bayesian hierarchical spatial Poisson models. They use random effects at state and county levels to account for spatial heterogeneity and spatial dependence	Adjusts for five county-level covariates (percent adults over 65, poverty, lifetime smoking, obesity, and temperature).	Uses long-term exposure data calculated as average daily exposure for 2001 to 2008	Yes	Abstract RATIONALE: Short-term effects of air pollution exposure on respiratory disease mortality are well established. However, few studies have examined the effects of long-term exposure and, among those that have, results are inconsistent. OBJECTIVE: To evaluate long-term association between ambient ozone, fine particulate matter (PM2.5, particles with aerodynamic diameter of 2.5 micrometers or less) and chronic lower respiratory disease (CLRD) mortality in the contiguous United States. METHODS: We fit Bayesian hierarchical spatial Poisson models, adjusting for five county-level covariates (percent adults aged ≥65 years, poverty, lifetime smoking, obesity, and temperature), with random effects at state and county levels to account for spatial heterogeneity and spatial dependence. MEASUREMENTS AND MAIN RESULTS: We derived county-level average daily exposure levels for ambient ozone and PM2.5 for 2001-2008 from the U.S. Environmental Protection Agency's down-scaled estimates and obtained 2007-2008 CLRD deaths from the National Center for Health Statistics. Exposure to ambient ozone was associated with increased rate of CLRD deaths, with a rate ratio of 1.05 (95% credible interval, 1.01-1.09) per 5-ppb increase in ozone; the association between ambient PM2.5 and CLRD mortality was positive but statistically insignificant (rate ratio 1.068, 95% credible interval, 0.995-1.146). CONCLUSIONS: This is the first national study that links air pollution exposure data with CLRD mortality for 3109 contiguous U.S. counties. Ambient ozone may be associated with increased rate of death from CLRD in the contiguous United States.

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Hart, J.E., Liao, X., Hong, B., Puett, R.C., Yanosky, J.D., Suh, H., Kiomourtzoglou, M., Spiegelman, D., Laden, F.	The Association of Long-Term Exposure to PM2.5 on All-Cause Mortality in the Nurses' Health Study and the Impact of Measurement-Error Correction	2015	Environmental Health	PM2.5	All-cause non-accidental (ICD-9: 0-799, ICD-10: A00-R99)	United States	Participants in Nurses' Health Study, still alive in 2000	Estimates the effect of long-term PM2.5 exposure on all-cause mortality, adjusting for measurement error	Yes	Assigned time-varying average PM2.5 in the year before each death, and then used time-varying Cox proportional hazards models to estimate hazard ratios. Estimated for measure error using risk-set regression calibration	Controls for time-varying potential confounders like age, race, physical activity, BMI, family history, smoking, diet, individual- and area-level SES. Corrects for bias due to exposure measurement error using risk set regression calibration for time-varying exposures.	Used average exposure over the year before death	Yes	Abstract Background Long-term exposure to particulate matter less than 2.5 μm in diameter (PM2.5) has been consistently associated with risk of all-cause mortality. The methods used to assess exposure, such as area averages, nearest monitor values, land use regressions, and spatio-temporal models in these studies are subject to measurement error. However, to date, no study has attempted to incorporate adjustment for measurement error into a long-term study of the effects of air pollution on mortality. Methods We followed 108,767 members of the Nurses' Health Study (NHS) 2000–2006 and identified all deaths. Biennial mailed questionnaires provided a detailed residential address history and updated information on potential confounders. Time-varying average PM2.5 in the previous 12-months was assigned based on residential address and was predicted from either spatio-temporal prediction models or as concentrations measured at the nearest USEPA monitor. Information on the relationships of personal exposure to PM2.5 of ambient origin with spatio-temporal predicted and nearest monitor PM2.5 was available from five previous validation studies. Time-varying Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95 percent confidence intervals (95%CI) for each 10 μg/m3 increase in PM2.5. Risk-set regression calibration was used to adjust estimates for measurement error. Results Increasing exposure to PM2.5 was associated with an increased risk of mortality, and results were similar regardless of the method chosen for exposure assessment. Specifically, the multivariable adjusted HRs for each 10 μg/m3 increase in 12-month average PM2.5 from spatio-temporal prediction models were 1.13 (95%CI:1.05, 1.22) and 1.12 (95%CI:1.05, 1.21) for concentrations at the nearest EPA monitoring location. Adjustment for measurement
Jerrett, M., Burnett, R.T., Beckerman, B.S., Turner, M.C., Krewski, D., Thurston, G., Martin, R.V., van Donkelaar, A., Hughes, E., Shi, Y., Gapstur, S.M., Thun, M.J., Pope, C.A.	Spatial Analysis of Air Pollution and Mortality in California	2013	Respiratory and Critical Care Medicine	PM2.5, O3, NO2	Cardiovascular disease (ICD-9: 390-429, ICD-10:I01-I59), ischemic heart disease (ICD-9: 410-414, ICD-10:I20-I25), stroke (ICD-9: 430-438, ICD-10: I60-I69), respiratory disease, lung cancer (ICD-9: 162, ICD-10: C34), all-cause *Paper does not include specific ICD codes, so I have assigned them to the best of my ability.	California	California adults from American Cancer Society Cancer Prevention II Study	Assesses the associations of PM2.5, O3, and NO2 with the risk of mortality in California adults	Yes (with ischemic heart disease mortality and all causes combined)	Assigned exposure for PM2.5 to subjects' addresses using an advanced remote sensing model coupled with atmospheric modeling, applied to monthly average monitoring data from 112 sites. Assessed the association between air pollution and mortality (CVD, IHD, stroke, respiratory disease, lung cancer, all other, all causes) using standard and multilevel Cox proportional hazards models.	Controlled for individual-level variables for lifestyle, diet, demographics, ocupation, and education and ecological variables at the county level. Also control for residence in a metropolitan area. Acknowledges the potential for bias from intercorrelation among the various pollutants.	Used long-term averaged exposure rates. Exposures appear to be averaged over different year ranges for different pollutants. For PM2.5, seems to be over 1998 to 2002	Yes	Rationale: Although substantial scientific evidence suggests that chronic exposure to ambient air pollution contributes to premature mortality, uncertainties exist in the size and consistency of this association. Uncertainty may arise from inaccurate exposure assessment. Objectives: To assess the associations of three types of air pollutants (fine particulate matter, ozone [O3], and nitrogen dioxide [NO2]) with the risk of mortality in a large cohort of California adults using individualized exposure assessments. Methods: For fine particulate matter and NO2, we used land use regression models to derive predicted individualized exposure at the home address. For O3, we estimated exposure with an inverse distance weighting interpolation. Standard and multilevel Cox survival models were used to assess the association between air pollution and mortality. Measurements and Main Results: Data for 73,711 subjects who resided in California were abstracted from the American Cancer Society Cancer Prevention II Study cohort, with baseline ascertainment of individual characteristics in 1982 and follow-up of vital status through to 2000. Exposure data were derived from government monitors. Exposure to fine particulate matter, O3, and NO2 was positively associated with ischemic heart disease mortality. NO2 (a marker for traffic pollution) and fine particulate matter were also associated with mortality from all causes combined. Only NO2 had significant positive association with lung cancer mortality. Conclusions: Using the first individualized exposure assignments in this important cohort, we found positive associations of fine particulate matter, O3, and NO2 with mortality. The positive associations of NO2 suggest that traffic pollution relates to premature death.

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Kiomourtzoglou, M, Austin, E., Koutrakis, P., Dominici, F., Schwartz, J., Zanobetti, A.	PM2.5 and Survival Among Older Adults: Effect Modification by Particulate Composition	2015	Epidemiology	PM2.5	All-cause	81 US cities	Medicare enrollees (>=65 years)	Investigates the impact of PM2.5 exposure on "survival" and the variation of this effect across clusters of cities with similar PM2.5 composition	Yes	Use time-varying annual PM2.5 averages from ambient central monitoring sites, then run Cox models for cities to determine the effect of PM2.5 on mortality. They then pool city-specific effects using a random effects meta-regression, and assess effect modification by cluster membership	They control for individual data on previous cardiopulmonary-related hospitalizations and stratify analysis by follow-up time, age, gender, and race. Look at effect modification by membership in clusters determined by PM2.5 composition.	Use long-term exposure data, with time-varying annual PM2.5 averages.	Yes	BACKGROUND: Fine particulate (PM2.5) air pollution has been consistently linked to survival, but reported effect estimates are geographically heterogeneous. Exposure to different types of particle mixtures may explain some of this variation. METHODS: We used k-means cluster analyses to identify cities with similar pollution profiles, (ie, PM2.5 composition) across the United States. We examined the impact of PM2.5 on survival, and its variation across clusters of cities with similar PM2.5 composition, among Medicare enrollees in 81 US cities (2000-2010). We used time-varying annual PM2.5 averages, measured at ambient central monitoring sites, as the exposure of interest. We ran by-city Cox models, adjusting for individual data on previous cardiopulmonary-related hospitalizations and stratifying by follow-up time, age, gender, and race. This eliminates confounding by factors varying across cities and long-term trends, focusing on year-to-year variations of air pollution around its city-specific mean and trend. We then pooled the city-specific effects using a random effects meta-regression. In this second stage, we also assessed effect modification by cluster membership and estimated cluster-specific PM2.5 effects. RESULTS: We followed more than 19 million subjects and observed more than 6 million deaths. We found a harmful impact of annual PM2.5 concentrations on survival (hazard ratio = 1.11 [95% confidence interval = 1.01, 1.23] per 10 μg/m). This effect was modified by particulate composition, with higher effects observed in clusters containing high concentrations of nickel, vanadium, and sulfate. For instance, our highest effect estimate was observed in cities with harbors in the Northwest, characterized by high nickel, vanadium, and elemental carbon concentrations (1.9 [1.1, 3.3]). We observed null or negative associations in clusters with high oceanic and crustal particles.
Kloog, I., Ridgway, B., Koutrakis, P., Coull, B., Schwartz, JD	Long- and Short-Term Exposure to PM2.5 and Mortality: Using Novel Exposure Models	2013	Epidemiology	PM2.5	All-cause (short term) Cardiovascular and Respiratory diseases (long term) *The text does not specify ICD codes or anything more specific than these broad categories	Massachusetts	All deaths in Massachusetts	Evaluate the effect of long- and short-term exposure to PM2.5 on mortality rates	Yes	Estimate acute effects of PM2.5 exposure by regressing mortality rate for geographic cell and day on short-term exposure by matching geocoded mortality data with spatially detailed exposure data. Examine long-term exposure using relative incidence analysis.	Controls for socioeconomic factors and a surrogate for long-term smoking history, temperature. Test for effect modification by death location using interaction term between in-hospital death and short-term exposure. Look for modification of long term effect by low and high education groups, and for modification of short- and long-term effects by whether near to or far from monitors. Address misclassification issue	Uses current and previous day exposure for acute effects of exposure (sensitivity checks with longer lags) and separately estimates long-term effect	Yes	Background—Many studies have reported associations between ambient particulate matter (PM) and adverse health effects, focused on either short-term (acute) or long-term (chronic) PM exposures. For chronic effects, the studied cohorts have rarely been representative of the population. We present a novel exposure model combining satellite aerosol optical depth and land use data to investigate both the long- and short-term effects of PM2.5 exposures on population mortality in Massachusetts, United States, for the years 2000–2008. Methods—All deaths were geocoded. We performed two separate analyses: a time-series analysis (for short-term exposure) where counts in each geographic grid cell were regressed against cell-specific short-term PM2.5 exposure, temperature, socioeconomic data, lung cancer rates (as a surrogate for smoking), and a spline of time (to control for season and trends). In addition, for long-term exposure, we performed a relative incidence analysis using two long-term exposure metrics: regional 10 × 10 km PM2.5 predictions and local deviations from the cell average based on land use within 50 m of the residence. We tested whether these predicted the proportion of deaths from PM-related causes (cardiovascular and respiratory diseases). Results—For short-term exposure, we found that for every 10-μg/m3 increase in PM2.5 exposure there was a 2.8% increase in PM-related mortality (95% confidence interval [CI] = 2.0–3.5). For the long-term exposure at the grid cell level, we found an odds ratio (OR) for every 10-μg/m3 increase in long-term PM2.5 exposure of 1.6 (CI = 1.5–1.8) for particle-related diseases. Local PM2.5 had an OR of 1.4 (CI = 1.3– 1.5), which was independent of and additive to the grid cell effect. Conclusions—We have developed a novel PM2.5 exposure model based on remote sensing data to assess both short- and long-term human exposures. Our approach allows us to gain spatial resolution in acute effects and an assessment of long-term effects in the entire

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Krall, J.R., Anderson, G.B., Dominici, F., Bell, M.L., Peng, R.D.	Short-Term Exposure to Particulate Matter Constituents and Mortality in a National Study of U.S. Urban Communities	2013	Environmental Health Perspectives	PM2.5	All-cause non-accidental (ICD-9: 0-799, ICD-10: A00-R99)	72 urban US communities	All deaths	Evaluates the national, season-specific, and region-specific short-term associations between mortality and PM2.5 constituents	Yes	Estimate mortality effects of seven PM2.5 constituent species using Poisson time-series regression model and controlling for time and weather	Allows seasonal effect modification with interaction terms. Controlled for region-specific fixed effects by fitting separate community-specific single-pollutant models. Does not account for exposure misclassification, and does not allow controls for potential confounders to differ by location	Looks at short-term effects using average of same and previous day PM2.5	Yes	BACKGROUND: Although the association between PM2.5 mass and mortality has been extensively studied, few national-level analyses have estimated mortality effects of PM2.5 chemical constituents. Epidemiologic studies have reported that estimated effects of PM2.5 on mortality vary spatially and seasonally. We hypothesized that associations between PM2.5 constituents and mortality would not vary spatially or seasonally if variation in chemical composition contributes to variation in estimated PM2.5 mortality effects. OBJECTIVES: We aimed to provide the first national, season-specific, and region-specific associations between mortality and PM2.5 constituents. METHODS: We estimated short-term associations between nonaccidental mortality and PM2.5 constituents across 72 urban U.S. communities from 2000 to 2005. Using U.S. Environmental Protection Agency (EPA) Chemical Speciation Network data, we analyzed seven constituents that together compose 79-85% of PM2.5 mass: organic carbon matter (OCM), elemental carbon (EC), silicon, sodium ion, nitrate, ammonium, and sulfate. We applied Poisson time-series regression models, controlling for time and weather, to estimate mortality effects. RESULTS: Interquartile range increases in OCM, EC, silicon, and sodium ion were associated with estimated increases in mortality of 0.39% [95% posterior interval (PI): 0.08, 0.70%], 0.22% (95% PI: 0.00, 0.44), 0.17% (95% PI: 0.03, 0.30), and 0.16% (95% PI: 0.00, 0.32), respectively, based on single-pollutant models. We did not find evidence that associations between mortality and PM2.5 or PM2.5 constituents differed by season or region. CONCLUSIONS: Our findings indicate that some constituents of PM2.5 may be more toxic than others and. therefore. regulating PM total mass alone may
Kravchenko, J., Akushevich, I., Abernethy, A.P., Holman, S., Ross, W.G., Lyerly, H.K.	Long-Term Dynamics of Death Rates of Emphysema, Asthma, and Pneumonia and Improving Air Quality	2014	International Journal of Chronic Obstructive Pulmonary Disease	O3, SO2, NO2, CO, PM2.5, PM10	Emphysema (ICD-9: 492, ICD-10: J43), asthma (ICD-9: 493, ICD-10: J45, J46), pneumonia (ICD-9: 480.0, 480.1, 480.2, 480. 9, 485, 486, 487.0, 487.1, ICD-10: J11.00, J11.1, J12.0, J12.1, J12,2, J12.9, J18.0, J18.9)	North Carolina	All deaths	Analyze the associations between changes in state-wide average concentrations of pollutants and death rates of emphysema, asthma, and pneumonia	No	Use log-linear model to evaluate associations between long-term concentrations of ozone, SO2, NO2, CO, PM2.5 and PM10 for 5-year age groups. Produce age-adjusted death rates using standard 2000 NC population. After state-level analysis, did county-level analysis for those with data.	Included controls for age group-specific smoking prevalence and seasonal fluctuations of disease-specific respiratory deaths. They do not include factors like changes in socioeconomic status, because they say other studies have reported that race and social factors of small effect modification. They do not control for other changes over time, because they are looking at a monthly time-step.	Uses long-term exposure, with monthly concentrations	Yes	BACKGROUND: The respiratory tract is a major target of exposure to air pollutants, and respiratory diseases are associated with both short- and long-term exposures. We hypothesized that improved air quality in North Carolina was associated with reduced rates of death from respiratory diseases in local populations. MATERIALS AND METHODS: We analyzed the trends of emphysema, asthma, and pneumonia mortality and changes of the levels of ozone, sulfur dioxide (SO2), nitrogen dioxide (NO2), carbon monoxide (CO), and particulate matters (PM2.5 and PM10) using monthly data measurements from air-monitoring stations in North Carolina in 1993-2010. The log-linear model was used to evaluate associations between air-pollutant levels and age-adjusted death rates (per 100,000 of population) calculated for 5-year age-groups and for standard 2000 North Carolina population. The studied associations were adjusted by age group-specific smoking prevalence and seasonal fluctuations of disease-specific respiratory deaths. RESULTS: Decline in emphysema deaths was associated with decreasing levels of SO2 and CO in the air, decline in asthma deaths-with lower SO2, CO, and PM10 levels, and decline in pneumonia deaths-with lower levels of SO2. Sensitivity analyses were performed to study potential effects of the change from International Classification of Diseases (ICD)-9 to ICD-10 codes, the effects of air pollutants on mortality during summer and winter, the impact of approach when only the underlying causes of deaths were used, and when mortality and air-quality data were analyzed on the county level. In each case, the results of sensitivity analyses demonstrated stability. The importance of analysis of pneumonia as an underlying cause of death was also highlighted. CONCLUSION: Significant associations were observed between decreasing death

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Lepeule, J., Laden, F., Dockery, D., Schwartz, J.	Chronic Exposure to Fine Particles and Mortality: An Extended Follow-up of the Harvard Six Cities Study From 1974 to 2009	2012	Environmental Health Perspectives	PM2.5	All-cause, cardiovascular (ICD-9:400.0-440.9, ICD-10: I10.0-I70.9), lung-cancer (ICD-9: 162, ICD-10: C33.0-C34.9), chronic obstructive pulmonary disease (ICD-9: 490.0-496.0, ICD-10: J40.0-J47.0)	Six cities in eastern and midwestern U.S. (Watertown, MA, Kingston and Harriman, TE, parts of St. Louis, MI, Steubenville, OH, Portage, Wyocena, and Pardeeville, WI, Topeka, KA	Adults from the six cities	Tests the robustness of the association between chronic exposure to PM2.5 and mortality observed in original Harvard 6-cities study. Tests model specifications, association with specific causes of death etc.	Yes	Uses Cox proportional hazards model, stratified by sex, 1-year age groups, and time in the study. Also tests Poisson model with dummy variables for each year of follow-up, test various other model specifications.	Adjusts for possible case-level confounders, like smoking status, educational level, BMI. Acknowledge risk fo remaining confounders, like risk factors arisign after enrollment or unmeasured factors that co-vary with PM2.5, possible misclassification of cause of death. They limit the potential for residual cross-sectional confouding by relying on both between- and within-city contrasts in exposure. Check for effect modification by smoking status.	Uses second-degree polynomial distributed lag model to allow effects of exposure to be distributed from 1 to 5 years before death or censor	Yes	BACKGROUND: Epidemiologic studies have reported associations between fine particles (aerodynamic diameter ≤ 2.5 μm; PM2.5) and mortality. However, concerns have been raised regarding the sensitivity of the results to model specifications, lower exposures, and averaging time. OBJECTIVE: We addressed these issues using 11 additional years of follow-up of the Harvard Six Cities study, incorporating recent lower exposures. METHODS: We replicated the previously applied Cox regression, and examined different time lags, the shape of the concentration-response relationship using penalized splines, and changes in the slope of the relation over time. We then conducted Poisson survival analysis with time-varying effects for smoking, sex, and education. RESULTS: Since 2001, average PM2.5 levels, for all six cities, were < 18 μg/m3. Each increase in PM2.5 (10 μg/m3) was associated with an adjusted increased risk of all-cause mortality (PM2.5 average on previous year) of 14% [95% confidence interval (CI): 7, 22], and with 26% (95% CI: 14, 40) and 37% (95% CI: 7, 75) increases in cardiovascular and lung-cancer mortality (PM2.5 average of three previous years), respectively. The concentration-response relationship was linear down to PM2.5 concentrations of 8 μg/m3. Mortality rate ratios for PM2.5 fluctuated over time, but without clear trends despite a substantial drop in the sulfate fraction. Poisson models produced similar results. CONCLUSIONS: These results suggest that further public policy efforts that reduce fine particulate matter air pollution are likely to have continuing public health benefits.
Moolgavkar, S.H., McClellan, R.O., Dewanji, A., Turim, J., Luebeck, E.G., Edwards, E.	Time-Series Analyses of Air Pollution and Mortality in the United States: A Subsampling Approach	2013	Environmental Health Perspectives	PM10, O3, CO, NO2, SO2	All-cause non-accident	108 United States cities	All deaths, 1987-2000, from NMMAPS	Estimates maximum likelihoods of the common national effects of criteria pollutants on mortality	Use subsampling, where they randomly choose 4 cities without replacement from the 108 cities, and estimate the common pollutant effect for each sample. Ran 5,000 bootstrap cycles. Fit an over-dispersed Poisson model to the randomly chosen 4 cities. Investigate the shape of the concentration-response relationship for city-specific confounders, day of week effects, and time trends	Control for temperature and relative humidity in each of the 4 cities in each sample. Also control for day of the week, temporal trends, mean temperature on the previous day, and mean dew-point temperature--should control	Use a 1-day lag for pollutant exposure, i.e. 24-hr average pollutant concentration	Yes	No	Background: Hierarchical Bayesian methods have been used in previous papers to estimate national mean effects of air pollutants on daily deaths in time-series analyses. Objectives: We obtained maximum likelihood estimates of the common national effects of the criteria pollutants on mortality based on time-series data from ≤ 108 metropolitan areas in the United States. Methods: We used a subsampling bootstrap procedure to obtain the maximum likelihood estimates and confidence bounds for common national effects of the criteria pollutants, as measured by the percentage increase in daily mortality associated with a unit increase in daily 24-hr mean pollutant concentration on the previous day, while controlling for weather and temporal trends. We considered five pollutants [PM10, ozone (O3), carbon monoxide (CO), nitrogen dioxide (NO2), and sulfur dioxide (SO2)] in single- and multipollutant analyses. Flexible ambient concentration–response models for the pollutant effects were considered as well. We performed limited sensitivity analyses with different degrees of freedom for time trends. Results: In single-pollutant models, we observed significant associations of daily deaths with all pollutants. The O3 coefficient was highly sensitive to the degree of smoothing of time trends. Among the gases, SO2 and NO2 were most strongly associated with mortality. The flexible ambient concentration–response curve for O3 showed evidence of nonlinearity and a threshold at about 30 ppb. Conclusions: Differences between the results of our analyses and those reported from using the Bayesian approach suggest that estimates of the quantitative impact of pollutants depend on the choice of statistical approach, although results are not directly comparable because they are based on different data. In addition, the estimate of the O3-mortality coefficient depends on the amount of smoothing of time trends.

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Bart Ostro, J. Hu, D.Goldberg, P. Reynolds, A. Hertz, L. Bernstein, and M. J. Kleeman	Associations of Mortality with Long-Term Exposures to Fine and Ultrafine Particles, Species and Sources: Results from the California Teachers Study Cohort	2015	Environmental Health Perspectives	PM, Ultrafines	all-cause, cardiovascular, ischemic heart disease (IHD), and respiratory mortality	California	statewide cohort of > 100,000 women from the California Teachers Study, aged 30 and older	What is the effect of exposure to ultrafine particles, PM2.5, and the constituents of both pollutants on all-cause, cardiovascular, ischemic heart disease, and respiratory mortality among women in CA?	observed significant positive associations between IHD mortality and both fine and ultrafine particle species and sources.	Cox proportional hazards model	Controlled for twenty individual-level covariates, including smoking	No.	yes	Background: Although several cohort studies report associations between chronic exposure to fine particles (PM2.5) and mortality, few have studied the effects of chronic exposure to ultrafine (UF) particles. In addition, few studies have estimated the effects of the constituents of either PM2.5 or UF particles. Methods: We used a statewide cohort of > 100,000 women from the California Teachers Study who were followed from 2001 through 2007. Exposure data at the residential level were provided by a chemical transport model that computed pollutant concentrations from > 900 sources in California. Besides particle mass, monthly concentrations of 11 species and 8 sources or primary particles were generated at 4-km grids. We used a Cox proportional hazards model to estimate the association between the pollutants and all-cause, cardiovascular, ischemic heart disease (IHD), and respiratory mortality. Results: We observed statistically significant ($p < 0.05$) associations of IHD with PM2.5 mass, nitrate, elemental carbon (EC), copper (Cu), and secondary organics and the sources gas- and dieselfueled vehicles, meat cooking, and high-sulfur fuel combustion. The hazard ratio estimate of 1.19 (95% CI: 1.08, 1.31) for IHD in association with a 10-μg/m3 increase in PM2.5 is consistent with findings from the American Cancer Society cohort. We also observed significant positive associations between IHD and several UF components including EC, Cu, metals, and mobile sources. Conclusions: Using an emissions-based model with a 4-km spatial
Sacks, J.D., Ito, K., Wilson, W.e., Neas, L.M.	Impact of Covariate Models on the Assessment of the Air Pollution-Mortailty Association in a Single- and Multipollutant Context	2012	American Journal of Epidemiology	PM2.5, trace elements, CO, NO2, SO2, O3	Cardiovascular mortality (ICD-9: 390-429)	Philadelphia County, PA	All deaths, all ages	Uses daily speciation data to create a more clear interpretation of lagged associations, and examines air pollutant-mortality associations through a common dimension-reduction method.	No	Performed time-series analysis using a priori regression models from multicity epidemiologic studies. Tried 6 regression models that adjust for temporal trends and weather covariates. Used single-pollutant regression models to look at cardiovascular mortality associations, and then also tried multipollutant models. Checked for evidence of residual confounding or model misspecification in regression models using method developed by Flanders et al.	Controlled for season, temperature, and temporal trends using various methods. Controlled for multicollinearity by calculating the concurvity of each individual pollutant and source factor. Looked at multipollutant models to control for copollutant confounding.	Looked at associations of mortality with same day and previos day exposures	Yes	With the advent of multicity studies, uniform statistical approaches have been developed to examine air pollution-mortality associations across cities. To assess the sensitivity of the air pollution-mortality association to different model specifications in a single and multipollutant context, the authors applied various regression models developed in previous multicity time-series studies of air pollution and mortality to data from Philadelphia, Pennsylvania (May 1992–September 1995). Single-pollutant analyses used daily cardiovascular mortality, fine particulate matter (particles with an aerodynamic diameter ≤2.5 μm; PM2.5), speciated PM2.5, and gaseous pollutant data, while multipollutant analyses used source factors identified through principal component analysis. In single-pollutant analyses, risk estimates were relatively consistent across models for most PM2.5 components and gaseous pollutants. However, risk estimates were inconsistent for ozone in all-year and warm-season analyses. Principal component analysis yielded factors with species associated with traffic, crustal material, residual oil, and coal. Risk estimates for these factors exhibited less sensitivity to alternative regression models compared with single-pollutant models. Factors associated with traffic and crustal material showed consistently positive associations in the warm season, while the coal combustion factor showed consistently positive associations in the cold season. Overall, mortality risk estimates examined using a source-oriented approach yielded more stable and precise risk estimates, compared with single-pollutant analyses.

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Shi, L., Zanobetti, A., Kloog, I., Coull, B.A., Koutrakis, P., Melly, S. J., Schwartz, J.D.	Low-Concentration PM2.5 and Mortality: Estimating Acute and Chronic Effects in a Population-Based Study	2015	Environmental Health Perspectives	PM2.5	All-cause	New England (CT, MA, NH, ME, RI, VT)	>=65 years, people who died between 2003 and 2008	Estimates the effect of low-concentration on PM2.5 on mortality-- Note: restricts analysis to annual concentrations below 10 0 µg/m3 or daily concentrations below 30 µg/m3	Yes (short- and long-term with mutual adjustment, and short-term without mutual adjustment)	Uses Poisson regressions to simultaneously estimate acute and chronic effects, with mutual adjustment for short- and long-term exposure and controls for area-based confounders. Used satellite pollution data and mortality records from Medicare for 2003 to 2008	Controls for selection bias associated with non-random missing data in satellite pollution data. Controls for temperature, socio-economic variables, county-level smoking characteristics, day of the week. Subtracting long-term average exposure from short-term exposure should ensure that differences between ZIP codes in PM2.5 do not contribute to short-term effect estimate, so short-term effect is not confounded by variables that differ across ZIP codes. Acknowledge possible incompleteness of individual level controls. Allowed effect modification by population size.	Used same and previous day average for acute exposure, with sensitivity analysis, and calculated long-term exposure as 365-day moving average ending on date of death. Defined short-term exposure as difference between 2-day average and long-term average	Yes	BACKGROUND: Both short- and long-term exposures to fine particulate matter (PM2.5) are associated with mortality. However, whether the associations exist below the new EPA standards (12 µg/m3 of annual average PM2.5, 35 µg/m3 daily) is unclear. In addition, it is not clear whether results of previous time series studies (fit in larger cities) and cohort studies (fit in convenience samples) are generalizable to the general population. OBJECTIVES: To estimate the effects of low-concentration PM2.5 on mortality. METHODS: High resolution (1 × 1 km) daily PM2.5 predictions, derived from satellite aerosol optical depth retrievals, were employed. Poisson regressions were applied to the Medicare population (age>=65) in New England to simultaneously estimate the acute and chronic effects, with mutual adjustment for short- and long-term exposure, as well as area-based confounders. Models were also restricted to annual concentrations below 10 µg/m3 or daily concentrations below 30 µg/m3. RESULTS: PM2.5 was associated with increased mortality. In the cohort, 2.14% (95% CI: 1.38, 2.89%) and 7.52% (95% CI: 1.95, 13.40%) increases were estimated for each 10 µg/m3 increase in short- (2 day) and long-term (1 year) exposures, respectively. The associations still held for analyses restricted to low-concentration PM2.5 exposures. The corresponding estimates were 2.14% (95% CI: 1.34, 2.95%) and 9.28% (95% CI: 0.76, 18.52%). Penalized spline models of long-term exposure indicated a higher slope for mortality in association with exposures above versus below 6 µg/m3. In contrast, the association between short-term exposure and mortality appeared to be linear across the entire exposure distribution. CONCLUSIONS:
Thurston, G.D., Jiyoung Ahn, K. R. Cromar,Y. Shao, H. R. Reynolds, M. Jerrett, C. C. Lim, R. Shanley, Y. Park, and R. B. Hayes	Ambient Particulate Matter Air Pollution Exposure and Mortality in the NIH-AARP Diet and Health Cohort	2015	Environmental Health Perspectives	PM2.5	Hazard ratio for all-cause, CVD, respiratory disease	Six states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and two metropolitan areas (Detroit, MI and Atlanta, GA)	517,041 men and women enrolled in the National Institutes of Health-AARP cohort, ages 50 and up.	Particulate matter air pollution levels have been declining in recent years in the US.. so it is important to test these associations in another large U.S. cohort with detailed individual-level risk factor information on participants,especially one for which pollution exposures can be estimated at the individual participant residence level, and in more recent lower PM2.5 exposure years	yes for total and CVD mortality; analyses of California residents alone also yielded statistically significant PM2.5 mortality HR's for total and CVD mortality	Cox Proportional Hazard models yielded Hazard Ratio (HR) estimates per 10 µg/m3 of PM2.5 exposure	adjusted for the following individual covariates and potential risk factors at enrollment: race, education , marital status , Body Mass Index , alcohol consumption, and smoking history	No.	yes	Background: Outdoor fine particulate matter (PM2.5) has been identified as a global health threat, but the number of large U.S. prospective cohort studies with individual participant data remains limited, especially at lower recent exposures. Objectives: To test the relationship between long-term exposure PM2.5 and death risk from all non-accidental causes, cardiovascular (CVD), and respiratory diseases in 517,041 men and women enrolled in the National Institutes of Health-AARP cohort. Methods: Individual participant data were linked with residence PM2.5 exposure estimates across the continental U.S for a 2000-2009 follow up period when matching census-tract level PM2.5 exposure data were available. Participants enrolled ranged from 50-71 yrs. of age, residing in 6 U.S. States and 2 cities. Cox Proportional Hazard models yielded Hazard Ratio (HR) estimates per 10 µg/m3 of PM2.5 exposure. Results: PM2.5 exposure was significantly associated with total mortality (HR= 1.03, 95% CI =1.00, 1.05) and CVD mortality (HR=1.10, 95% CI=1.05, 1.15), but the association with respiratory mortality was not statistically significant (HR=1.05, 95% CI=0.98,1.13). A significant association was found with respiratory mortality only among never smokers (HR=1.27; 95% CI: 1.03, 1.56). Associations with 10 µg/m3 PM2.5 exposures in yearly participant residential annual mean, or in metropolitan area-wide mean, were consistent with baseline exposure model results. Associations with PM2.5 were similar when adjusted for ozone exposures. Analyses of California residents alone also yielded

Table 1. Mortality

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Vanos, J.K., Cakmak, S., Kalkstein, L.S., Yagouti, A.	Association of Weather and Air Pollution Interactions on Daily Mortality in 12 Canadian Cities	2015	Air Quality, Atmosphere and Health	NO2, O3, SO2, PM2.5	All-cause non-accident	12 Canadian cities	All deaths, 1981-2008	Investigates the short-term effects of exposure to air pollution on the relative risk of mortality	For each city and weather type, estimate a risk ratio due to exposure to each air pollutant using a distributed lag nonlinear model. Also look at interactive effects of exposure to two pollutants. Adjust for temporal variability using a categorical variable for day of week, and apply a natural cubic spline of time with one knot at each of 30, 120, 180, and 365 days of observation for monthly, 3-month, 6-month, and yearly time effects. Then pool selected models for each city into one estimate using a random effects model.	Look at effect modification by presence of other pollutant to reduce copollutant confounding. Remove temporal variability, and control for mean air temperature. Look at effect modification by type of weather.	Apply lags of 0-6 days for each pollutant, where total estimate summarizes effects of cumulative exposure over the previous days	Yes	Yes	It has been well established that both meteorological attributes and air pollution concentrations affect human health outcomes. We examined all cause nonaccident mortality relationships for 28 years (1981–2008) in relation to air pollution and synoptic weather type (encompassing air mass) data in 12 Canadian cities. This study first determines the likelihood of summertime extreme air pollution events within weather types using spatial synoptic classification. Second, it examines the modifying effect of weather types on the relative risk of mortality (RR) due to daily concentrations of air pollution (nitrogen dioxide, ozone, sulfur dioxide, and particulate matter <2.5 µm). We assess both single- and two-pollutant interactions to determine dependent and independent pollutant effects using the relatively new time series technique of distributed lag nonlinear modeling (DLNM). Results display dry tropical (DT) and moist tropical plus (MT+) weathers to result in a fourfold and twofold increased likelihood, respectively, of an extreme pollution event (top 5 % of pollution concentrations throughout the 28 years) occurring. We also demonstrate statistically significant effects of single-pollutant exposure on mortality ($p < 0.05$) to be dependent on summer weather type, where stronger results occur in dry moderate (fair weather) and DT or MT+ weather types. The overall average single-effect RR increases due to pollutant exposure within DT and MT+ weather types are 14.9 and 11.9 %, respectively. Adjusted exposures (two-way pollutant effect estimates) generally results in decreased RR estimates, indicating that the pollutants are not independent. Adjusting for ozone significantly lowers 67 % of the single-pollutant RR estimates and reduces model variability, which demonstrates that ozone significantly controls a portion of the mortality signal from the model. Our findings demonstrate the mortality risks of air pollution exposure to differ by weather type, with increased accuracy obtained when accounting for interactive effects through adjustment for dependent pollutants using a DLNM.
Villeneuve, P.J., Weichenthal, S.A., Crouse, D., Miller, A.B., To, T., Martin, R.V., van Donkelaar, A., Wall, C., Burnett, R.T.	Long-term Exposure to Fine Particulate Matter Air Pollution and Mortality Among Canadian Women	2015	Epidemiology	PM2.5	Coronary heart disease (ICD-9:410-414, ICD-10: I20-I25), cerebrovascular disease (ICD-9: 430-438, ICD-10: I60-I69), cardiovascular diseases combined (ICD-9: 400-440, ICD-10: I00-I99), all-cause non-accidental (ICD-9: 0-799, ICD-10: A00-V99), nonmalignant respiratory disease (ICD-9: 460-519, ICD-10: J00-J99), cancer (ICD-9: 140-239, ICD-10: C00-C99), lung cancer (ICD-9: 162, ICD-10: C33-C34)	Canada	Participants in the Canadian National Breast Screening Study between 1980 and 1985	Identify the association between long-term PM2.5 exposure and several causes of death	Yes (in particular, with nonaccidental and ischemic heart disease mortality)	Calculated individual-level estimates of long-term PM2.5 exposure and then used Cox proportional hazards models. Made concentration-response functions for cancer, ischemic heart disease, cardiovascular disease, and nonaccidental mortality	Note: most PM2.5 exposure is at low levels. Controlled for individual covariates like marital status, occupation, and education attained and neighborhood SES covariates. Looked at effect modification by place of birth (in Canada or elsewhere), whether participants had moved during first phase of follow-up, and whether they smoked. Did a formal threshold analysis for nonaccidental mortality, cardiovascular mortality, cancer mortality, and ischemic heart disease mortality. Acknowledges the potential for misclassification in exposure assignments	Used long-term exposure defined as average between 1998 and 2006	Yes	
Weichenthal, S., Villeneuve, P.J., Burnett, R.T., van Donkelaar, A., Martin, R.V., Jones, R.R., DellaValle, C.T., Sandler, D.P., Ward, M.H., Hoppin, J.A.	Long-Term Exposure to Fine Particular Matter: Association with Nonaccidental and Cardiovascular Mortality in the Agricultural Health Study Cohort	2014	Environmental Health Perspectives	PM2.5	All-cause non-accidental (ICD-9: <800, ICD-10:<V01), cardiovascular mortality (ICD-9: 400-440, ICD-10: I10-I70), ischemic heart disease (ICD-9: 412, 414, ICD-10: I25), cerebrovascular disease (ICD9: 430-438, ICD-10: I60-I69), lung cancer (ICD-9: 162, ICD-10: C34)	Primarily Iowa and North Carolina	U.S. Agricultural Health Study cohort	Examines the relationship between long-term PM2.5 exposure and non-accidental mortality in rural populations	Yes (with cardiovascular mortality among men, but no significant association with nonaccidental mortality in full cohort)	Assigned long-term PM2.5 exposure to subjects at enrollment, and estimated hazard ratios using Cox proportional hazards models. Graphed concentration-response functions usign natural splines for PM2.5 with two degrees of freedom using adjusted Cox survival models.	All models controlled for sex, state of enrollment, and birth year category. Race was not included as a control because almost all subjects were white. Moderately adjusted model also controlled for BMI and pack-years of smoking, and the most adjusted model controlled for SE factors and other lifestyle factors. Checked for effect modification by sex, state of enrollment, BMI, and time spent outdoors. Also checked for effect modification by occupational sources of PM2.5. Acknowledges potential for misclassification.	Uses six year average PM2.5 exposure to assess long-term exposure	Yes	

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Zanobetti, A., Austin, E., Coull, B.A., Schwartz, J., Koutrakis, P.	Health Effects of Multi-Pollutant Profiles	2014	Environmental International	PM2.5	All-cause non-accidental (ICD-9: 0-799, ICD-10: A00-R99)	greater Boston area: Middlesex, Norfolk, and Suffolk counties	All deaths	Evaluates whether the effect of PM2.5 on total mortality differed by distinct pollutant mixtures in Boston between 1999 and 2009	Yes	Used all-cause non-accidental daily mortality as the outcome of interest, and used two-day moving PM2.5 concentrations for the whole area. Using data for PM2.5 components, grouped days into 5 clusters. Then did Poisson generalized additive model, controlling for long-term trend and seasonality with natural cubic regression spline, day of the week indicators, for weather using natural cubic spline for same and previous day temperature, and for dew point temp. Then used interaction terms between PM2.5 and component cluster.	Provides controls for long-term time trend, seasonality, weather. Allows for effect modification by clusters of PM2.5 composition, and checked for effect modification by season.	Allows for some lag by using two-day moving PM2.5 average concentrations.	Yes	Background: The association between exposure to particle mass and mortality is well established; however, there are still uncertainties as to whether certain chemical components are more harmful than others. Moreover, understanding the health effects associated with exposure to pollutants mixtures may lead to new regulatory strategies. Objectives: Recently we have introduced a new approach that uses cluster analysis to identify distinct air pollutant mixtures by classifying days into groups based on their pollutant concentration profiles. In Boston during the years 1999–2009, we examined whether the effect of PM2.5 on total mortality differed by distinct pollution mixtures. Methods: We applied a time series analysis to examine the association of PM2.5 with daily deaths. Subsequently, we included an interaction term between PM2.5 and the pollution mixture clusters. Results: We found a 1.1 % increase (95% CI: 0.0, 2.2) and 2.3% increase (95% CI: 0.9–3.7) in total mortality for a 10 μg/m3 increase in the same day and the two-day average of PM2.5 respectively. The association is larger in a cluster characterized by high concentrations of the elements related to primary traffic pollution and oil combustion emissions with a 3.7% increase (95% CI: 0.4, 7.1) in total mortality, per 10 μg/m3 increase in the same day average of PM2.5. Conclusions: Our study shows a higher association of PM2.5 on total mortality during days with a strong contribution of traffic emissions, and fuel oil combustion. Our proposed method to create multi-pollutant profiles is robust, and provides a promising tool to identify multi-pollutant mixtures which can be linked to the health effects.

Table 2. Birth and Pregnancy Outcomes

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Basu, R., Harris, M., Sie, L., Malig, B., Broadwin, R., Green, R.	Effects of Fine Particulate Matter and its Constituents on Low Birth Weigth Among Full-Term Infants in California	2014	Environmental Research	PM2.5	Low Birth Weight	California	Infants born between 2000 and 2006 to mothers in California, singleton live full-term births with gestational age 37-44 weeks with available data	Evaluates relationships between prenatal exposure to PM2.5 and birth weight and looks at how specific PM2.5 constituents contribute to that risk	Yes	Performed linear regression analyses relating birth weight to continuous measures of PM2.5 and constituent exposure, with a separate model used for each exposure variable. Present results as change in birth weight associated with each interquartile range increase in trimester and full gest. period exposures. Also did logistic regression analyses, and present results as percent change in risk of LBW	Controlled for mothers' race/ethnicity, age, educational attainment, gestational age, month of birth, infant sex, temperature and humidity readings. Also did analyses stratified by season of birth, adjusted for region of California, and included zip code-level controls for SES. Also did analysis stratified by maternal age, race/ethnicity, education to check for effect modification. Did tests for linearity with quadratic terms on pollutants.	Calculated exposure over gestational period and for each trimester as averages of weekly exposure means	Yes	Relationships between prenatal exposure to fine particles (PM2.5) and birth weight have been observed previously. Few studies have investigated specific constituents of PM2.5, which may identify sources and major contributors of risk. We examined the effects of trimester and full gestational prenatal exposures to PM2.5 mass and 23 PM2.5 constituents on birth weight among 646,296 term births in California between 2000 and 2006. We used linear and logistic regression models to assess associations between exposures and birth weight and risk of low birth weight (LBW; <2500g), respectively. Models were adjusted for individual demographic characteristics, apparent temperature, month and year of birth, region, and socioeconomic indicators. Higher full gestational exposures to PM2.5 mass and several PM2.5 constituents were significantly associated with reductions in term birth weight. The largest reductions in birth weight were associated with exposure to vanadium, sulfur, sulfate, iron, elemental carbon, titanium, manganese, bromine, ammonium, zinc, and copper. Several of these PM2.5 constituents were associated with increased risk of term LBW. Reductions in birth weight were generally larger among younger mothers and varied by race/ethnicity. Exposure to specific constituents of PM2.5, especially traffic-related particles, sulfur constituents, and metals, were associated with decreased birth weight in California.
DeFranco, E., Hall, E., Hossain, M., Chen, A., Haynes, E.N., Jones, D., Ren, S., Lu, L., Muglia, L.	Air Pollution and Stillbirth Risk: Exposure to Airborne Particulate Matter During Pregnancy is Associated with Fetal Death	2015	PLoS One	PM2.5	Stillbirth	Ohio	Singleton births at 20-42 weeks of gestation without known major congenital anomalies 2006-2010, and w/ mother's residence within 10 of PM2.5 monitor	Evaluates the association between exposure to PM2.5 and stillbirth	Yes (with third trimester exposure)	Compared demographic, medical, and delivery characteristics of stillbirths to those of live births using t-test for continuous variable comparisons and X^2 tests for categorical variables. Estimated the association between stillbirth risk and high PM2.5 levels using generalized estimating equation model with logit link function.	Adjusted analysis for maternal age, race, education level, quantity of prenatal care, cigarette smoking status, season of conception. Did sensitivity analyses for more strict residential distance-to-monitor cut-off. Acknowledges potential for confounding by other pollutant exposure or unmeasured sociodemographic and pregnancy risks for stillbirth, which could be spatially-correlated. Possible misclassification bias from exposure data.	Calculated monthly averages of PM2.5 for each station, and then derived average PM2.5 exposure level for each trimester	Yes	**Objective:** To test the hypothesis that exposure to fine particulate air pollution (PM2.5) is associated with stillbirth. **Study Design:** Geo-spatial population-based cohort study using Ohio birth records (2006-2010) and local measures of PM2.5, recorded by the EPA (2005-2010) via 57 monitoring stations across Ohio. Geographic coordinates of the mother's residence for each birth were linked to the nearest PM2.5 monitoring station and monthly exposure averages calculated. The association between stillbirth and increased PM2.5 levels was estimated, with adjustment for maternal age, race, education level, quantity of prenatal care, smoking, and season of conception. **Results:** There were 349,188 live births and 1,848 stillbirths of non-anomalous singletons (20-42 weeks) with residence ≤10 km of a monitor station in Ohio during the study period. The mean PM2.5 level in Ohio was 13.3 μg/m3 [±1.8 SD, IQR(Q1: 12.1, Q3: 14.4, IQR: 2.3)], higher than the current EPA standard of 12 μg/m3. High average PM2.5 exposure through pregnancy was not associated with a significant increase in stillbirth risk, adjOR 1.21(95% CI 0.96,1.53), nor was it increased with high exposure in the 1st or 2nd trimester. However, exposure to high levels of PM2.5 in the third trimester of pregnancy was associated with 42% increased stillbirth risk, adjOR 1.42(1.06,1.91). **Conclusions:** Exposure to high levels of fine particulate air pollution in the third trimester of pregnancy is associated with increased stillbirth risk. Although the risk increase associated with high PM2.5 levels is modest, the potential impact on overall stillbirth rates could be robust as all pregnant women are potentially at risk.
Ebisu, K., Bell, M.L.	Airborne PM2.5 Chemical Components and Low Birth Weight in the Northeastern and Mid-Atlantic Regions of the United States	2012	Environmental Health Perspectives	PM2.5, PM10, CO, NO2, O3, SO2	Low Birth Weight	northeastern and mid-Atlantic U.S.	All births 2000-2007	Examines whether birth weight is affected by PM2.5, PM10, and gaseous pollutants	Close to significant	Calculated exposures during gestation and each trimester for each pollutant. Characterized births as low or normal birth weight, and then used logistic regression with adjustment for various birth-specific and regional controls	Controlled for maternal race, marital status, tobacco consumption during pregnancy, alcohol consumption during pregnancy, highest education, age, infant sex, gestational length, when trimester prenatal care began, first in birth order, delivery method, average apparent temperature for each trimester, season of birth, and year of birth., regional indicators. Estimated two-pollutant models for pollutants that showed statistically significant associations with LBW in single-pollutant models and were not highly correlated with each other, and allowed effect modification by sex, race	Calculates average exposure during gestation and each trimester	Yes	**Background:** Previous studies on air pollutants and birth outcomes have reported inconsistent results. Chemical components of particulate matter ≤ 2.5 μm (PM2.5) composition are spatially - heterogeneous, which might contribute to discrepancies across PM2.5 studies. **Objectives:** We explored whether birth weight at term is affected by PM2.5, PM10 (PM ≤ 10 μm), and gaseous pollutants. **Methods:** We calculated exposures during gestation and each trimester for PM2.5 chemical components, PM10, PM2.5, carbon monoxide, nitrogen dioxide, ozone, and sulfur dioxide for births in 2000-2007 for states in the northeastern and mid-Atlantic United States. Associations between exposures and risk of low birth weight (LBW) were adjusted by family and individual characteristics and region. Interaction terms were used to investigate whether risk differs by race or sex. **Results:** Several PM2.5 chemical components were associated with LBW. Risk increased 4.9% (95% CI: 3.4, 6.5%), 4.7% (3.2, 6.2%), 5.7% (2.7, 8.8%), and 5.0% (3.1, 7.0%) per interquartile range increase of PM2.5 aluminum, elemental carbon, nickel, and titanium, respectively. Other PM2.5 chemical components and gaseous pollutants showed associations, but were not statistically significant in multipollutant models. The trimester associated with the highest relative risk differed among pollutants. Effect estimates for PM2.5 elemental carbon and nickel were higher for infants of white mothers than for those of African-American mothers, and for males than females. **Conclusions:** Most exposure levels in our study area were in compliance with U.S. Environmental Protection Agency air pollution standards; however, we identified associations between PM2.5 components and LBW. Findings suggest that some PM2.5 components may be more harmful than others, and that some groups may be particularly susceptible.

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Faiz, A.S., Rhoads, G.G., Demissie, K., Lin, Y., Kruse, L., Rich, D.Q.	Does Ambient Air Pollution Trigger Stillbirth?	2013	Epidemiology	PM2.5, CO, NO2, SO2	Stillbirth	New Jersey	Stillbirths 1998-2004	Investigates whether sudden increase in the mean ambient air pollutant concentration immediately before delivery triggers stillbirth	Yes (for various lag periods, not modified by maternal risk factors)	For each stillbirth, assign concentration of air pollutants from closest monitoring site within 10 km of maternal residence. Use a time-stratified case-crossover design and conditional logistic regression to estimate relative odds of stillbirth associated with IQR increase in mean pollutant concentrations.	Evaluate effect modification by maternal risk factors.	Look at mean pollutant concentrations on lag day 2 and lag days 2 through 6 before delivery.	Yes	**Objective:** We previously reported an increased risk of stillbirth associated with increases in trimester-specific ambient air pollutant concentrations. Here, we consider whether sudden increase in the mean ambient air pollutant concentration immediately before delivery triggers stillbirth. **Methods:** We used New Jersey linked fetal death and hospital discharge data and hourly ambient air pollution measurements from particulate matter ≤ 2.5 mm (PM2.5), carbon monoxide (CO), nitrogen dioxide (NO2), and sulfur dioxide (SO2) monitors across New Jersey for the years 1998-2004. For each stillbirth, we assigned the concentration of air pollutants from the closest monitoring site within 10 km of the maternal residence. Using a time-stratified case-crossover design and conditional logistic regression, we estimated the relative odds of stillbirth associated with interquartile range (IQR) increases in the mean pollutant concentrations on lag day 2 and lag days 2 through 6 before delivery, and whether these associations were modified by maternal risk factors. **Results:** The relative odds of stillbirth increased with IQR increases in the mean concentrations of CO (odds ratio [OR] = 1.20, 95% confidence interval [CI] = 1.05-1.37), SO2 (OR = 1.11, 95% CI = 1.02-1.22), NO2 (OR = 1.11, 95% CI = 0.97-1.26), and PM2.5 (OR = 1.07, 95% CI = 0.93-1.22) 2 days before delivery. We found similar associations with increases in pollutants 2 through 6 days before delivery. These associations were not modified by maternal risk factors. **Conclusion:** Short-term increases in ambient air pollutant concentrations immediately before delivery may trigger stillbirth.
Gray, S.C., Edwards, S.E., Schultz, B.D., Miranda, M.L.	Assessing the Impact of Race, Social Factors and Air Pollution on Birth Outcomes: A Population-Based Study	2014	Environmental Health	PM2.5, O3	Low birth weight, birth weight, preterm birth, small for gestational age	North Carolina	All registered livebirths, singletons, no diagnosed congenital anomalies at the time of birth	Examines the joint effects of air pollution and measures of SES in a population level analysis of pregnancy outcomes in North Carolina.	Yes (with reductions in birth weight, LBW, and SGA)	Used linear and logistic mixed regression models. Represented birthweight as a continuous outcome variable, and the others as binary outcomes.	Control for gestatoinal age, maternal race/ethnicity, maternal education, maternal age at delivery, trimester prenatal care began m tobacco use during pregnancy, marital status at delivery, year of birth, parity, infant sex, and census tract-level median household income.	Calculated average exposure over full pregnancy	Yes	Background: Both air pollution exposure and socioeconomic status (SES) are important indicators of children's health. Using highly resolved modeled predictive surfaces, we examine the joint effects of air pollution exposure and measures of SES in a population level analysis of pregnancy outcomes in North Carolina (NC). Methods: Daily measurements of particulate matter <2.5 μm in aerodynamic diameter (PM2.5) and ozone (O3) were calculated through a spatial hierarchical Bayesian model which produces census-tract level point predictions. Using multilevel models and NC birth data from 2002-2006, we examine the association between pregnancy averaged PM2.5 and O3, individual and area-based SES indicators, and birth outcomes. Results: Maternal race and education, and neighborhood household income were associated with adverse birth outcomes. Predicted concentrations of PM2.5 and O3 were also associated with an additional effect on reductions in birth weight and increased risks of being born low birth weight and small for gestational age. Conclusions: This paper builds on and complements previous work on the relationship between pregnancy outcomes and air pollution exposure by using 1) highly resolved air pollution exposure data; 2) a five-year population level sample of pregnancies; and 3) including personal and areal level measures of social determinants of pregnancy outcomes. Results show a stable and negative association between air pollution exposure and adverse birth outcomes. Additionally, the more socially disadvantaged populations are at a greater risk; controlling for both SES and environmental stressors provides a better understanding of the contributing factors to poor children's health outcomes.

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Ha, S., Hu, H., Roussos-Ross, D., Haidong, K., Roth, J., Xu, X.	The Effects of Air Pollution on Adverse Birth Outcomes	2014	Environmental Research	PM2.5, O3	Term low birth weight, preterm delivery (PTD), and very PTD	Florida	All singleton live births in Florida 2004-2005 with data, excluding outlier birth weights and gestational age	Studies the association between prenatal exposure to PM2.5 and O3 and the risk of adverse birth outcomes	Yes (exposure from each trimester is significant, with strongest effect in the second trimester)	Used univariate and multivariate logistic regression models. Later did multi-pollutant models to control for confounding by other pollutants. For all analyses, compared births with a defined negative outcome with healthy births.	Controls for covariates including infant's gender, maternal age, gestational age, maternal education, maternal race, marital status, prenatal care, pregnancy tobacco use, pregnancy alcohol consumption, maternal risk factors maternal infection, maternal complications, season of conception, etc. Used census block-level median household income and unemployment categories. Did capture area sensitivity analysis looking only at births within 5 miles of monitor stations.	Looked at average pollutant concentration in each trimester	Yes	**Background:** Air pollution has been shown to have adverse effects on many health outcomes including cardiorespiratory diseases and cancer. However, evidence on the effects of prenatal exposure is still limited. The purpose of this retrospective cohort study is to evaluate the effects of prenatal exposure to air pollutants including particulate matter with aerodynamic diameter less than 2.5 μm (PM2.5) and ozone (O3) on the risk of adverse birth outcomes (ABOs) including term low birth weight (LBW), preterm delivery (PTD) and very PTD (VPTD). **Methods:** singleton births from 2004 to 2005 in Florida were included in the study (N=423,719). Trimester-specific exposures to O3 and PM2.5 at maternal residence at delivery were estimated using the National Environmental Public Health Tracking Network data, which were interpolated using Hierarchical Bayesian models.**Results:** After adjustment for potential confounders such as demographics, medical and lifestyle factors PM2.5 exposures in all trimesters were found to be significantly and positively associated with the risk of all ABOs. Second-trimester exposure had the strongest effects. For an interquartile range (IQR) increase in PM2.5 during the second trimester, the risk of term LBW, PTD and VPTD increased by 3% [95% confidence interval (CI): 1-6%)], 12% (11-14%) and 22% (18-25%), respectively. O3 was also found to be positively associated with PTD and VPTD with the strongest effects over the whole pregnancy period [3% (1-5%) for PTD and 13% (7-19%) for VPTD for each IQR increase]. However, O3 was observed to have protective effects on term LBW. Results were consistent for multi-pollutant models. **Conclusion:** PM2.5 has consistent adverse effects on ABOs whereas O3 has inconsistent effects. These findings warrant further investigation.
Harris, G., Thompson, W.D., Fitzgerald, E., Wartenberg, D.	The Association of PM2.5 with Full Term Low Birth Weight at Different Spatial Scales	2015	Environmental Research	PM2.5	Full term low birth weight	CT, ME, MN, NJ, NY, UT, WI	Births 2001-2004	Assesses if there is an association between exposure to PM2.5 and low birth weight, and whether that association varies according to spatial and temporal resolution of the exposure or according to timing of the exposure during pregnancy	Yes (with highest association during first trimester, but diminished with finer spatial resolution)	Used logistic regression models to estimate odds ratios of PM2.5 exposure with full term birth weight, initially running regressions separately for each state and then pooling all state data together. Finally, included a state by PM exposure interaction term in the pooled data model. Modeled the exposure/response relationship as loglinear. Run analysis at different spatial scales, using county-level exposure and then "grid-level" for a few states	Checked for non-linearity by using a quadratic term. Adjusted models for mothers' age, martial status, education, race/ethnicity, prenatal care, sex of the child, smoking status, presence of an pregnancy complications. Also adjusted for census block-level SES variables. Acknowledge possibility of misclassification bias in county-level exposure analysis. Also census-block SES data might leave room for confounding.	Consider four exposure periods: full gestation period and three trimesters	Yes	There is interest in determining the relationship between fine particulate matter air pollution and various health outcomes, including birth outcomes such as term low birth weight. Previous studies have come to different conclusions. In this study we consider whether the effect may vary by location and gestational period. We also compare results when using different spatial resolutions for the air concentration estimates. Among the seven states considered, New Jersey and New York had the highest PM2.5 levels (average full gestation period exposures of 13 μg/m(3)) and the largest rate of low birth weight births (2.6 and 2.8%, respectively); conversely Utah and Minnesota had the lowest PM2.5 levels (9 μg/m(3)) and the lowest rates of low birth weight births (2.1 and1.9%, respectively). There is an association between PM2.5 exposure and low birth weight in New York for the full gestation period and all three trimesters, in Minnesota for the full gestation period and the first and third trimesters, and in New Jersey for the full gestation period and the first trimester. When we pooled the data across states, the OR for the full gestation period was 1.030 (95% CI: 1.022-1.037) and it was highest for the first trimester (OR 1.018; CI: 1.013-1.022) and decreasing during the later trimesters. When we used a finer spatial resolution, the strengths of the associations tended to diminish and were no longer statistically significant. We consider reasons why these differences may occur and their implications for evaluating the effects of PM2.5 on birth outcomes.

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Hu, H., Ha, S., Henderson, B.H., Warner, T.D., Roth, J., Kan, H., Xu, X.	Association of Atmospheric Particulate Matter and Ozone with Gestational Diabetes Mellitus	2015	Environmental Health Perspectives	PM2.5, O3	Gestational diabetes mellitus	Florida	Live singleton births Jan 2004-Dec 2005, no prevous preterm births or prepregnancy diabetes mellitus, no congential abnormalities etc.	Examines the association between GDM and two ambient air pollutants (PM2.5, O3)	Yes (but less so in copollutant model)	Examined distribution of categorical covariates and continuous exposures between women with GDM and without GDM. Ran logistic regression models to investigate associations between risk of GDM and exposure to air pollution during different trimesters of prenancy. Ran sensitivity analysis testing for potential bias from using indicator for missing data.	Ran an unadjusted model and model adjusting for maternal age, race/ethnicity, education, marital status, prenatal care, season and year of conception, urbanization, and median household income at census block group-level. Evaluated co-pollutant logistic models to assess potential confounding. Ran sensitivity analyses to test for potential misclassification of exposure etc.	Daily concentrations averaged over each of the first two trimesters and full gestational period	Yes	**Background:** Ambient air pollution has been linked to the development of gestational diabetes mellitus (GDM). However, evidence of the association is very limited, and no study has estimated the effects of ozone. **Methods:** We used Florida birth vital statistics records to investigate the association between the risk of GDM and two air pollutants (PM2.5 and O3) among 410,267 women who gave birth in Florida between 2004 and 2005. Individual air pollution exposure was assessed at women's home address at time of delivery using the Hierarchical Bayesian space-time statistical model. We further estimated associations between air pollution exposures during different trimesters and GDM. **Results:** After controlling for nine covariates, increased odds of GDM with per 5 µg/m3 increase in PM2.5 (ORTrimester1=1.16; 95% CI: 1.11, 1.21; ORTrimester2=1.15; 95% CI: 1.10, 1.20; ORPregnancy=1.20; 95% CI: 1.13, 1.26) and per 5 ppb increase in O3 (ORTrimester1=1.09; 95% CI: 1.07, 1.11; ORTrimester2=1.12; 95% CI: 1.10, 1.14; ORPregnancy=1.18; 95% CI: 1.15, 1.21) were observed during both the first trimester and second trimester as well as the full pregnancy in single-pollutant models. Comparing to the single-pollutant model, the ORs for O3 were almost identical in the co-pollutant model. However, the ORs for PM2.5 during the first trimester and the full pregnancy attenuated, and no association was observed for PM2.5 during the second trimester in the co-pollutant model (OR=1.02; 95% CI: 0.98, 1.07).**Conclusion:** This population-based study suggests that exposure to air pollution during pregnancy is associated with increased risk of GDM in Florida, USA.
Hyder, A., Lee, H.J., Koutrakis, P., Belanger, K., Bell, M.L.	PM2.5 Exposure and Birth Outcomes: Use of Satellite- and Monitor-Based Data	2014	Epidemiology	PM2.5	Mean birth weight at term birth, low birth weight at term, small for gestational age, and preterm birth	CT and MA	All births 2000-2006	Evaluates the effect of PM2.5 exposure on birth outcomes using existing monitoring data and emerging method of modeled estimates based on satellite data	Yes (for low birth weight, not preterm birth)	Used date of birth and gestational age to establish start and end dates for gestational exposure and used two methods for PM2.5 exposure assessment: monitor data and modeled estimates based on satellite data. Calculated trimester-specific and overall exposure during gestation based on mother's residence. Used logistic regression for binary outcomes (term LBW, SGA, preterm birth) and linear regression for birth weight	Controlled for mother's age, marital status, education, race/ethnicity, prenatal care, smoking, type of birth, season of conception, medical risk factors, medical risk due to previous preterm birth of SGA, baby's sex, gestational age, year of conception, trimester-specific apparent temperature, and state of residence	Looks at average exposure during gestational period and for each trimester	Yes	**Background:** Air pollution may be related to adverse birth outcomes. Exposure information from land-based monitoring stations often suffers from limited spatial coverage. Satellite data offer an alternative data source for exposure assessment. **Methods:** We used birth certificate data for births in Connecticut and Massachusetts, United States (2000-2006). Gestational exposure to PM2.5 was estimated from US Environmental Protection Agency monitoring data and from satellite data. Satellite data were processed and modeled by using two methods-denoted satellite (1) and satellite (2)-before exposure assessment. Regression models related PM2.5 exposure to birth outcomes while controlling for several confounders. Birth outcomes were mean birth weight at term birth, low birth weight at term (<2500 g), small for gestational age (SGA, <10th percentile for gestational age and sex), and preterm birth (<37 weeks). **Results:** Overall, the exposure assessment method modified the magnitude of the effect estimates of PM2.5 on birth outcomes. Change in birth weight per interquartile range (2.41 µg/m) increase in PM2.5 was -6 g (95% confidence interval = -8 to -5), -16 g (-21 to -11), and -19 g (-23 to -15), using the monitor, satellite (1), and satellite (2) methods, respectively. Adjusted odds ratios, based on the same three exposure methods, for term low birth weight were 1.01 (0.98-1.04), 1.06 (0.97-1.16), and 1.08 (1.01-1.16); for SGA, 1.03 (1.01-1.04), 1.06 (1.03-1.10), and 1.08 (1.04-1.11); and for preterm birth, 1.00 (0.99-1.02), 0.98 (0.94-1.03), and 0.99 (0.95-1.03). **Conclusions:** Under exposure assessment methods, we found associations between PM2.5 exposure and adverse birth outcomes particularly for birth weight among term births and for SGA. These results add to the growing concerns that air pollution adversely affects infant health and suggest that analysis of health consequences based on satellite-based exposure assessment can provide additional useful information.

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Kloog, I., Melly, S.J., Ridgway, W.L., Coull, B.A., Schwartz, J.	Using New Satellite Based Exposure Methods to Study the Association Between Pregnancy PM2.5 Exposure, Premature Birth and Birth Weight in Massachusetts	2012	Environmental Health	PM2.5	Preterm delivery	Massachusetts	All singleton live births Jan 1, 2000- Dec 31, 2008	Evaluates the association between premature birth and birth weight with exposure to ambient PM2.5 levels during pregnancy	Yes (significant negative relation with birth weight and small significant positive association with premature birth)	Performed a linear mixed regression model using birth weight among full term births as outcome and a logistic mixed regression model using preterm/full term birth as the outcome. Regressed on mean PM2.5 exposure prior to delivery. Used a random intercept for census tract to capture unmeasured similarities in persons in the same neighborhood.	Controlled for open space and individual-level mother's race, mother's years of education, Kotelchuck index of adequacy of prenatal care utilization, gestational age, cigarettes smoked, chronic conditions of mother, previous occurrence of preterm birth, gender of infant, median income at census tract-level.	Look at exposure 30 days, 90 days, and 270 days before the delivery date	Yes	**Background:** Adverse birth outcomes such as low birth weight and premature birth have been previously linked with exposure to ambient air pollution. Most studies relied on a limited number of monitors in the region of interest, which can introduce exposure error or restrict the analysis to persons living near a monitor, which reduces sample size and generalizability and may create selection bias. **Methods:** We evaluated the relationship between premature birth and birth weight with exposure to ambient particulate matter (PM2.5) levels during pregnancy in Massachusetts for a 9-year period (2000–2008). Building on a novel method we developed for predicting daily PM2.5 at the spatial resolution of a 10x10km grid across New-England, we estimated the average exposure during 30 and 90 days prior to birth as well as the full pregnancy period for each mother. We used linear and logistic mixed models to estimate the association between PM2.5 exposure and birth weight (among full term births) and PM2.5 exposure and preterm birth adjusting for infant sex, maternal age, maternal race, mean income, maternal education level, prenatal care, gestational age, maternal smoking, percent of open space near mothers residence, average traffic density and mothers health. **Results:** Birth weight was negatively associated with PM2.5 across all tested periods. For example, a 10 μg/m3 increase of PM2.5 exposure during the entire pregnancy was significantly associated with a decrease of 13.80 g [95% confidence interval (CI) =−21.10, -6.05] in birth weight after controlling for other factors, including traffic exposure. The odds ratio for a premature birth was 1.06 (95% confidence interval (CI) = 1.01–1.13) for each 10 μg/m3 increase of PM2.5 exposure during the entire pregnancy period. **Conclusions:** The presented study suggests that exposure to PM2.5 during the last month of pregnancy contributes to risks for lower birth weight and preterm birth in infants.
Laurent, O., Hu, J., Li, L., Cockburn, M., Escobedo, L., Kleeman, M.J., Wu, J.	Sources and Contents of Air Pollution Affecting Term Low Birth Weight in Los Angeles County, California, 2001-2008	2014	Environmental Research	PM2.5, NO2, O3	Low Birth Weight	Los Angeles County, CA	Singleton livebirths with plausible combinations of birth weight and gestational age, no birth defects, 2001-2008	Studies the relationships between LBW in term born infants and exposures to particles by size fraction, source, and chemical composition, and complementary components of air pollution	Yes (with significant effect modification by socioeconomic status, chronic hypertension, diabetes, BMI)	Estimated generalized additive models, using a logistic link function with a quasi-binomial distribution. Did sensitivity analysis looking at the effect of adjustent for population density, diabetes, chronic hypertension, and preeclampsia.	Adjusted for maternal race/ethnicity, education level, parity, trimester of pregnancy during which primary care began and infant's gender. Also adjusted for maternal age, length of gestation and median household income by census block group. Tried controlling for both seasonal and long-term temporal trends using a smoothed function of the day of conception. Looks at adjustment for maternal height, BMI, and weight gain during pregnancy. Looked at effect modification by maternal race/ethnicity, education, median block group income, hypertension, diabetes, and preeclampsia. Evaluated correlation between pollutants, but seems to use single pollutant models--unsure	Looked at average pollutant concentration for entire pregnancy and for each trimester	Yes	Background: Low birth weight (LBW, <2500 g) has been associated with exposure to air pollution, but it is still unclear which sources or components of air pollution might be in play. The association between ultrafine particles and LBW has never been studied. Objectives: To study the relationships between LBW in term born infants and exposure to particles by size fraction, source and chemical composition, and complementary components of air pollution in Los Angeles County (California, USA) over the period 2001–2008. Methods: Birth certificates (n=960,945) were geocoded to maternal residence. Primary particulate matter (PM) concentrations by source and composition were modeled. Measured fine PM, nitrogen dioxide and ozone concentrations were interpolated using empirical Bayesian kriging. Traffic indices were estimated. Associations between LBW and air pollution metrics were examined using generalized additive models, adjusting for maternal age, parity, race/ethnicity, education, neighborhood income, gestational age and infant sex. Results: Increased LBW risks were associated with the mass of primary fine and ultrafine PM, with several major sources (especially gasoline, wood burning and commercial meat cooking) of primary PM, and chemical species in primary PM (elemental and organic carbon, potassium, iron, chromium, nickel, and titanium but not lead or arsenic). Increased LBW risks were also associated with total fine PM mass, nitrogen dioxide and local traffic indices (especially within 50 m from home), but not with ozone. Stronger associations were observed in infants born to women with low socioeconomic status, chronic hypertension, diabetes and a high body mass index. Conclusions: This study supports previously reported associations between traffic-related pollutants and LBW and suggests other pollution sources and components, including ultrafine particles, as possible risk factors.

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Lee, P.C., Roberts, J.M., Catov, J.M., Talbott, E.O., Ritz, B.	First Trimester Exposure to Ambient Air Pollution, Pregnancy Complications and Adverse Birth Outcomes in Allegheny County, PA	2013	Maternal and Child Health Journal	PM10, PM2.5, O3	Preeclampsia, gestational hypertension, preterm delivery	Allegheny County, PA	Live singleton births at Magee-Women's Hospital between 1997 and 2002	Examines the association between air pollution during the first trimester and pregnancy complications and poor birth outcomes	Yes (with preeclampsia, gestational hypertension, preterm delivery)	Performed multiple logistic regression with robust variance estimators to account for non-independence, since many women lived within the same zip code. Treated pollutant concentrations as continuous variables and reported associations as per IQR and per-unit increases.	Controlled for maternal age, race/ethnicity, parity, # cigarettes smoked during pregnancy, season of birth, and year of conception. Considered several other potential confounders, but did not include. Conducted sensitivity analyses stratified by maternal race/ethnicity and smoking status. Acknowledge the potential for misclassification of exposure because participants may have moved.	Looked at average air pollution concentrations over the first trimester	Yes	Despite numerous studies of air pollution and adverse birth outcomes, few studies have investigated preeclampsia and gestational hypertension, two pregnancy disorders with serious consequences for both mother and infant. Relying on hospital birth records, we conducted a cohort study identifying 34,705 singleton births delivered at Magee-Women's Hospital in Pittsburgh, PA between 1997 and 2002. Particle (<10 μm-PM10; <2.5 μm-PM2.5) and ozone (O3) exposure concentrations in the first trimester of pregnancy were estimated using the space-time ordinary Kriging interpolation method. We employed multiple logistic regression estimate associations between first trimester exposures and preeclampsia, gestational hypertension, preterm delivery, and small for gestational age (SGA) infants. PM2.5 and O3 exposures were associated with preeclampsia (adjusted OR = 1.15, 95% CI = 0.96-1.39 per 4.0 μg/m(3) increase in PM2.5; adjusted OR = 1.12, 95% CI = 0.89-1.42 per 16.8 ppb increase in O3), gestational hypertension (for PM2.5 OR = 1.11, 95 % CI = 1.00-1.23; for O3 OR = 1.12, 95 % CI = 0.97 1.29), and preterm delivery (for PM2.5 ORs = 1.10, 95% CI = 1.01-1.20; for O3 ORs = 1.23, 95% CI = 1.01-1.50). Smaller 5-8 % increases in risk were also observed for PM10 with gestational hypertension and SGA, but not preeclampsia. Our data suggest that first trimester exposure to particles, mostly PM2.5, and ozone, may increase the risk of developing preeclampsia and gestational hypertension, as well as preterm delivery and SGA.
Mobasher, Z., Salam, M.T., Goodwin, T.M., Lurmann, F., Ingles, S.A., Wilson, M.L.	Associations Between Ambient Air Pollution and Hypertensive Disorders of Pregnancy	2013	Environmental Research	CO, NO2, O3, PM10, PM2.5	Hypertensive Disorders of Pregnancy	Southern California	Women giving birth in Los Angeles 1999-2008 at Los Angeles County+USC Women's and Children's Hospital, predominately Hispanic	Investigates the role of trimester-specific ambient air pollution on risk for hypertensive disorder of pregnancy	Yes (with 1st trimester exposure, modified by BMI)	Retrospective case-control study. Performed correlation analysis to determine Pearson's correlation coefficients for all air pollutants. Then used unconditional logistic regression to examine the association between ambient air pollution and odds of hypertensive disorder of pregnancy	Adjusted analysis for maternal age, parity, maternal smoking status, exposure to secondhand smoke during pregnancy, indicator of calendar year of pregnancy, BMI. Acknowledge the possibility of exposure misclassification, response rate may introduce bias.	Uses average pollution in each trimester	Yes	**Background:** Exposure to ambient air pollution is linked to adverse pregnancy outcomes. Previous reports examining the relationship between ambient air pollution and Hypertensive Disorders of Pregnancy have been inconsistent. **Objectives:** We evaluated the effects of ambient air pollution on the odds of Hypertensive Disorder of Pregnancy and whether these associations varied by body mass index (BMI). **Methods:** We conducted a retrospective, case-control study among 298 predominantly Hispanic women (136 clinically confirmed cases) who attended the Los Angeles County+University of Southern California Women's and Children's Hospital during 1996–2008. Trimester-specific carbon monoxide (CO), nitrogen dioxide (NO2), ozone (O3), and particulate matter with aerodynamic diameter <10 μm and <2.5 μm (PM10, PM2.5) exposure were estimated based on 24-hour exposure level at residential address. Logistic regression models were fitted to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for two standard deviation increase in exposure levels. **Results:** Exposures to CO and PM2.5 in the 1st trimester were significantly associated with Hypertensive Disorders of Pregnancy, and these associations were modified by BMI. In non-obese women (BMI <30), 1st trimester exposures to PM2.5 and CO were significantly associated with increased odds of Hypertensive Disorder of Pregnancy (ORs per 2-standard deviation increase in PM2.5 (7 μg/m3) and CO (1 ppm) exposures were 9.10 [95% CI: 3.33–24.6] and 4.96 [95% CI: 1.85–13.31], respectively). Additionally, there was a significantly positive association between exposure to O3 in the 2nd trimester and Hypertensive Disorder of Pregnancy (OR per 15 ppb=2.05; 95% CI: 1.22–3.46).**Conclusion:** Among non-obese women, 1st trimester exposure to PM2.5 and carbon monoxide are associated with increased odds of Hypertensive Disorder of Pregnancy.

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Padula, A.M., Tager, I.B., Carmichael, S.L., Hammond, S.K., Yang, W., Lurmann, F., Shaw, G.M.	Ambient Air Pollution and Traffic Exposures and Congenital Heart Defects in the San Joaquin Valley of California	2014	Paediatric and Perinatal Epidemiology	CO, NO2, PM10, PM2.5, O3	Congenital heart defects--heterotaxia, d-Transposition of the great arteries, tetralogy of fallot, double outlet right ventricle (TGA and other)	San Joaquin Valley, CA	All births in San Joaquin valley	Investigates the association between ambient air pollution and congenital heart defects	Yes (with transposition of great arteries and inversely associated with perimembranous ventricular septal defects)	Cases included live births, stillbirths, and pregnancy terminations with congenital heart defects, and controls were non-malformed live-born infants randomly selected from birth hospitals to represent the population. First analyzed the association between pollutants and traffic metrics. Then did multivariate logistic regression analyses to estimate adjusted odds ratios.	In analysis adjusted for maternal race/ethnicity, education, and early prenatal vitamin use. Considered other controls, like maternal age, parity, infant sex, year of birth etc., but did not include them. Investigated effect modification by cigarette smoking. Acknowledge that they may have misclassified exposure, particularly if vulnerable windows for certain heart defects are narrower than they expected. Also potential bias from early fetal loss, possible other confounders	Used average air pollution measurements from the first and second month of pregnancy	Yes	**Background:** Congenital anomalies are a leading cause of infant morbidity and mortality. Studies suggest associations between environmental contaminants and some anomalies, although evidence is limited. **Methods:** We used data from the California Center of the National Birth Defects Prevention Study and the Children's Health and Air Pollution Study to estimate the odds of 27 congenital heart defects with respect to quartiles of seven ambient air pollutant and traffic exposures in California during the first 2 months of pregnancy, 1997-2006 (n = 822 cases and n = 849 controls). **Results:** Particulate matter < 10 microns (PM10) was associated with pulmonary valve stenosis [adjusted odds ratio (aOR)Fourth Quartile = 2.6] [95% confidence intervals (CI) 1.2, 5.7] and perimembranous ventricular septal defects (aORThird Quartile = 2.1) [95% CI 1.1, 3.9] after adjusting for maternal race/ethnicity, education and multivitamin use. PM2.5 was associated with transposition of the great arteries (aORThird Quartile = 2.6) [95% CI 1.1, 6.5] and inversely associated with perimembranous ventricular septal defects (aORFourth Quartile = 0.5) [95% CI 0.2, 0.9]. Secundum atrial septal defects were inversely associated with carbon monoxide (aORFourth Quartile = 0.4) [95% CI 0.2, 0.8] and PM2.5 (aORFourth Quartile = 0.5) [95% CI 0.3, 0.8]. Traffic density was associated with muscular ventricular septal defects (aORFourth Quartile = 3.0) [95% CI 1.2, 7.8] and perimembranous ventricular septal defects (aORThird Quartile = 2.4) [95% CI 1.3, 4.6], and inversely associated with transposition of the great arteries (aORFourth Quartile = 0.3) [95% CI 0.1, 0.8]. **Conclusions:** PM10 and traffic density may contribute to the occurrence of pulmonary valve stenosis and ventricular septal defects, respectively. The results were mixed for other pollutants and had little consistency with previous studies.
Pedersen, M., Stayner, L., Slama, R., Sorenson, M., Figueras, F., Nieuwenhuijsen, M.J., Raaschou-Nielsen, O., Dadvand, P.	Ambient Air Pollution and Pregnancy-Induced Hypertensive Disorders: A Systematic Review and Meta-Analysis	2014	Hypertension	NO2, NOx, CO, O3, PM10, PM2.5	Gestational hypertension, preeclampsia		Nine studies were conducted in the United States, 5 in Europe, and 3 in Iran, Japan, and Australia	Systematically reviews and meta-analyzes studies to investigate the association between exposure to ambient air pollution and pregnancy-induced hypertensive disorders	Yes	Gathered epidemiological studies that were in English, published between December 2009-December 2013, and ultimately used 17. Then calculated combined risk estimates using random-effect models.		Looks at long-term exposure	Yes	Pregnancy-induced hypertensive disorders can lead to maternal and perinatal morbidity and mortality, but the cause of these conditions is not well understood. We have systematically reviewed and performed a meta-analysis of epidemiological studies investigating the association between exposure to ambient air pollution and pregnancy-induced hypertensive disorders including gestational hypertension and preeclampsia. We searched electronic databases for English language studies reporting associations between ambient air pollution and pregnancy-induced hypertensive disorders published between December 2009 and December 2013. Combined risk estimates were calculated using random-effect models for each exposure that had been examined in ≥4 studies. Heterogeneity and publication bias were evaluated. A total of 17 articles evaluating the impact of nitrogen oxides (NO2, NOX), particulate matter (PM10, PM2.5), carbon monoxide (CO), ozone (O3), proximity to major roads, and traffic density met our inclusion criteria. Most studies reported that air pollution increased risk for pregnancy-induced hypertensive disorders. There was significant heterogeneity in meta-analysis, which included 16 studies reporting on gestational hypertension and preeclampsia as separate or combined outcomes; there was less heterogeneity in findings of the 10 studies reporting solely on preeclampsia. Meta-analyses showed increased risks of hypertensive disorders in pregnancy for all pollutants except CO. Random-effect meta-analysis combined odds ratio associated with a 5-μg/m3 increase in PM2.5 was 1.57 (95% confidence interval, 1.26-1.96) for combined pregnancy-induced hypertensive disorders and 1.31 (95%confidence interval, 1.14-1.50) for preeclampsia [corrected]. Our results suggest that exposure to air pollution increases the risk of pregnancy-induced hypertensive disorders.

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Pereira, G., Belanger, K., Ebisu, K., Bell, M.L.	Fine Particulate Matter and Risk of Preterm Birth in Connecticut in 2000-2006: a Longitudinal Study	2014	American Journal of Epidemiology	PM2.5	Pre-term birth	Connecticut	Women who gave vaginal birth between 2000 and 2006 with data, lived close to monitor, gave birth at least twice during study period	Assessed whether a woman has more risk of preterm delivery when she has elevated exposure to ambient PM2.5 during pregnancy	Not quite, but very close	Calculated rate of preterm birth by race for the reference population by year of conception and compared this rate with the temporal trend in mean PM2.5. Partitioned spatiotemporal variation in exposure by using random intercepts models fit with Proc Mixed. Matched pregnancies by mother, and estimated separate models for each trimester and for whole-pregnancy exposure	Adjusted for average number of cigarettes smoked per day, maternal age, parity. Checked sensitivity of results to adjustments for carbon monoxide, nitrogen dioxide, sulfur dioxide, ambient max temp, area-level socioeconomic factors.	Used average exposure for each trimester and for the whole pregnancy	Yes	Several studies have examined associations between particulate matter with aerodynamic diameter of 2.5 μm or less (PM2.5) and preterm birth, but it is uncertain whether results were affected by individual predispositions (e.g., genetic factors, social conditions) that might vary considerably between women. We tested the hypothesis that a woman is at greater risk of preterm delivery when she has had elevated exposure to ambient PM2.5 during a pregnancy than when she has not by comparing pregnancies in the same woman. From 271,204 births, we selected 29,175 women who had vaginal singleton livebirths at least twice in Connecticut in 2000-2006 (n = 61,688 births). Analyses matched pregnancies to the same woman. Adjusted odds ratios per interquartile range (2.33-μg/m(3)) increase in PM2.5 in the first trimester, second trimester, third trimester, and whole pregnancy were 1.07 (95% confidence interval (CI): 1.00, 1.15), 0.96 (95% CI: 0.90, 1.03), 1.03 (95% CI: 0.97, 1.08), and 1.13 (95% CI: 1.01, 1.28), respectively. Among Hispanic women, the odds ratio per interquartile range increase in whole-pregnancy exposure was 1.31 (95% CI: 1.00, 1.73). Pregnancies with elevated PM2.5 exposure were more likely to result in preterm birth than were other pregnancies to the same woman at lower exposure. Associations were most pronounced in the first trimester and among Hispanic women.
Rappazzo, K.M., Daniels, J.L., Messer, L.C., Poole, C., Lobdell, D.T.	Exposure to Fine Particulate Matter During Pregnancy and Risk of Preterm Birth Among Women in New Jersey, Ohio, and Pennsylvania, 2000-2005	2014	Environmental Health Perspectives	PM2.5	Preterm birth	New Jersey, Pennsylvania, Ohio	Singleton births that competed at least 20 weeks of gestation during 2000-2005, no birth defects	Examines the association between ambient PM2.5 and risk of preterm birth	Yes (with exposure during fourth week of gestation, week of birth, and 2 weeks before birth)	Estimated adjusted risk differences using modified Poisson regression with an identity link. Estimated absolute effect measures. Modeled each category of preterm birth separately as a dichotomous outcome, and included those at risk of PTB at a given time point as appropriate, treating PM2.5 as a continuous variable. Besides looking at weekly exposure, evaluated average exposure during trimesters and entire pregnancy for sake of comparison with other studies.	Identified possible confounders using directed acyclic graph analysis. Controlled for maternal race/ethnicity, education level, marital status, age at delivery, smoking status, prenatal care initiation, parity, daily average ozone. Assessed effect modification by ozone, state, region, and population density. Performed sensitivity analysis to include temperature and season of conception, and included smoking. Acknowledge possibility of exposure misclassification, and residual confounding from census block-level SES data, bias from women who couldn't be geolocated etc.	Estimated exposure as during each week of gestation anchored from last menstrual period, and each week lagged from birth	Yes	**Background:** Particulate matter ≤ 2.5 μm in aerodynamic diameter (PM2.5) has been variably associated with preterm birth (PTB). **Methods:** We assembled a cohort of singleton pregnancies that completed ≥ 20 weeks of gestation during 2000–2005 using live birth certificate data from three states (Pennsylvania, Ohio, and New Jersey) (n = 1,940,213; 8% PTB). We estimated mean PM2.5 exposures for each week of gestation from monitor-corrected Community Multi-Scale Air Quality modeling data. RDs were estimated using modified Poisson linear regression and adjusted for maternal race/ethnicity, marital status, education, age, and ozone. **Results:** RD estimates varied by exposure window and outcome period. Average PM2.5 exposure during the fourth week of gestation was positively associated with all PTB outcomes, although magnitude varied by PTB category [e.g., for a 1-μg/m3 increase, RD = 11.8 (95% CI: –6, 29.2); RD = 46 (95% CI: 23.2, 68.9); RD = 61.1 (95% CI: 22.6, 99.7); and RD = 28.5 (95% CI: –39, 95.7) for preterm births during 20–27, 28–31, 32–34, and 35–36 weeks, respectively]. Exposures during the week of birth and the 2 weeks before birth also were positively associated with all PTB categories. **Conclusions:** Exposures beginning around the time of implantation and near birth appeared to be more strongly associated with PTB than exposures during other time periods. Because particulate matter exposure is ubiquitous, evidence of effects of PM2.5 exposure on PTB, even if small in magnitude, is cause for concern.
Robledo, C.A., Mendola, P., Yeung, E., Mannisto, T., Sundaram, R., Liu, D., Ying, Q., Sherman, S., Grantz, K.L.	Preconception and Early Pregnancy Air Pollution Exposures and Risk of Gestational Diabetes Mellitus	2015	Environmental Research	PM2.5, PM10, NOx, CO, SO2, O3	Gestational diabetes mellitus (ICD-9: 648.8)	United States	Singleton births without pregestational diabetes, Participants in Consortium on Safe Labor	Investigates the association between critera air pollutants regulated by the US EPA and the risk of gestational diabetes mellitus	No	First calcualted Spearman rank correlations between each pollutants. Then fitted binary regression models with the log link function to estimate relative risks for IQR increase for each pollutant. Used a first order autoregressive covariance structure to account for within-cluster correlation for women with more than one singleton pregnancy during study period. Made separate models for air pollutants during each exposure window.	Assessed potential confounding by maternal characteristics, including parity, marital status, insurance status, hospital type, prenatal history of smoking and alcohol, study sites. Looked at effect modification by maternal BMI. Also looked at multi-pollutant models to look at confounding by other pollutants.	Included pre-conception exposure (91 days before last menstrual period), average exposure during 1st trimester, weekly averages for gestational weeks 1 through 24	Yes	Background: Air pollution has been linked to gestational diabetes mellitus (GDM) but no studies have evaluated impact of preconception and early pregnancy air pollution exposures on GDM risk. Methods: Electronic medical records provided data on 219,952 singleton deliveries to mothers with (n=11,334) and without GDM (n=208,618). Average maternal exposures to particulate matter (PM) ≤ 2.5μm (PM2.5) and PM2.5 constituents, PM ≤ 10μm (PM10), nitrogen oxides (NOx), carbon monoxide, sulfur dioxide (SO2) and ozone (O3) were estimated for the 3-month preconception window, first trimester, and gestational weeks 1-24 based on modified Community Multiscale Air Quality models for delivery hospital referral regions. Binary regression models with robust standard errors estimated relative risks (RR) for GDM per interquartile range (IQR) increase in pollutant concentrations adjusted for study site, maternal age and race/ethnicity. Results: Preconception maternal exposure to NOX (RR=1.09, 95% CI: 1.04, 1.13) and SO2 (RR=1.05, 1.01, 1.09) were associated with increased risk of subsequent GDM and risk estimates remained elevated for first trimester exposure. Preconception O3 was associated with lower risk of subsequent GDM (RR=0.93, 0.90, 0.96) but risks increased later in pregnancy. Conclusion: Maternal exposures to NOx and SO2 preconception and during the first few weeks of pregnancy were associated with increased GDM risk. O3 appeared to increase GDM risk in association with mid-pregnancy exposure but not in earlier time windows. These common exposures merit further investigation.

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Salihu, H.M., Ghaji, N., Mbah, A.K., Alio, A.P., August, E.M., Boubakari, I.	Particulate Pollutants and Racial/Ethnic Disparity in Feto-Infant Morbidity Outcomes	2012	Maternal and Child Health Journal	PM2.5, PM10, PM10-2.5	Low birth weight (<2500 g), very low birth weight (<1500 g), preterm birth (<37 weeks), very preterm birth (<33 weeks), and small for gestational age	Hillsborough County, Florida	All singleton live births, 2000-2007	Evaluates the impact of exposure to PM10, PM2.5, and PM10-2.5 on fetal morbidity outcomes, with the unique feature of delineating differential effects on racial/ethnic subgroups.	Yes (with greatest risk for very low birth weight)	Compared baseilne characteristics between women who were exposed and those who were not using Chi-square test for categorical variables and t-tests for continuous variables. Constructed regressino models and assessed goodness-of-fit using the -2 log likelihood ratio test. Estimated significant of main effects using the Wald test.	Allowed effect modification by exposure to other particulate categories. Controlled for race/ethnicity, maternal age, marital status, education level, parity, cigarette smoking during pregnancy, adequacy of prenatal care, and maternal pregnancy complications. They acknowledge the possibility of confounding by other pollutants. Looked at effect modification by race and other characteristics.	Looked at average exposure ovre the whole pregnancy	Yes	We sought to assess the association between air particulate pollutants and feto-infant morbidity outcomes across racial/ethnic subgroups. This is a retrospective cohort study from 2000 through 2007 based on three linked databases: (1) The Florida Hospital Discharge database; (2) The vital statistics records of singleton live births in Florida; (3) Air pollution and meteorological data from the Environmental Protection Agency. Using computerized mathematical modeling, we assigned exposure values of the air pollutants of interest (PM2.5, PM10 and the PM coarse fraction [PM10− PM2.5]) to mothers over the period of pregnancy based on Euclidean minimum distance from the air pollution monitoring sites. The primary outcomes of interest were: low birth weight, very low birth weight, preterm birth, very preterm birth, and small for gestational age (SGA). We used adjusted odds ratios to approximate relative risks. We observed increased risk for overall feto-infant morbidity outcome in women exposed to any of the three particulate pollutants (values above the median). Exposed women had increased odds for low birth weight, very low birth weight and preterm birth with the greatest risk being that for very low birth weight (AOR = 1.27, 95% CI = 1.08–1.49). Black women exposed to any particulate pollutant had the greatest odds for all the morbidity outcomes, most pronounced for very low birth weight (AOR = 3.32, 95% CI = 2.56–4.30). Environmental particulate pollutants are associated with adverse feto-infant outcomes among exposed women, especially blacks. Black–white disparity in adverse fetal outcomes is widened in the presence of these pollutants, which provide a target for intervention.
Savitz, D.A., Elston, B., Bobb, J.F., Cloughterty, J.E., Dominici, F., Ito, K., Johnson, S., McAlexander, T., Ross, Z., Shmool, J.L., Matte, T.D., Wellenius, G.A.	Ambient Fine Particulate Matter, Nitrogen Dioxide, and Hypertensive Disorders of Pregnancy in New York City	2015	Epidemiology	PM2.5, NO2	Gestational hypertension, mild preeclampsia, severe preeclampsia	New York City		Investigates the association between PM2.5 and NO2 and the development of hypertensive disorders of pregnancy		**Cannot see methodology because I cannot access the full text.	Controls for individual risk factors, socioeconomic conditions, and delivery hospital. **Cannot see more without accessing the full text.	Looks at average exposure during the first and second trimester	**Cannot see estimates without accessing full text	Background: Previous studies suggested a possible association between fine particulate matter air pollution (PM2.5) and nitrogen dioxide (NO2) and the development of hypertensive disorders of pregnancy, but effect sizes have been small and methodologic weaknesses preclude firm conclusions. Methods: We linked birth certificates in New York City in 2008-2010 to hospital discharge diagnoses and estimated air pollution exposure based on maternal address. The New York City Community Air Survey provided refined estimates of PM2.5 and NO2 at the maternal residence. We estimated the association between exposures to PM2.5 and NO2 in the first and second trimester and risk of gestational hypertension, mild preeclampsia, and severe preeclampsia among 268,601 births. Results: In unadjusted analyses, we found evidence of a positive association between both pollutants and gestational hypertension. However, after adjustment for individual covariates, socioeconomic deprivation, and delivery hospital, we did not find evidence of an association between PM2.5 or NO2 in the first or second trimester and any of the outcomes. Conclusions: Our data did not provide clear evidence of an effect of ambient air pollution on hypertensive disorders of pregnancy. Results need to be interpreted with caution considering the quality of the available exposure and health outcome measures and the uncertain impact of adjusting for hospital. Relative to previous studies, which have tended to identify positive associations with PM2.5 and NO2, our large study size, refined air pollution exposure estimates, hospital-based disease ascertainment, and little risk of confounding by socioeconomic deprivation, does not provide evidence for an association.

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Stingone, J.A., Luben, T.J., Daniels, J.L, Fuentes, M., Richardson, D.B., Aylsworth, A.S,. Herring, A.H., Anderka, M., Botto, L., Correa, A., Gilboa, S.M., Langlois, P.H., Mosley, B., Shaw, G.M>, Siffel, C., Olshan, A.F.	Maternal Exposure to Criteria Air Pollutants and Congenital Heart Defects in Offspring: Results from the National Birth Defects Prevention Study	2014	Environmental Health Perspectives	CO, NO2, O3, PM10, PM2.5, SO2	Simple, isolated congenital heart defects with no extra-cardiac birth defects present		Participants in National Birth Defects Prevention Study, live births and stillbirths > 20 weeks gestation or at least 500 g	Investigates the association between maternal exposure to air pollutants during weeks 2-8 of pregnancy and their associations with congenital heart defects	Yes (with hypoplastic left heart syndrome, inversely associated with atrial septal defects, some attenuation of results by multipollutant models)	Construfted two-stage hierarchical regression models to account for correlation between estimates and partially address multiple inference. In first stage, ran uconditional, polytomous logistic regression model of individual CHDs on exposure defined as either all 1-week average exposure or single 7-week average. Looked at sensitivity to changes in the model specification.	Controled for maternal age, race/ethnicity, educational attainment, household income, tobacco smoking in the first month of pregnancy, alcohol consumption during the first trimester, maternal nativity. Also controlled for distance to closest major road, prepregnancy BMI, maternal occupational status. Looked at multipollutant models using a principal component analysis.	Calculated average pollutant concentration for weeks 2-8 of pregnancy and 1-week averages for each week	Yes	Background: Epidemiologic literature suggests that exposure to air pollutants is associated with fetal development. Objectives: We investigated maternal exposures to air pollutants during weeks 2-8 of pregnancy and their associations with congenital heart defects. Methods: Mothers from the National Birth Defects Prevention Study, a nine-state case-control study, were assigned 1-week and 7-week averages of daily maximum concentrations of carbon monoxide, nitrogen dioxide, ozone, and sulfur dioxide and 24-hr measurements of fine and coarse particulate matter using the closest air monitor within 50 km to their residence during early pregnancy. Depending on the pollutant, a maximum of 4,632 live-birth controls and 3,328 live-birth, fetal-death, or electively terminated cases had exposure data. Hierarchical regression models, adjusted for maternal demographics and tobacco and alcohol use, were constructed. Principal component analysis was used to assess these relationships in a multipollutant context. Results: Positive associations were observed between exposure to nitrogen dioxide and coarctation of the aorta and pulmonary valve stenosis. Exposure to fine particulate matter was positively associated with hypoplastic left heart syndrome but inversely associated with atrial septal defects. Examining individual exposure-weeks suggested associations between pollutants and defects that were not observed using the 7-week average. Associations between left ventricular outflow tract obstructions and nitrogen dioxide and between hypoplastic left heart syndrome and particulate matter were supported by findings from the multipollutant analyses, although estimates were attenuated at the highest exposure levels. Conclusions: Using daily maximum pollutant levels and exploring individual exposure-weeks revealed some positive associations between certain pollutants and defects and suggested potential windows of susceptibility during pregnancy.
Symanski, E., Davila, M., McHugh, M.K., Waller, D.K., Zhang, X., Lai, D.	Maternal Exposure to Fine Particulate Pollution During Nattow Gestational Periods and Newborn Health in Harris County, Texas	2014	Maternal and Child Health Journal	PM2.5	Preterm birth and small for gestational age	Harris County, Texas	All live births, Jan 1, 2005-Dec 31, 2007	Examine association between three categories of PTB and term SGA and PM2.5 during periods of gestation		Performed correlation analyses for all exposure metrics. Then used logistic regression analyses to examine the associations between PTB and term SGA as outcomes and the air pollution metrics as predictors. Performed separate analysis for each outcome, each of which included different 4-week chunks from gestational period.	Controlled for birth season, mother's smoking status, race, level of education, age, BMI, receipt of Women, Infants, and Children services, trimester prenatal care initiated, parity, and type of payment for delivery	Mean exposure for every weeks of pregnancy		It remains unclear when the fetus is most susceptible to the effects of particulate air pollution. We conducted a population-based study in a large urban area to evaluate associations between preterm birth (PTB) and fetal growth and exposures to fine particles (PM2.5) during narrow periods of gestation. We identified 177,816 births during 2005–2007 among mothers who resided in Harris County, Texas at the time of delivery. We created three mutually exclusive categories of mildly (33–36 completed weeks of gestation), moderately (29–32 weeks of gestation), and severely (20–28 weeks of gestation) PTB, and among full term infants, we identified those who were born small for their gestational age. Using routine air monitoring data, we generated county-level daily time series of estimated ambient air levels of PM2.5 and then computed exposure metrics during every 4 weeks of a mother's pregnancy. We evaluated associations in each 4-week period using multiple logistic regression. A 10 µg/m3 increase in PM2.5 exposure in the first 4 weeks of pregnancy significantly increased the odds of mildly, moderately and severely PTB by 16, 71 and 73 %, respectively. Associations were stronger when infants with birth defects were excluded. Our findings indicate an association between PM2.5 and PTB, with stronger associations for moderately and severely PTB infants. Efforts should continue to implement stricter air quality standards and improve ambient air quality.

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Tanner, J.P., Salemi, J.L., Stuart, A.L., Yu, H., Jordan, M.M., DuClos, C., Cavicchia, P., Correia, J.A., Watkins, S.M., Kirby, R.S.	Associations Between Exposure to Ambient Benzene and PM2.5 During Pregnancy and the Risk of Selected Birth Defects in Offspring	2015	Environmental Research	PM2.5	Birth defects (ICD-9: 740-759.9., ICD-10: Q codes), which include spina bifida, orofacial clefts, CCHDs	Florida	Singleton infants born from 2000-2009	Assesses the association between maternal-fetal exposure to ambient benzene and PM2.5 and several types of birth defect	Yes (with non-isolated truncus arteriosis, total anomalous pulmonary venous return, coarctation of the aorta, interrupted aortic arch, isolated and non-isolated critical congenital heart defect)	Performed multivariate Poisson regressions to estimate adjusted prevalence ratios, using exposure concentration quartiles where the lowest quartile was used as the exposure reference group. Stratified analysis by isolated and non-isolated birth defect cases.	Adjusted the models for a number of potential confounders, including maternal race/ethnicity, maternal nativity, maternal age in years, maternal education, maternal marital status, parity, block group median household income, infant's birth cohort and sex	Average exposure at 3-4 weeks for spina bifida, 3-8 weeks for CCHDs, cleft lip used 3-8 weeks, cleft palate 5-12 weeks, combo cleft lip cleft palate 3-12 weeks	Yes	**Objective:** A growing number of studies have investigated the association between air pollution and the risk of birth defects, but results are inconsistent. The objective of this study was to examine whether maternal exposure to ambient PM2.5 or benzene increases the risk of selected birth defects in Florida. **Methods:** We conducted a retrospective cohort study of singleton infants born in Florida from 2000 to 2009. Isolated and non-isolated birth defect cases of critical congenital heart defects, orofacial clefts, and spina bifida were identified from the Florida Birth Defects Registry. Estimates of maternal exposures to PM2.5 and benzene for all case and non-case pregnancies were derived by aggregation of ambient measurement data, obtained from the US Environmental Protection Agency Air Quality System, during etiologically relevant time windows. Multivariable Poisson regression was used to estimate adjusted prevalence ratios (aPRs) and 95% confidence intervals (CIs) for each quartile of air pollutant exposure. **Results:** Compared to the first quartile of PM2.5 exposure, higher levels of exposure were associated with an increased risk of non-isolated truncus arteriosus (aPR4th Quartile, 8.80; 95% CI, 1.11-69.50), total anomalous pulmonary venous return (aPR2nd Quartile, 5.00; 95% CI, 1.10-22.84), coarctation of the aorta (aPR4th Quartile, 1.72; 95% CI, 1.15-2.57; aPR3rd Quartile, 1.60; 95% CI, 1.07-2.41), interrupted aortic arch (aPR4th Quartile, 5.50; 95% CI, 1.22-24.82), and isolated and non-isolated any critical congenital heart defect (aPR3rd Quartile, 1.13; 95% CI, 1.02-1.25; aPR4th Quartile, 1.33; 95% CI, 1.07-1.65). Mothers with the highest level of exposure to benzene were more likely to deliver an infant with an isolated cleft palate (aPR4th Quartile, 1.52; 95% CI, 1.13-2.04) or any orofacial cleft (aPR4th Quartile, 1.29; 95% CI, 1.08-1.56). An inverse association was observed between exposure to benzene and non-isolated pulmonary atresia (aPR4th Quartile, 0.19; 95% CI, 0.04-0.84). **Conclusion:** Our results suggest a few associations between exposure to ambient PM2.5 or benzene and specific birth defects in Florida. However, many related
Vinikoor-Imler, L.C., Davis, J.A., Meyer, R.E., Luben, T.J.	Early Prenatal Exposure to Air Pollution and its Associations with Birth Defects in a State-Wide Birth Cohort From North Carolina	2013	Birth Defects Research Part A: Clinical and Molecular Teratology	PM2.5, O3	Birth defects	North Carolina	All NC resident singleton live births 2003-2005	Examines association between various birth defects and predicted concentrations of pollutants in both single- and co-pollutant models	No	Performed binomial regression to estimate association between a one-unit change in IQR for PM2.5 and O3 concentrations and each birth defect category in single and copollutant models.	Controlled for confounding with maternal age, maternal race/ethnicity, rural-urban continuum codes. Considered but did not include others, like maternal education, parity, maternal smoking, marital status etc. Acknowledge potential exposure misclassification.	Average exposure during weeks 3-8 of pregnancy	Yes	**Background:** Few studies have examined the potential relationship between air pollution and birth defects. The objective of this study was to investigate whether maternal exposure to particulate matter (PM2.5) and ozone (O3) during pregnancy is associated with birth defects among women living throughout North Carolina. **Methods:** Information on maternal and infant characteristics was obtained from North Carolina birth certificates and health service data (2003-2005) and linked with information on birth defects from the North Carolina Birth Defects Monitoring Program. The 24-hr PM2.5 and O3 concentrations were estimated using a hierarchical Bayesian model of air pollution generated by combining modeled air pollution predictions from the U.S. Environmental Protection Agency's Community Multi-Scale Air Quality model with air monitor data from the Environmental Protection Agency's Air Quality System. Maternal residence was geocoded and assigned pollutant concentrations averaged over weeks 3 to 8 of gestation. Binomial regression was performed and adjusted for potential confounders. **Results:** No association was observed between either PM2.5 or O3 concentrations and most birth defects. Positive effect estimates were observed between air pollution and microtia/anotia and lower limb deficiency defects, but the 95% confidence intervals were wide and included the null. **Conclusion:** Overall, this study suggested a possible relationship between air pollution concentration during early pregnancy and certain birth defects (e.g., microtia/anotia, lower limb deficiency defects), although this study did not have the power to detect such an association. The risk for most birth defects does not appear to be affected by ambient air pollution.
Vinikoor-Imler, L.C., Stewart, T.G., Luben, T.J., Davis, J.A., Langlois, P.H.	An Exploratory Analysis of the Relationship Between Ambient Ozone and Particulate Matter Concentrations During Early Pregnancy and Selected Birth Defects in Texas	2015	Environmental Pollution	PM2.5, O3	Birth defects: anencephaly, spinal bifida, hydrocephalus, anotia or microtia, conotruncal heart defects, septal heart defects, atrioventricular septal defects, obstructive heart defects, anomalous pulmonary venous return, oral clefts, esophageal atresia, intestinal atresia, biliary atresia, hypospadias, longitudinal limb deficiency defects, transverse limb deficiency defects, craniosynostosis, diaphragmatic hernia, omphalocele, gastroschisis	Texas	All singleton live births 2002-2006	Examines associations between O3 and PM2.5 concentrations	No	Calculated exposure using heirarchical Bayesian model combining data from air monitors with estimates from EPA's CMZQ model. Calculated associations using logistic regression in single-pollutant models and co-pollutant models.	Covariates included prenatal care in first trimester, number of previous live births, maternal age, maternal education, maternal race/ethnicity, urbanicity. Performed co-pollutant and single-pollutant models to evaluate confounding.	Average concentrations during the first trimester	Yes	We performed an exploratory analysis of ozone (O3) and fine particulate matter (PM2.5) concentrations during early pregnancy and multiple types of birth defects. Data on births were obtained from the Texas Birth Defects Registry (TBDR) and the National Birth Defects Prevention Study (NBDPS) in Texas. Air pollution concentrations were previously determined by combining modeled air pollution concentrations with air monitoring data. The analysis generated hypotheses for future, confirmatory studies; although many of the observed associations were null. The hypotheses are provided by an observed association between O3 and craniosynostosis and inverse associations between PM2.5 and septal and obstructive heart defects in the TBDR. Associations with PM2.5 for septal heart defects and ventricular outflow tract obstructions were null using the NBDPS. Both the TBDR and the NBPDS had inverse associations between O3 and septal heart defects. Further research to confirm the observed associations is warranted.

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Wilhelm, M., Ghosh, J.K., Su, J., Cockburn, M., Jerrett, M., Ritz, B.	Traffic-Related Air Toxics and Term Low Birth Weight in Los Angeles County, California	2012	Environmental Health Perspectives	NO, NO2, NOx, PM10, PM2.5	Low Birth Weight	Los Angeles county, California	All singleton live births 1 June 2004- 30 March 2006	Examine the odds of term LBW when mothers are exposed to high levels of traffic-related air pollutants prenatally	Yes (presented for PM2.5 from specific sources)	Calculated correlation coefficients and performed factor analysis to examine clustering among various air pollution exposure metrics. Then examined associations between air pollution exposure and odds of term LBW using single- and multiple-variable logistic regression models.	Adjusted analysis for maternal age, race/ethnicity, education, and parity, and gestational age, gestational age squared. Also tried controlling for sex of infant, prenatal care, payment source for prenatal care, whether mother was born in US, maternal birthplace, and SES measure. Tried to reduce misclassification by looking only at women within a certain distance of monitoring stations.	Uses average exposure during first trimester, second trimester, and through entire pregnancy	Yes	**Background:** Numerous studies have linked criteria air pollutants with adverse birth outcomes, but there is less information on the importance of specific emission sources, such as traffic, and air toxics. **Objectives:** We used three exposure data sources to examine odds of term low birth weight (LBW) in Los Angeles, California, women when exposed to high levels of traffic-related air pollutants during pregnancy. **Methods:** We identified term births during 1 June 2004 to 30 March 2006 to women residing within 5 miles of a South Coast Air Quality Management District (SCAQMD) Multiple Air Toxics Exposure Study (MATES III) monitoring station. Pregnancy period average exposures were estimated for air toxics, including polycyclic aromatic hydrocarbons (PAHs), source-specific particulate matter < 2.5 µm in aerodynamic diameter (PM2.5) based on a chemical mass balance model, criteria air pollutants from government monitoring data, and land use regression (LUR) model estimates of nitric oxide (NO), nitrogen dioxide (NO2) and nitrogen oxides (NOx). Associations between these metrics and odds of term LBW (< 2,500 g) were examined using logistic regression. **Results:** Odds of term LBW increased approximately 5% per interquartile range increase in entire pregnancy exposures to several correlated traffic pollutants: LUR measures of NO, NO2, and NOx, elemental carbon, and PM2.5 from diesel and gasoline combustion and paved road dust (geological PM2.5). **Conclusions:** These analyses provide additional evidence of the potential impact of traffic-related air pollution on fetal growth. Particles from traffic sources should be a focus of future studies.
Xu, X., Hu, H., Ha, S., Roth, J.	Ambient Air Pollution and Hypertensive Disorder of Pregnancy	2014	Journal of Epidemiology and Community Health	NO2, SO2, PM2.5, O3, CO	Hypertensive disorders of pregnancy (gestational hypertension, pre-eclampsia, eclampsia during pregnancy)	Jacksonville, Florida	All singleton live births, no congenital abnormalities, no outlier birth weights or gestational ages	Investigates the associations between air pollutants and the risk of hypertensive disorders of pregnancy	Yes (for PM2.5 in full pregnancy and second trimester)	X^2 tests and t tests used to compare the distributions of categorical and continuous independent variables between women with HDP and those without HDP. Used logistic regression models to estimate association between exposure to different air pollutants and gestational hypertension during the three trimesters and full gestation. Air pollutants analyzed in separate models.	Included controls for census tract-level median household income, individual-level marital status, maternal age, race, education, smoking during pregnancy, season of birth, prenatal care, year of conception. Also ran two-pollutant logistic models to assess confounding by copollutants. Developed multipollutant score for each participant during different gestational periods, studied effect of combined air pollutants. Acknowledges potential for selection bias, possible misclassification.	Average concentrations during trimesters and full pregnancy	Yes	**Background:** Ambient air pollution has been implicated in the development of hypertensive disorders of pregnancy (HDP). However, evidence of the association between air pollution and HDP is still limited, and the effects of gaseous air pollutants on HDP and their time windows of exposure have not been well studied. **Methods:** We used the Florida birth registry data to investigate the associations between air pollutants (NO2, SO2, PM2.5, O3 and CO) and the risks of HDP in 22 041 pregnant women in Jacksonville, Florida, USA from 2004 to 2005. Further, we examined whether air pollution exposure during different time windows defined by trimesters and the entire pregnancy had different effects on HDP. **Results:** The single-pollutant logistic regression model showed that exposure to four pollutants during the full pregnancy period was significantly associated with prevalence of HDP after adjusting for covariates: NO2 (OR=1.21, 95% CI 1.09 to 1.35), PM2.5 (OR=1.24, 95% CI 1.08 to 1.43), SO2 (OR=1.13, 95% CI 1.01 to 1.25) and CO (OR=1.12, 95% CI 1.03 to 1.22) per IQR increase. Similar effects were observed when first trimester exposure to NO2, SO2 and CO, and second trimester exposures to PM2.5 were examined. Consistent results were confirmed in multiple-pollutant models. **Conclusions:** This study suggests that exposure to high levels of air pollution during early pregnancy and the full gestational period was associated with increased prevalence of HDP in Florida, USA.
Zhu, X., Liu, Y., Chen, Y., Yao, C., Che, Z. Cao, J.	Maternal Exposure to Fine Particulate Matter (PM2.5) and Pregnancy Outcomes: a Meta-Analysis	2015	Environmental Science and Pollution Research	PM2.5	Change in birth weight, low birth weight, preterm birth, small for gestational age, stillbirth	19 of 25 studies from the U.S. and Canada, 5 from California	Pregnant women	Synthetically quantifies the relationships between maternal exposure to PM2.5 during pregnancy and pregnancy outcomes, including change in birth weight, low birth weight, preterm birth, small for gestational age, stillbirth	Yes (with LBW, preterm birth, SGA, but not stillbirth, for different gestational exposure periods)	Chose 25 studies that gave appropriate quantitative evaluation of relationships, adjusted for other risk factors, published in English, did trimester-specific or entire pregnancy exposure. 8 of 25 were cohort studies, 16 were cross-sectional studies, and 1 was a case-control study.	Studies typically control for factors like tobacco and alcohol use during pregnancy, mother's marital status, race, age, education etc.	Studies look at trimester-specific exposure or exposure over entire pregnancy	Yes	A growing body of evidence has investigated the association between maternal exposure to PM2.5 (particulate matter with aerodynamic diameter 2.5 µm) during pregnancy and adverse pregnancy outcomes. However, the results of those studies are not consistent. To synthetically quantify the relationship between maternal exposure to PM2.5 during pregnancy and pregnancy outcomes (the change in birth weight, low birth weight (LBW), preterm birth (PTB), small for gestational age (SGA), and stillbirth), a meta-analysis of 25 published observational epidemiological studies that met our selection criteria was conducted. Results suggested a 10 µg/m(3) increase in PM2.5 was positively associated with LBW (odds ratio (OR) = 1.05; 95 % confidence interval (CI), 1.02-1.07), PTB (OR= 1.10; 95 % CI, 1.03-1.18), and SGA (OR = 1.15; 95 % CI, 1.10-1.20) based on entire pregnancy exposure, and pooled estimate of decrease in birth weight was 14.58 g (95 % CI, 9.86-19.31); however, there was no evidence of a statistically significant effect of per 10 µg/m(3) increase in PM2.5 exposure on the risk of stillbirth (OR = 1.18; 95 % CI, 0.69-2.04). With respect to three different gestation periods, no significant risks were found in PTB, stillbirth, and the first trimester on the change of birth weight with a 10 µg/m(3) increase in PM2.5. In this study, a comprehensive quantitative analysis of the results show that PM2.5 can increase the risk of LBW, PTB, and SGA; pregnant women need to take effective measures to reduce PM2.5 exposure.

Table 2. Birth and Pregnancy Outcomes

Authors	Title	Year Published	Journal Published	Pollutant(s) Studied	Causes of Mortality or Morbidity Considered	Geographic scope	Population studied	Study question	Statistically significant relationships?	Analysis method	Controls for factors that could obscure relationship?	Assesses potential lag between exposure and outcome?	Reports uncertainty?	Abstract
Zhu, Y., Zhang, C., Liu, D., Grantz, K.L., Wallace, M., Mendola, P.	Maternal Ambient Air Pollution Exposure Preconception and During Early Gestation and Offspring Congenital Orofacial Defects	2015	Environmental Research	CO, NOx, O3, PM2.5, PM10, SO2	Orofacial defects (isolated/multiple cleft palate and cleft lip with or without cleft palate)	United States	Consortium on Safe Labor	Investigates the association between maternal exposure to various air pollutants with risks of orofacial defects		Performed separate analysis for each outcome and exposure window of interest combination. Estimate generalized estimating equations to calculate robust standard errors accounting for clustering due to multiple pregnancies of the same woman. Performed sensitivity analysis excluding multiple gestation pregnancies and infants born to women with preexisting or gestational diabetes.	Controlled for site/region, maternal age, race/ethnicity, marital status, insurance, prepregnancy body mass index, nulliparity, season of conception, smoking and/or alcohol consumption during pregnancy, multiple birth, preexisting or gestational diabetes mellitus. Performed simulation extrapolation procedures to correct for potential exposure misclassification. I believe they did not do co-pollutant models.	Three months preconception and early gestation (both an average over weeks 3-8 and weekly averages from weeks 1 through 10)	Yes	**Background:** Maternal air pollution exposure has been related to orofacial clefts but the literature is equivocal. Potential chronic preconception effects have not been studied. **Objectives:** Criteria air pollutant exposure during three months preconception and gestational weeks 3-8 was studied in relation to orofacial defects. **Methods:** Among 188,102 live births and fetal deaths from the Consortium on Safe Labor (2002-2008), 63 had isolated cleft palate (CP) and 159 had isolated cleft lip with or without cleft palate (CL ±CP). Exposures were estimated using a modified Community Multiscale Air Quality model. Logistic regression with generalized estimating equations adjusted for site/region and maternal demographic, lifestyle and clinical factors calculated the odds ratio (OR) and 95% CI per interquartile increase in each pollutant.**Results**: Preconception, carbon monoxide (CO; OR=2.24; CI: 1.21, 4.16) and particulate matter (PM) ≤10μm (OR=1.72; CI: 1.12, 2.66) were significantly associated with CP, while sulfur dioxide (SO2) was associated with CL ±CP (OR=1.93; CI: 1.16, 3.21). During gestational weeks 3-8, CO remained a significant risk for CP (OR=2.74; CI: 1.62, 4.62) and nitrogen oxides (NOx; OR=3.64; CI: 1.73, 7.66) and PM ≤2.5μm (PM2.5; OR=1.74; CI: 1.15, 2.64) were also related to the risk. Analyses by individual week revealed that positive associations of NOx and PM2.5 with CP were most prominent from weeks 3-6 and 3-5, respectively. **Conclusions:** Exposure to several criteria air pollutants preconception and during early gestation was associated with elevated odds for CP, while CL ±CP was only associated with preconception SO2 exposure.

Table 3. Cardiovascular

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Atkinson, R.W., Kang, S., Anderson, H.R., Mills, I.C., Walton, H.A.	Epidemiological Time Series Studies of PM2.5 and Daily Mortality and Hospital Admissions: a Systematic Review and Meta-Analysis	2014	Thorax	PM2.5	All-cause mortality, IHD mortality, stroke mortality, COPD (excl. asthma) mortality, hospital admissions for cardiovascular and respiratory diseases: all ages: cardiovascular, respiratory, 65+ years: cardiovascular, COPD incl astha, COPD excl asthma, lower resp infection, respiratory, IHD, heart failure, cardiac, stroke, dysrhythmia; 0-14: respiratory, asthma	Worldwide, but provides estimates specific to WHO American Region A (U.S., Canada, Cuba)	For different health endpoints, considers all ages, 65+ years, 0-14 years	Assesses the evidence for associations between PM2.5 and daily mortality and hospital admissions for a range of diseases and ages using a comprehensive review and meta-analysis	Yes	Did a systematic, comprehensive review of 110 peer-reviewed time series studies published through May 2011. Within each WHO region, did a two stage meta-analysis, first pooling single-city estimates and then pooling these summary estimates with the selected multicity study estimates to get a WHO region-specific summary estimates. In WHO American Region A, had 33 total mortality studies, 31 hospital admission studies.	They assessed small study bias in single-city estimates and selected multicity estimates. They choose studies that attempt to control for confounding factors like season, lont-term temporal trends and meteorological conditions	Studies vary in the time lag they study for short-term effects.	Yes	**Background:** Short-term exposure to outdoor fine particulate matter (particles with a median aerodynamic diameter <2.5 μm (PM2.5)) air pollution has been associated with adverse health effects. Existing literature reviews have been limited in size and scope. **Methods:** We conducted a comprehensive, systematic review and meta-analysis of 110 peer-reviewed time series studies indexed in medical databases to May 2011 to assess the evidence for associations between PM2.5 and daily mortality and hospital admissions for a range of diseases and ages. We stratified our analyses by geographical region to determine the consistency of the evidence worldwide and investigated small study bias. **Results:** Based upon 23 estimates for all-cause mortality, a 10 μg/m3 increment in PM2.5 was associated with a 1.04% (95% CI 0.52% to 1.56%) increase in the risk of death. Worldwide, there was substantial regional variation (0.25% to 2.08%). Associations for respiratory causes of death were larger than for cardiovascular causes, 1.51% (1.01% to 2.01%) vs 0.84% (0.41% to 1.28%). Positive associations with mortality for most other causes of death and for cardiovascular and respiratory hospital admissions were also observed. We found evidence for small study bias in single-city mortality studies and in multicity studies of cardiovascular disease. **Conclusions:** The consistency of the evidence for adverse health effects of short-term exposure to PM2.5 across a range of important health outcomes and diseases supports policy measures to control PM2.5 concentrations. However, reasons for heterogeneity in effect estimates in different regions of the world require further investigation. Small study bias should also be considered in assessing and quantifying health risks from PM2.5.
Beckerman, B.S., Jerrett, M., Finkelstein, M., Kanaroglou, P., Brook, J.R., Arain, M.A., Sears, M.R., Stieb, D., Balmes, J., Chapman, K.	The Association Between Chronic Exposure to Traffic-Related Air Pollution and Ischemic Heart Disease	2012	Journal of Toxicology and Environmental Health, Part A	NO2, PM2.5, O3	Ischemic heart disease (ICD-9-CM: 412-414)	Toronto, Canada	Patients referred during 1992-1999 to pulmonary clinic at Toronto Western Hospital	Looks at the association between IHD and air pollutants	No	Uses a modified Poisson regression to produce relative risk estimates. Primary analysis is of NO2 concentrations, but considers PM2.5 and O3 as confounders. **I cannot see more detail without accessing the full text.	Controlled with individual and neighborhood-level covariates.		Yes	Increasing evidence links air pollution to the risk of cardiovascular disease. This study investigated the association between ischemic heart disease (IHD) prevalence and exposure to traffic-related air pollution (nitrogen dioxide [NO_2], fine particulate matter [$PM_{2.5}$], and ozone [O_3]) in a population of susceptible subjects in Toronto. Local (NO_2) exposures were modeled using land use regression based on extensive field monitoring. Regional exposures ($PM_{2.5}$, O_3) were modeled as confounders using inverse distance weighted interpolation based on government monitoring data. The study sample consisted of 2360 patients referred during 1992 to 1999 to a pulmonary clinic at the Toronto Western Hospital in Toronto, Ontario, Canada, to diagnose or manage a respiratory complaint. IHD status was determined by clinical database linkages (ICD-9-CM 412-414). The association between IHD and air pollutants was assessed with a modified Poisson regression resulting in relative risk estimates. Confounding was controlled with individual and neighborhood-level covariates. After adjusting for multiple covariates, NO_2 was significantly associated with increased IHD risk, relative risk (RR) = 1.33 (95% confidence interval [CI]: 1.2, 1.47). Subjects living near major roads and highways had a trend toward an elevated risk of IHD, RR = 1.08 (95% CI: 0.99, 1.18). Regional $PM_{2.5}$ and O_3 were not associated with risk of IHD.

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Bell, M.L, Ebisu, K., Leaderer, B.P., Gent, J.F., Lee, H.J., Koutrakis, P., Wang, Y., Dominici, F., Peng, R.D.	Associations of PM2.5 Constituents and Sources with Hospital Admissions: Analysis of Four Counties in Connecticut and Massachusetts (USA) for Person >= 65 Years of Age	2014	Environmental Health Perspectives	PM2.5	Cause of admission: respiratory disease [chronic obstructive pulmonary disease (ICD-9-CM: 490-492) and respiratory tract infection (ICD-9-CM: 464-466, 480-487)] and cardiovascular disease [heart failure (ICD-9-CM: 428), heart rhythm disturbances (ICD-9-CM: 426-427), cerebrovascular events (ICD-9-CM: 430-438), ischemic heart disease (ICD-9-CM: 410-414, 429), peripheral vascular disease (ICD-9-CM: 440-448)]	New Haven County, CT, Hartford County, CT, Fairfield County, CT, Hampden County, MA	Medicare enrollees (>= 65) in four counties enrolled in fee-for-service plan August 2000-Feb 2004	Evaluates the relative risks of cardiovascular and respiratory hospitalizations associated with short-term exposure to PM2.5 constituents and sources.		Calculated monthly number of beneficiaries in each county and linked this with inpatient claims data to identify patients discharged from acute-care hospitals. Calculated daily numbers of admissions. Performed time-series analysis to estimate associations using a log-linear Poisson regression model.	Control for temperature, dew point temperature, region. Used co-pollutant models for constituents that had significant single-pollutant effects and did not correlate too highly.	Considered single-day lags of exposure using same day of hospitalization, previous day, and two days previous.	Yes	**Background:** Epidemiological studies have demonstrated associations between short-term exposure to PM2.5 and hospital admissions. The chemical composition of particles varies across locations and time periods. Identifying the most harmful constituents and sources is an important health and regulatory concern. **Objectives:** We examined pollutant sources for associations with risk of hospital admissions for cardiovascular and respiratory causes. **Methods:** We obtained PM2.5 filter samples for four counties in Connecticut and Massachusetts and analyzed them for PM2.5 elements. Source apportionment was used to estimate daily PM2.5 contributions from sources (traffic, road dust, oil combustion, and sea salt as well as a regional source representing coal combustion and other sources). Associations between daily PM2.5 con- stituents and sources and risk of cardiovascular and respiratory hospitalizations for the Medicare population (> 333,000 persons ≥ 65 years of age) were estimated with time-series analyses (August 2000–February 2004). **Results:** PM2.5 total mass and PM2.5 road dust contribution were associated with cardiovascular hospitalizations, as were the PM2.5 constituents calcium, black carbon, vanadium, and zinc. For respiratory hospitalizations, associations were observed with PM2.5 road dust, and sea salt as well as aluminum, calcium, chlorine, black carbon, nickel, silicon, titanium, and vanadium. Effect esti- mates were generally robust to adjustment by co-pollutants of other constituents. An interquartile range increase in same-day PM2.5 road dust (1.71 µg/m3) was associated with a 2.11% (95% CI: 1.09, 3.15%) and 3.47% (95% CI: 2.03, 4.94%) increase in cardiovascular and respiratory admissions, respectively. **Conclusions:** Our results suggest some particle sources and constituents are more harmful than others and that in this Connecticut/Massachusetts region the most harmful particles include black carbon, calcium, and road dust PM2.5.
Bell, M.L., Ebisu, K., Leaderer, B.P., Gent, J.F., Lee, H.J., Koutrakis, P., Wang, Y., Dominici, F., Peng, R.D.	Associations of PM2.5 Constituents and Sources with Hospital Admissions: Analysis of Four Counties in Connecticut and Massachusetts (USA) for Persons >= 65 Years of Age	2014	Environmental Health Perspectives	PM2.5	Cardiovascular and respiratory hospital admissions, with cause of admission from chronic obstructive pulmonary disease (ICD-9: 490-492), respiratory tract infection (ICD-9: 464-466, 480-487), cardiovascular disease (ICD-9:428, 426-427, 430-438, 410-414, 429, 440-448)	Four counties in CT and MA	Medicare beneficiaries (>= 65 years)	Examines associations between pollutant sources and the risk of hospital admissions for cardiovascular and respiratory causes		Obtained PM2.5 filter samples for four counties in CT and MA and analyzed them for PM2.5 elements, then used source apportionment to estimate contributions to daily PM2.5 from various sources. Used time-series analysis to estimate associations between PM2.5 sources or constituents and daily cardiovascular or respiratory hospitalization using a log-linear Poisson regression	Allowed effect modification by pollutant source, PM2.5 constituent, controlled for day or week, temperature, de point temperature, and indicator for region	Considered same-day, one-day lags, and two-day lags	Yes	**Background:** Epidemiological studies have demonstrated associations between short-term exposure to PM2.5 and hospital admissions. The chemical composition of particles varies across locations and time periods. Identifying the most harmful constituents and sources is an important health and regulatory concern. **Objectives:** We examined pollutant sources for associations with risk of hospital admissions for cardiovascular and respiratory causes. **Methods:** We obtained PM2.5 filter samples for four counties in Connecticut and Massachusetts and analyzed them for PM2.5 elements. Source apportionment was used to estimate daily PM2.5 contributions from sources (traffic, road dust, oil combustion, and sea salt as well as a regional source representing coal combustion and other sources). Associations between daily PM2.5 constituents and sources and risk of cardiovascular and respiratory hospitalizations for the Medicare population (> 333,000 persons ≥ 65 years of age) were estimated with time-series analyses (August 2000–February 2004). **Results:** PM2.5 total mass and PM2.5 road dust contribution were associated with cardiovascular hospitalizations, as were the PM2.5 constituents calcium, black carbon, vanadium, and zinc. For respiratory hospitalizations, associations were observed with PM2.5 road dust, and sea salt as well as aluminum, calcium, chlorine, black carbon, nickel, silicon, titanium, and vanadium. Effect estimates were generally robust to adjustment by co-pollutants of other constituents. An interquartile range increase in same-day PM2.5 road dust (1.71 µg/m3) was associated with a 2.11% (95% CI: 1.09, 3.15%) and 3.47% (95% CI: 2.03, 4.94%) increase in cardiovascular and respiratory admissions, respectively. **Conclusions:** Our results suggest some particle sources and constituents are more harmful than others and that in this Connecticut/Massachusetts region the most harmful particles include black carbon, calcium, and road dust PM2.5.

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Bell, M.L., Son, J.Y., Peng, R.D., Wang, Y., Dominici, F.	Brief Report: Ambient PM2.5 and Risk of Hospital Admissions: Do Risks Differ for Men and Women?	2015	Epidemiology	PM2.5	Risk of cause-specific cardiovascular and respiratory hospitalizations (I can't access full text to see specifics)	213 U.S. counties	Medicare beneficiaries (>= 65) for 1999-2000	Estimates the associations between PM2.5 exposure and risk of cause-specific cardiovascular and respiratory hospitalizations, and whether these associations differ between men and women		Use Bayesian hierarchical modeling to estimate associations.	?	?	Yes	**Background:** While strong evidence exists for associations between fine particles (PM2.5) and health, less is known about whether associations differ by sex. **Methods:** We used Bayesian hierarchical modeling to estimate associations between PM2.5, based on ambient monitors, and risk of cause-specific cardiovascular and respiratory hospitalizations for about 12.6 million Medicare beneficiaries (>65 years) residing in 213 US counties for 1999-2010. **Results:** Point estimates were higher for women than men for almost all causes of hospitalization. PM2.5 risks were higher for women than men for respiratory tract infection, cardiovascular, and heart rhythm disturbance admissions. A 10 μg/m(3) increase in same-day PM2.5 was associated with a 1.13% increased risk of heart rhythm disturbance admissions for women (95% posterior interval [PI]: 0.63%, 1.63%), and 0.03% for men (95% PI: -0.48%, 0.55%). Differences remained after stratification by age and season. **Conclusions:** Women may be more susceptible to PM2.5-related hospitalizations for some respiratory and cardiovascular causes.
Ensor, K.B., Raun, L.H., Persse, D.	A Case-Crossover Analysis of Out-of-Hospital Cardiac Arrest and Air Pollution	2013	Circulation	PM2.5, O3, NO2, SO2, CO	Out of hospital cardiac arrest	Houston, TX	All non-dead-on-arrival adults >=18 from Houston Fire Department EMS calls 2004-2011	Studies the association between air pollution and risk of out-of-hospital cardiac arrest.	Yes	Used a time-stratified case-crossover design coupled with conditional logistic regression. Uses ambient air pollution concentrations at times when the study individual is not experiencing the OHCA health event as reference for each case. Use conditional logistic regression to estimate the association of pollution and increased relative risk of health event. Did sensitivity analysis with single lag models to look at hour and day time scales. Implemented constrained distributed lag models to estimate the cumulative effect over 2-hour average or 2-day average increments.	Case-crossover design should control for individual-level confounders. When there was a significant association between individual pollutants and OHCA, looked at potential confounding between pollutants by estimating correlations and including pollutants as covariates in the model. Looked at effect modification by age, sex, race, and season. Acknowledge the possibility of exposure time misclassification and selection bias from not including individuals dead on arrival.	Assessed lags on hourly and daily time scale, for 1-8 lag hours and 1-5 day lags	Yes	**Background:** Evidence of an association between the exposure to air pollution and overall cardiovascular morbidity and mortality is increasingly found in the literature. However, results from studies of the association between acute air pollution exposure and risk of out-of-hospital cardiac arrest (OHCA) are inconsistent for fine particulate matter, and, although pathophysiological evidence indicates a plausible link between OHCA and ozone, none has been reported. Approximately 300 000 persons in the United States experience an OHCA each year, of which >90% die. Understanding the association provides important information to protect public health. **Methods and Results:** The association between OHCA and air pollution concentrations hours and days before onset was assessed by using a time-stratified case-crossover design using 11 677 emergency medical service–logged OHCA events between 2004 and 2011 in Houston, Texas. Air pollution concentrations were obtained from an extensive area monitor network. An average increase of 6 μg/m3 in fine particulate matter 2 days before onset was associated with an increased risk of OHCA (1.046; 95% confidence interval, 1.012–1.082). A 20-ppb ozone increase for the 8-hour average daily maximum was associated with an increased risk of OHCA on the day of the event (1.039; 95% confidence interval, 1.005–1.073). Each 20-ppb increase in ozone in the previous 1 to 3 hours was associated with an increased risk of OHCA (1.044; 95% confidence interval, 1.004–1.085). Relative risk estimates were higher for men, blacks, or those aged >65 years. **Conclusions:** The findings confirm the link between OHCA and fine particulate matter and introduce evidence of a similar link with ozone.

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Kiomourtzoglou, M.A., Coull, B.A., Dominici, F., Koutrakis, P., Schwartz, J., Suh, H.	The Impact of Source Contribution Uncertainty on the Effects of Source-Specific PM2.5 on Hospital Admissions: A Case Study in Boston, MA	2014	Journal of Exposure Science and Environmental Epidemiology	PM2.5	ER admissions for CVD	Boston, MA	Medicare beneficiaries (>= 65) for 2003-2010	Assesses the impact of uncertainty on the effect estimates of particulate sources on emergency cardiovascular disease admissions. Despite this focus on uncertainty of sources, also do "base health analysis" of effect of PM2.5 on CVD ER admissions		Identified PM2.5 sources using positive matrix factorization and absolute principle component analysis and looked at the effect on emergency CVD hospital admissions. Propagated uncertainty in source contributions using a block bootstrap procedure, and estimated average across-methods source-specific effect estimates using bootstrap procedure. For "base health analysis," do case-crossover analysis using time-stratified approach, choosing control dates bidirectionally. Ran conditional logistic regressions	Eliminates confounding by personal characteristics that do not change over and limits confounding by seasonality and long-term trends by using case-crossover analysis and bidirectional control days. Adjusted for same-day temperature, same-day dew point, and 2-day moving averaged temperature, adjusted for PM2.5 to control for previous associations with health outcomes, differential correlation with factors included in the model, and with other pollutants not included that could confound results.	Looked at associations for moving averages of 1, 2, 4, 6, and 7 days	Yes	Epidemiologic studies of particulate sources and adverse health do not account for the uncertainty in the source contribution estimates. Our goal was to assess the impact of uncertainty on the effect estimates of particulate sources on emergency cardiovascular (CVD) admissions. We examined the effects of PM2.5 sources, identified by positive matrix factorization (PMF) and absolute principle component analysis (APCA), on emergency CVD hospital admissions among Medicare enrollees in Boston, MA, during 2003-2010, given stronger associations for this period. We propagated uncertainty in source contributions using a block bootstrap procedure. We further estimated average across-methods source-specific effect estimates using bootstrap samples. We estimated contributions for regional, mobile, crustal, residual oil combustion, road dust, and sea salt sources. Accounting for uncertainty, same-day exposures to regional pollution were associated with an across-methods average effect of 2.00% (0.18, 3.78%) increase in the rate of CVD admissions. Weekly residual oil exposures resulted in an average 2.12% (0.19, 4.22%) increase. Same-day and 2-day exposures to mobile-related PM2.5 were also associated with increased admissions. Confidence intervals when accounting for the uncertainty were wider than otherwise. Agreement in PMF and APCA results was stronger when uncertainty was considered in health models. Accounting for uncertainty in source contributions leads to more stable effect estimates across methods and potentially to fewer spurious significant associations.
Kloog, I., Coull, B.A., Zanobetti, A., Koutrakis, P., Schwartz, J.D.	Acute and Chronic Effects of Particles on Hospital Admissions in New England	2012	PLoS One	PM2.5	Hospital admissions for cardiovascular or respiratory diagnoses among the elderly (65+): respiratory (ICD-9: 460-519), cardiovascular disease (ICD-9: 390-429), stroke (ICD-9: 430-436), diabetes (ICD-9: 250)	New England: CT, ME, MA, NH, RI, VT	Medicare beneficiaries (>= 65 years)	Assess the association betweenshort term and long term PM2.5 exposure and hospital admissions among the elderly		Matched admissions counts by zip code to exposure estimates. Make use of the equivalence between Poisson regression and the piecewise constant proportional hazard model, allowing them to model the time to a hospital admission as a function of both long- and short-term exposure. Check for linearity by fitting a piecewise linear model	Controlled for temperature with the same moving average as PM2.5, age, percent minorities, median income, and percent of people with no high school education. For sensitivity analysis, analyzed other averaging periods and the addition of land use and temporal variables	For short-term exposure, used mean of same and day before, and long-term exposure calculated as the mean exposure in each zip-code. Also define short term as difference between the two-day average and the long-term average.	Yes	**Background:** Many studies have reported significant associations between exposure to PM2.5 and hospital admissions, but all have focused on the effects of short-term exposure. In addition all these studies have relied on a limited number of PM2.5 monitors in their study regions, which introduces exposure error, and excludes rural and suburban populations from locations in which monitors are not available, reducing generalizability and potentially creating selection bias. **Methods:** Using our novel prediction models for exposure combining land use regression with physical measurements (satellite aerosol optical depth) we investigated both the long and short term effects of PM2.5 exposures on hospital admissions across New-England for all residents aged 65 and older. We performed separate Poisson regression analysis for each admission type: all respiratory, cardiovascular disease (CVD), stroke and diabetes. Daily admission counts in each zip code were regressed against long and short-term PM2.5 exposure, temperature, socio-economic data and a spline of time to control for seasonal trends in baseline risk. **Results:** We observed associations between both short-term and long-term exposure to PM2.5 and hospitalization for all of the outcomes examined. In example, for respiratory diseases, for every10-µg/m3 increase in short-term PM2.5 exposure there is a 0.70 percent increase in admissions (CI = 0.35 to 0.52) while concurrently for every10-µg/m3 increase in long-term PM2.5 exposure there is a 4.22 percent increase in admissions (CI = 1.06 to 4.75). **Conclusions:** As with mortality studies, chronic exposure to particles is associated with substantially larger increases in hospital admissions than acute exposure and both can be detected simultaneously using our exposure models.

Table 3. Cardiovascular

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Link, M.S., Luttmann-Gibson, H., Schwartz, J., Mittleman, M.A., Wessler, B., Gold, D.R., Dockery, D.W., Laden, F.	Acute Exposure to Air Pollution Triggers Atrial Fibrillation	2013	Journal of the American College of Cardiology	PM2.5, NO2, SO2, O3	Atrial fibrillation	Boston area	Patients followed at the Tufts Medical Center Cardiac Arrhythmia Center, over 18, within 50 km of Harvard Supersite air quality monitor	Evaluates the association of air pollution with the onset of atrial fibrillation.	Yes (just for time periods right before the event)	Used a case-crossover design to allow for investigation of the acute effects of exposure to air pollution, comparing subject's exposures before the time of the event to distribution of exposure estimated from separate control periods. Analyze these matched sets using conditional logistic regression. Selected control periods using bidirectional time-stratified approach by matching on weekday and hour of day within same calendar month	Case-crossover design controls for all time-invariant individual-specific factors. Acknowledges issue of exposure misclassification due to method of air pollution modeling.	Used average air pollution for 24-hours prior to AF. Looked at 2 hours, 6 hours, 12, hours, and 48 hours before in sensitivity analysis	Yes	**Objectives:** This study sought to evaluate the association of air pollution with the onset of atrial fibrillation (AF). **Background:** Air pollution in general and more specifically particulate matter has been associated with cardiovascular events. Although ventricular arrhythmias are traditionally thought to convey the increased cardiovascular risk, AF may also contribute. **Methods:** Patients with dual chamber implantable cardioverter-defibrillators (ICDs) were enrolled and followed prospectively. The association of AF onset with air quality including ambient particulate matter <2.5 μm aerodynamic diameter (PM2.5), black carbon, sulfate, particle number, NO2, SO2, and O3 in the 24 h prior to the arrhythmia was examined utilizing a case-crossover analysis. In sensitivity analyses, associations with air pollution between 2 and 48 h prior to the AF were examined. **Results:** Of 176 patients followed for an average of 1.9 years, 49 patients had 328 episodes of AF lasting ≥ 30 s. Positive but nonsignificant associations were found for PM2.5 in the prior 24 h, but stronger associations were found with shorter exposure windows. The odds of AF increased by 26% (95% confidence interval: 8% to 47%) for each 6.0 μg/m(3) increase in PM2.5 in the 2 h prior to the event (p = 0.004). The odds of AF were highest at the upper quartile of mean PM2.5. **Conclusions:** PM was associated with increased odds of AF onset within hours following exposure in patients with known cardiac disease. Air pollution is an acute trigger of AF, likely contributing to the pollution-associated adverse cardiac outcomes observed in epidemiological studies.
Madrigano, J., Kloog, I., Goldberg, R., Coull, B.A., Mittleman, M.A., Schwartz, J.	Long-Term Exposure to PM2.5 and Incidence of Acute Myocardial Infarction	2013	Environmental Health Perspectives	PM2.5	Acute myocardial infarction	Greater Worcester, MA	Worcester Heart Attack Study	Examines how long-term exposure to area particulate matter affects the onset of acute myocardial infarction, distinguishing between the effect of area and local particulate pollution on incidence of AMI. Randomly select controls from resident lists. Ran logistic regression models. First ran model with separate terms for area and local PM2.5, and the second with a term for their sum.	Yes (with area PM2.5, and weakly with area+local PM2.5)	Case-control study: use a PM2.5 prediction model based on satellite aerosol optical depth measurements for area pollution predictions and local particulate pollution based on land use variables, and look at the effect of area and local particulate pollution on incidence of AMI. Randomly select controls from resident lists. Ran logistic regression models. First ran model with separate terms for area and local PM2.5, and the second with a term for their sum.	Match case and controls based on age, sex, and section of study area, and include finer age controls. Include higher-other interaction terms for those matching factors, and include measures of block group pop density and SES, distance to supermarkets, and distance to recreation areas. Use generalized estimating equations to account for any remaining correlation among subjects in the same block group, but some residual is likely because remaining SE and lifestyle factors vary spatially. Acknowledges potential exposure misclassification from controls moving address.	Look at long-term exposure, average for the year 2000	Yes	**Background:** A number of studies have shown associations between chronic exposure to particulate air pollution and increased mortality, particularly from cardiovascular disease, but fewer studies have examined the association between long-term exposure to fine particulate air pollution and specific cardiovascular events, such as acute myocardial infarction (AMI). **Objective**: We examined how long-term exposure to area particulate matter affects the onset of AMI, and we distinguished between area and local pollutants. **Methods:** Building on the Worcester Heart Attack Study, an ongoing community-wide investi- gation examining changes over time in myocardial infarction incidence in greater Worcester, Massachusetts, we conducted a case–control study of 4,467 confirmed cases of AMI diagnosed between 1995 and 2003 and 9,072 matched controls selected from Massachusetts resident lists. We used a prediction model based on satellite aerosol optical depth (AOD) measurements to generate both exposure to particulate matter ≤ 2.5 μm in diameter (PM2.5) at the area level (10 × 10 km) and the local level (100 m) based on local land use variables. We then examined the association between area and local particulate pollution and occurrence of AMI. **Results:** An interquartile range (IQR) increase in area PM2.5 (0.59 μg/m3) was associated with a 16% increase in the odds of AMI (95% CI: 1.04, 1.29). An IQR increase in total PM2.5 (area + local, 1.05 μg/m3) was weakly associated with a 4% increase in the odds of AMI (95% CI: 0.96, 1.11). **Conclusions:** Residential exposure to PM2.5 may best be represented by a combination of area and local PM2.5, and it is important to consider spatial gradients within a single metropolitan area when examining the relationship between particulate matter exposure and cardiovascular events.

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Neophytou, A.M., Costello, S., Brown, D.M., Picciotto, S., North, E.M., Hammond, S.K., Cullen, M.R., Eisen, E.A.	Marginal Structural Models in Occupational Epidemiology: Application in a Study of Ischemic Heart Disease Incidence and PM2.5 in the US Aluminum Industry	2014	American Journal of Epidemiology	PM2.5	Ischemic heart disease	United States	Actively employed aluminum workers	Effect of PM2.5 on Ischemic Heart Disease incidence among aluminum workers		Use a Cox marginal structural model and inverse probability weighting, which can be used to estimate risk in a cohort of active workers if there is a time-varying confounder (e.g. health status) affected by prior exposure. Stratified analysis by work process, and they used a composite risk score based on insurance claims as a time-varying measure of health status. Evaluates exposure only as exceeding or being below a cut-off	Controlled for individual factors like age, sex, race, job grade, and for smoking, height, and weight with varying availability.	Used average annual exposure in different areas of each plant from samples collected over 25 years	Yes	Marginal structural models (MSMs) and inverse probability weighting can be used to estimate risk in a cohort of active workers if there is a time-varying confounder (e.g., health status) affected by prior exposure-a feature of the healthy worker survivor effect. We applied Cox MSMs in a study of incident ischemic heart disease and exposure to particulate matter with aerodynamic diameter of 2.5 μm or less (PM2.5) in a cohort of 12,949 actively employed aluminum workers in the United States. The cohort was stratified by work process into workers in smelting facilities, herein referred to as "smelters" and workers in fabrication facilities, herein referred to as "fabricators." The outcome was assessed by using medical claims data from 1998 to 2012. A composite risk score based on insurance claims was treated as a time-varying measure of health status. Binary PM2.5 exposure was defined by the 10th-percentile cutoff for each work process. Health status was associated with past exposure and predicted the outcome and subsequent exposure in smelters but not in fabricators. In smelters, the Cox MSM hazard ratio comparing those always exposed above the cutoff with those always exposed below the cutoff was 1.98 (95% confidence interval: 1.18, 3.32). In fabricators, the hazard ratio from a traditional Cox model was 1.34 (95% confidence interval: 0.98, 1.83). Results suggest that occupational PM2.5 exposure increases the risk of incident ischemic heart disease in workers in both aluminum smelting and fabrication facilities.
Rich, D.Q., Ozkaynak, H., Crooks, J., Baxter, L., Burke, J., Ohman-Strickland, P., Thevent-Morrison, K., Kipen, H.M., Zhang, J.,Kostis, J.B., Lunden, M., Hodas, N., Turpin, B.J.	The Triggering of Myocardial Infarction by Fine Particles is Enhanced When Particles are Enriched in Secondary Species	2014	Environmental Science and Technology	PM2.5	Acute myocardial infarction	New Jersey	People 18>= years who were diagnosed with acute myocardial infarction	Evaluates whether the relative odds of transmural MI associated with increased PM2.5 concentration is modified by the PM2.5 composition	Not sure	Used a time-stratified case-crossover design, where each patient is a case during the period immediately before the MI and as a matched control during times when MI did not occur. Defined case periods as the 24 hour period before ER admission, while control periods were matched by day of the week, time of day, year, and month. Used a conditional logistic regression model stratified on each MI to regress case-control status against the mean PM2.5 concentration in the case period, including a natural spline of mean apparent temperature. Then estimated the risk of a transmural infarction associated with each interquartile range increase	Case-crossover design controls for time-invariant individual characteristics. Controlled for temperature. Study limited in that it could only use central site PM2.5 mass concentrations, biasing estimates towards the null.	Calculated ambient air pollution in 24 hours before MI using closest monitor to patient's residence	Yes	Previous studies have reported an increased risk of myocardial infarction (MI) associated with acute increases in PM concentration. Recently, we reported that MI/fine particle (PM2.5) associations may be limited to transmural infarctions. In this study, we retained data on hospital discharges with a primary diagnosis of acute myocardial infarction (using International Classification of Diseases ninth Revision [ICD-9] codes), for those admitted January 1, 2004 to December 31, 2006, who were ≥18 years of age, and were residents of New Jersey at the time of their MI. We excluded MI with a diagnosis of a previous MI and MI coded as a subendocardial infarction, leaving n = 1563 transmural infarctions available for analysis. We coupled these health data with PM2.5 species concentrations predicted by the Community Multiscale Air Quality chemical transport model, ambient PM2.5 concentrations, and used the same case-crossover methods to evaluate whether the relative odds of transmural MI associated with increased PM2.5 concentration is modified by the PM2.5composition/mixture (i.e., mass fractions of sulfate, nitrate, elemental carbon, organic carbon, and ammonium). We found the largest relative odds estimates on the days with the highest tertile of sulfate mass fraction (OR = 1.13; 95% CI = 1.00, 1.27), nitrate mass fraction (OR = 1.18; 95% CI = 0.98, 1.35), and ammonium mass fraction (OR = 1.13; 95% CI = 1.00 1.28), and the lowest tertile of EC mass fraction (OR = 1.17; 95% CI = 1.03, 1.34). Air pollution mixtures on these days were enhanced in pollutants formed through atmospheric chemistry (i.e., secondary PM2.5) and depleted in primary pollutants (e.g., EC). When mixtures were laden with secondary PM species (sulfate, nitrate, and/or organics), we observed larger relative odds of myocardial infarction associated with increased PM2.5 concentrations. Further work is needed to confirm these findings and examine which secondary PM2.5 component(s) is/are responsible for an acute MI response.

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Rodopoulou, S., Chalbot, M.C., Samoli, E., Dubois, D.w., San Filippo, B.D., Kavouras, I.G.	Air Pollution and Hospital Emergency Room and Admissions for Cardiovascular and Respiratory Diseases in Dona Ana County, New Mexico	2014	Environmental Research	PM10, PM2.5, O3	Respiratory (ICD-9: 493, 466, 490, 491, 492, 496, 480-486, 460-465) and cardiovascular (ICD-9: 410-414, 426-427, 402, 428, 390-459)	Dona Ana County, New Mexico	Residents of Dona Ana county, estimated separately for all ages and 65+	Evaluates the association between short-term exposure to ambient PM10, PM2.5, and O3 and respiratory and cardiovascular emergency room visits and hospitalizations		Used Poisson regression models allowing for overdispersion, allowed nonlinearity by using natural splines. Remove dlong-term trends and seasonal patterns with a natural cubic regression spline for each season and year. Estimate effects separately for all ages and 65+	Controlled for long-term time trends and seasonal patterns, as well as temperature, daily humidity. Evaluated effect modification by season and tried removing days with outlier pollution. Also tried doing two day average lag.	Uses same day and day before pollution, and then two-day moving average	Yes	**Introduction:** Doña Ana County in New Mexico regularly experiences severe air pollution episodes associated with windblown dust and fires. Residents of Hispanic/Latino origin constitute the largest population group in the region. We investigated the associations of ambient particulate matter and ozone with hospital emergency room and admissions for respiratory and cardiovascular visits in adults. **Methods:** We used trajectories regression analysis to determine the local and regional components of particle mass and ozone. We applied Poisson generalized models to analyze hospital emergency room visits and admissions adjusted for pollutant levels, humidity, temperature and temporal and seasonal effects. **Results:** We found that the sources within 500km of the study area accounted for most of particle mass and ozone concentrations. Sources in Southeast Texas, Baja California and Southwest US were the most important regional contributors. Increases of cardiovascular emergency room visits were estimated for PM10 (3.1% (95% CI: -0.5 to 6.8)) and PM10-2.5 (2.8% (95% CI: -0.2 to 5.9)) for all adults during the warm period (April-September). When high PM10 (>150µg/m(3)) mass concentrations were excluded, strong effects for respiratory emergency room visits for both PM10 (3.2% (95% CI: 0.5-6.0)) and PM2.5 (5.2% (95% CI: -0.5 to 11.3)) were computed. **Conclusions:** Our analysis indicated effects of PM10, PM2.5 and O3 on emergency room visits during the April-September period in a region impacted by windblown dust and wildfires.
Rodopoulou, S., Samoli, E., Chalbot, M.G., Kavouras, I.G.	Air Pollution and Cardiovascular and Respiratory Emergency Visits in Central Arkansas: A Time-Series Analysis	2015	Science of the Total Environment	PM2.5, O3	Emergency room visits for cardiovascular diagnoses (ICD-9: 401-459), hypertension (ICD-9: 401), hypertensive heart disease and heart failure (ICD-9: 402, 428), conduction disorders and cardiac dysrhythmias: (ICD-9: 426-427), cerebrovascular disease and stroke: (ICD-9: 430-438), respiratory diagnoses (ICD-9: 460-519), acute respiratory infections except acute bronchioloitis and bronchiolitis (ICD-9: 460-465), pneumonia (ICD-9: 480-486), asthma (ICD-9: 493), chronic obstructive pulmonary disease (ICD-9: 490-491-492-496)	Central Arkansas	Daily emergency room visits 2002-2012 among adults >=15	Studies the short-term effects of air pollution on cardiovascular and respiratory morbidity in the stroke and heart failure belt		Tallied daily hospital emergency counts and then linked these counts to lagged pollution exposure using overdispersed generalized linear Poisson regression models. Applied natural spline smooth functions to include the effect of time-varying covariates and calendar time on daily visits. Used natural cubic regression splint with 1.5 degrees of freedom for each season and year.	Controlled for temperature on day of visit, two previous days, average relative humidity with lags, dummy variables for the day of the week and holidays effect. Looked for confounding by other pollutants using two pollutant models. Also looked at effect modification by season, age, gender, and race.	Uses PM2.5 and O3 from day before visit for cardiovascular causes and on the two preceding days for respiratory causes. Experimented with other lags	Yes	**Background:** Heart disease and stroke mortality and morbidity rates in Arkansas are among the highest in the U.S. While the effect of air pollution on cardiovascular health was identified in traffic-dominated metropolitan areas, there is a lack of studies for populations with variable exposure profiles, demographic and disease characteristics. **Objective:** Determine the short-term effects of air pollution on cardiovascular and respiratory morbidity in the stroke and heart failure belt. **Methods:** We investigated the associations of fine particles and ozone with respiratory and cardiovascular emergency room visits during the 2002–2012 period for adults in Central Arkansas using Poisson generalized models adjusted for temporal, seasonal and meteorological effects. We evaluated sensitivity of the associations to mutual pollutant adjustment and effect modification patterns by sex, age, race and season. **Results:** We found effects on cardiovascular and respiratory emergencies for PM2.5 (1.52% [95% (confidence interval) CI: −1.10%, 4.20%]; 1.45% [95%CI: − 2.64%, 5.72%] per 10 μg/m3) and O3 (0.93% [95%CI: − 0.87%, 2.76%]; 0.76 [95%CI: − 1.92%, 3.52%] per 10 ppbv) during the cold period (October–March). The effects were stronger among whites, except for the respiratory effects of O3 that were higher among Blacks/African-Americans. Effect modification patterns by age and sex differed by association. Both pollutants were associated with increases in emergency room visits for hypertension, heart failure and asthma. Effects on cardiovascular and respiratory emergencies were observed during the cold period when particulate matter was dominated by secondary nitrate and wood burning. **Conclusion:** Outdoor particulate pollution during winter had an effect on cardiovascular morbidity in central Arkansas, the region with high stroke and hear**t disease incidence rates.**

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Talbott, E.O., Rager, J.R., Benson, S., Brink, L.A., Bilonick, R.A., Wu, C.	A Case-Crossover Analysis of the Impact of PM2.5 on Cardiovascular Disease Hospitalizations for Selected CDC Tracking States	2014	Environmental Research	PM2.5	Non-elective hospital admission for circulatory disease, including all circulatory disease, ischemic heart disease, acute myocardial infarction, heart failure, cardiac arrhythmia, cerebrovascular disease, and peripheral vascular disease (primary discharge diagnosis of ICD-9: 390-459)	FL, MA., NH, NJ, NM NY, WA	2001-2008 admissions for circulatory disease	Estimates the short-term association of PM2.5 with risk of hospitalization for circulatory diseases		Used EPA estimates for predicted daily PM2.5 concentrations derived from Community Multi-Scale Air Quality Model for each zip code. Then did time-stratified case-crossover study with conditional logistic regression. For control, compared level of ambient PM2.5 in the time period just before hospitalization with PM2.5 at referent period	Case-crossover design eliminates risk of confounding by invariant and slowly changing risk factors like age, gender etc. Adjusted all odds ratios for ozone, with the same lag as PM2.5 and for maximum apparent temperature on day of admission. Also assessed effect modification by time of year	Estimated four different lag periods: lag 0, lag 1, lag 2, and 3 day average	Yes	**Background:** Information is currently being collected by the CDC Environmental Public Health Tracking (EPHT) network on hospitalizations due to Acute Myocardial Infarction (AMI) and there is interest by CDC in exploring the relationship between fine particulate matter (PM2.5) and other cardiovascular (CVD) outcomes in the context of the EPHT program. The goal of this study was to assess the short term effects of daily PM(2.5) air pollution levels on hospitalizations for CVD for seven states within the CDC EPHT network (Florida, Massachusetts, New Hampshire, New Jersey, New Mexico, New York, and Washington). **Methods:** Hospitalization data was obtained for 2001-2008 admissions for circulatory disease (primary discharge diagnosis of ICD-9 codes 390-459) from data stewards in those states and included admission date, age, gender, and zip code of residence. We used CMAQ-derived predicted daily PM2.5 data as estimated by EPA at the centroid of each Census Bureau Zip Code Tabulation Area (ZCTA) and linked to zip code of patient residence. A time-stratified case-crossover study design with conditional logistic regression was used to evaluate the short-term association of PM2.5 on risk of non-elective hospitalizations for CVD. Specifically, we considered all circulatory disease, ischemic heart disease, acute myocardial infarction, heart failure, cardiac arrhythmia, cerebrovascular disease and peripheral vascular disease endpoints. **Results:** Data were obtained on over 7,500,000 hospitalizations for this time period. Mean annual PM2.5 exposure levels were lowest for New Mexico and Washington (6.5 µg/m3 PM2.5 and 8.4 µg/m3 PM2.5). New Jersey, New York and Massachusetts exhibited the highest annual averages for PM2.5, (12.8 µg/m3, 11.1 µg/m3 and 10.8 µg/m3), respectively. The Northeast states (Massachusetts, New Jersey, New Hampshire and New York) exhibited significant effects of PM2.5 during the cooler months across most disease categories after adjustment for ozone and maximum apparent temperature. Ischemic heart disease risk per 10 µg/m3 increase in PM2.5 varied from 1.02 to 1.05 for the cooler
Zanobetti, A., Coull, B.A., Gryparis, A., Kloog, I., Sparrow, D., Vokonas, P.S., Wright, R.O., Gold, D.R., Schwartz, J.	Associations Between Arrhythmia Episodes and Temporally and Spatially Resolved Black Carbon and Particulate Matter in Elderly Patients	2013	Occupational Environmental Medicine	BC, PM2.5	Arrhythmia episodes (bigeminy, trigeminy or couplets episodes) measured as ventricular ectopy	Greater Boston area	Elderly men, participants in Normative Aging Study, between 21 and 80 in 1963, still in the study in 2000	Investigates association between black carbon and PM2.5 and arrhythmia episodes	Yes (with effect modification by presence of a gene and obesity)	Use mixed effects models, described VE episodes as present or absent, and then applied mixed logistic regression models to account for correlation among measurements on the same subject across different medical visits.	Adjusted for individual-level confounders, including BMI, age, cumulative cigarette smoking, use of medication, having diabetes, alcohol consumption of 2 or more drinks/day, SES at individual and neighborhood level, 24-hr mean temperature, seasonality, and linear variable for year. Corrected for potential survival bias by using inverse probability weighting. Looked for effect modification by subgroups defined by diabetes, obesity, statin use, and by gene variants. No evidence of having done assessment of co-pollutant effects.	Looked at air pollution over previous 24 hours and for moving averages of 2, 3, and 4 previous days	Yes	**Objectives:** Ambient air pollution has been associated with sudden deaths, some of which are likely due to ventricular arrhythmias. Defibrillator discharge studies have examined the association of air pollution with arrhythmias in sensitive populations. No studies have assessed this association using residence-specific estimates of air pollution exposure. **Methods:** In the Normative Aging Study, we investigated the association between temporally-and spatially-resolved black carbon (BC) and PM2.5 and arrhythmia episodes (bigeminy, trigeminy or couplets episodes) measured as ventricular ectopy (VE) by 4-min electrocardiogram (ECG) monitoring in repeated measures of 701 subjects, during the years 2000 to 2010. We used a binomial distribution (having or not a VE episode) in a mixed effect model with a random intercept for subject, controlling for seasonality, temperature, day of the week, medication use, smoking, having diabetes, BMI and age. We also examined whether these associations were modified by genotype or phenotype. **Results:** We found significant increases in VE with both pollutants and lags; for the estimated concentration averaged over the three days prior to the health assessment we found increases in the odds of having VE with an OR of 1.52 (95% CI: 1.19–1.94) for an IQR (0.30 µg/m3) increase in BC and an OR of 1.39 (95% CI: 1.12–1.71) for an IQR (5.63 µg/m3) increase in PM2.5. We also found higher effects in subjects with the GSTT1 and GSTM1 variants and in obese (P-values<0.05). **Conclusion:** Increased levels of short-term traffic related pollutants may increase the risk of ventricular arrhythmia in elderly subjects.

Table 3. Cardiovascular

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Crouse, D.L., Peters, P.A., van Donkelaar, A., Goldberg, M.S., Villeneuve, P.J., Brion, O., Khan, S., Atari, D.O., Jerrett, M., Pope, C.A., Brauer, M., Brook, J.R., Martin, R.V., Stiev, D., Burnett, R.T.	Risk of Nonaccidental and Cardiovascular Mortality in Relation to Long-term Exposure to Low Concentrations of Fine Particulate Matter: A Canadian National-Level Cohort Study	2012	Environmental Health Perspectives	PM2.5	All-cause non-accident (ICD-9: <800, ICD-10: starting with A through R), ischemic heart disease (ICD-9: 410-414, ICD-10: I20-I25), cerebrovascular disease (ICD-9: 430-434, 436-438, ICD-10: I60-I69), cardiovascular disease (ICD-9:410-417, 420-438, 440-449, ICD-10: I20-I28, I30-I52, I60-I79), circulatory disease (ICD-9: 390-459, ICD-10: I00-I99)	Canada	>=25 years, Canadian residents, non-immigrant	Investigates the association between long-term exposure to ambient PM2.5 and non-accidental and cardiovascular mortality in nonimmigrant Canadian adults	Yes	Calculated hazard ratios, adjusting for individual-level and neighborhood covariates using both Cox proportional survival models and nested, spatial random-effect survival Cox models. Stratified analysis by single-year age groups and sex	Included controls for subjects' demographic and SE environment, population size of home community. Acknowledge issue of potential exposure misclassification due to mobility of subjects	Used long-term exposure defined as average of concentration from 2001 to 2006 for full cohort and then did sub-analysis of 11 cities using mean annual conc from 1987 to 2001.	Yes	Background: Few cohort studies have evaluated the risk of mortality associated with long-term exposure to fine particulate matter [≤ 2.5 µm in aerodynamic diameter (PM2.5)]. This is the first national-level cohort study to investigate these risks in Canada. Objective: We investigated the association between long-term exposure to ambient PM2.5 and cardiovascular mortality in nonimmigrant Canadian adults. Methods: We assigned estimates of exposure to ambient PM2.5 derived from satellite observations to a cohort of 2.1 million Canadian adults who in 1991 were among the 20% of the population mandated to provide detailed census data. We identified deaths occurring between 1991 and 2001 through record linkage. We calculated hazard ratios (HRs) and 95% confidence intervals (CIs) adjusted for available individual-level and contextual covariates using both standard Cox proportional survival models and nested, spatial random-effects survival models. Results: Using standard Cox models, we calculated HRs of 1.15 (95% CI: 1.13, 1.16) from nonaccidental causes and 1.31 (95% CI: 1.27, 1.35) from ischemic heart disease for each 10-µg/m3 increase in concentrations of PM2.5. Using spatial random-effects models controlling for the same variables, we calculated HRs of 1.10 (95% CI: 1.05, 1.15) and 1.30 (95% CI: 1.18, 1.43), respectively. We found similar associations between nonaccidental mortality and PM2.5 based on satellite-derived estimates and ground-based measurements in a subanalysis of subjects in 11 cities. Conclusions: In this large national cohort of nonimmigrant Canadians, mortality was associated with long-term exposure to PM2.5. Associations were observed with exposures to PM2.5 at concentrations that were predominantly lower (mean, 8.7 µg/m3; interquartile range, 6.2 µg/m3) than those reported previously.
Kloog, I., Coull, B.A., Zanobetti, A., Koutrakis, P., Schwartz, J.D.	Acute and Chronic Effects of Particles on Hospital Admissions in New England	2012	PLoS One	PM2.5	Hospital admissions for cardiovascular or respiratory diagnoses among the elderly (65+): respiratory (ICD-9: 460-519), cardiovascular disease (ICD-9: 390-429), stroke (ICD-9: 430-436), diabetes (ICD-9: 250)	New England: CT, ME, MA, NH, RI, VT	Medicare beneficiaries (>= 65 years)	Assess the association betweenshort term and long term PM2.5 exposure and hospital admissions among the elderly		Matched admissions counts by zip code to exposure estimates. Make use of the equivalence between Poisson regression and the piecewise constant proportional hazard model, allowing them to model the time to a hospital admission as a function of both long- and short-term exposure. Check for linearity by fitting a piecewise linear model	Controlled for temperature with the same moving average as PM2.5, age, percent minorities, median income, and percent of people with no high school education. For sensitivity analysis, analyzed other averaging periods and the addition of land use and temporal variables	For short-term exposure, used mean of same and day before, and long-term exposure calculated as the mean exposure in each zip-code. Also define short term as difference between the two-day average and the long-term average?	Yes	**Background:** Many studies have reported significant associations between exposure to PM2.5 and hospital admissions, but all have focused on the effects of short-term exposure. In addition all these studies have relied on a limited number of PM2.5 monitors in their study regions, which introduces exposure error, and excludes rural and suburban populations from locations in which monitors are not available, reducing generalizability and potentially creating selection bias. **Methods:** Using our novel prediction models for exposure combining land use regression with physical measurements (satellite aerosol optical depth) we investigated both the long and short term effects of PM2.5 exposures on hospital admissions across New-England for all residents aged 65 and older. We performed separate Poisson regression analysis for each admission type: all respiratory, cardiovascular disease (CVD), stroke and diabetes. Daily admission counts in each zip code were regressed against long and short-term PM2.5 exposure, temperature, socio-economic data and a spline of time to control for seasonal trends in baseline risk. **Results:** We observed associations between both short-term and long-term exposure to PM2.5 and hospitalization for all of the outcomes examined. In example, for respiratory diseases, for every10-µg/m3 increase in short-term PM2.5 exposure there is a 0.70 percent increase in admissions (CI = 0.35 to 0.52) while concurrently for every10-µg/m3 increase in long-term PM2.5 exposure there is a 4.22 percent increase in admissions (CI = 1.06 to 4.75). **Conclusions:** As with mortality studies, chronic exposure to particles is associated with substantially larger increases in hospital admissions than acute exposure and both can be detected simultaneously using our exposure models.

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Rodopoulou, S., Samoli, E., Chalbot, M.G., Kavouras, I.G.	Air Pollution and Cardiovascular and Respiratory Emergency Visits in Central Arkansas: A Time-Series Analysis	2015	Science of the Total Environment	PM2.5, O3	Emergency room visits for cardiovascular diagnoses (ICD-9: 401-459), hypertension (ICD-9: 401), hypertensive heart disease and heart failure (ICD-9: 402, 428), conduction disorders and cardiac dysrhythmias: (ICD-9: 426-427), cerebrovascular disease and stroke: (ICD-9: 430-438), respiratory diagnoses (ICD-9: 460-519), acute respiratory infections except acute bronchioloitis and bronchiolitis (ICD-9: 460-465), pneumonia (ICD-9: 480-486), asthma (ICD-9: 493), chronic obstructive pulmonary disease (ICD-9: 490-491-492-496)	Central Arkansas	Daily emergency room visits 2002-2012 among adults >=15	Studies the short-term effects of air pollution on cardiovascular and respiratory morbidity in the stroke and heart failure belt		Tallied daily hospital emergency counts and then linked these counts to lagged pollution exposure using overdispersed generalized linear Poisson regression models. Applied natural spline smooth functions to include the effect of time-varying covariates and calendar time on daily visits. Used natural cubic regression splint with 1.5 degrees of freedom for each season and year.	Controlled for temperature on day of visit, two previous days, average relative humidity with lags, dummy variables for the day of the week and holidays effect. Looked for confounding by other pollutants using two pollutant models. Also looked at effect modification by season, age, gender, and race.	Uses PM2.5 and O3 from day before visit for cardiovascular causes and on the two preceding days for respiratory causes. Experimented with other lags	Yes	**Background:** Heart disease and stroke mortality and morbidity rates in Arkansas are among the highest in the U.S. While the effect of air pollution on cardiovascular health was identified in traffic-dominated metropolitan areas, there is a lack of studies for populations with variable exposure profiles, demographic and disease characteristics. **Objective:** Determine the short-term effects of air pollution on cardiovascular and respiratory morbidity in the stroke and heart failure belt. **Methods:** We investigated the associations of fine particles and ozone with respiratory and cardiovascular emergency room visits during the 2002–2012 period for adults in Central Arkansas using Poisson generalized models adjusted for temporal, seasonal and meteorological effects. We evaluated sensitivity of the associations to mutual pollutant adjustment and effect modification patterns by sex, age, race and season. **Results:** We found effects on cardiovascular and respiratory emergencies for PM2.5 (1.52% [95% (confidence interval) CI: − 1.10%, 4.20%]; 1.45% [95%CI: − 2.64%, 5.72%] per 10 μg/m3) and O3 (0.93% [95%CI: − 0.87%, 2.76%]; 0.76 [95%CI: − 1.92%, 3.52%] per 10 ppbv) during the cold period (October–March). The effects were stronger among whites, except for the respiratory effects of O3 that were higher among Blacks/African-Americans. Effect modification patterns by age and sex differed by association. Both pollutants were associated with increases in emergency room visits for hypertension, heart failure and asthma. Effects on cardiovascular and respiratory emergencies were observed during the cold period when particulate matter was dominated by secondary nitrate and wood burning. **Conclusion:** Outdoor particulate pollution during winter had an effect on cardiovascular morbidity in central Arkansas, the region with high stroke and heart **disease incidence rates.**
Shin, H.H., Fann, N., Burnett, R.T., Cohen, A., Hubbell, B.J.	Outdoor Fine Particles and Nonfatal Strokes: Systematic Review and Meta-Analysis	2014	Epidemiology	PM2.5	Nonfatal ischemic stroke (ICD-9: 433-444), hemorrhagic stroke (ICD-9: 430-432), and cerebrovascular events (ICD-9: 430-438)	10 of 16 short-term studies were in North America and 3 of 4 long-term studies in U.S.	Varied	Does a systematic review and meta-analysis of studies of estimates of the effect of long- and short-term PM2.5 exposure on the incidence of non-fatal ischemic stroke, hemorrhagic stroke, and cerebrovascular disease		Identified 20 studies to include in meta-analysis. Then first evaluated the strength of the epidemiologic evidence supporting the relation between PM2.5 and cerebrovascular disease by performing a Bayesian random-effects meta-analysis treating unknown overall risk and heterogeneity as random variables to estimate pooled concentration-response relations. Then, reflect scientifically-based conclusions of causality on the epidemiologic evidence by asserting a nonnegative prior	Evaluate the possibility for publication bias, and acknowledges the possibility of bias because about 90% of short-term estimates came from a single study.	In short-term studies, preferentially selected risk estimates associated with distributed or cumulative lags, and where unavailable selected the lag with the largest risk estimate	Yes	**Background:** Epidemiologic studies find that long- and short-term exposure to fine particles (PM2.5) is associated with adverse cardiovascular outcomes, including ischemic and hemorrhagic strokes. However, few systematic reviews or meta-analyses have synthesized these results. **Methods:** We reviewed epidemiologic studies that estimated the risks of nonfatal strokes attributable to ambient PM2.5. To pool risks among studies we used a random-effects model and 2 Bayesian approaches. The first Bayesian approach assumes a normal prior that allows risks to be zero, positive or negative. The second assumes a gamma prior, where risks can only be positive. This second approach is proposed when the number of studies pooled is small, and there is toxicological or clinical literature to support a causal relation. **Results:** We identified 20 studies suitable for quantitative meta-analysis. Evidence for publication bias is limited. The frequentist meta-analysis produced pooled risk ratios of 1.06 (95% confidence interval = 1.00-1.13) and 1.007 (1.003-1.010) for long- and short-term effects, respectively. The Bayesian meta-analysis found a posterior mean risk ratio of 1.08 (95% posterior interval = 0.96-1.26) and 1.008 (1.003-1.013) from a normal prior, and of 1.05 (1.02-1.10) and 1.008 (1.004-1.013) from a gamma prior, for long- and short-term effects, respectively, per 10 μg/m PM2.5. **Conclusions:** Sufficient evidence exists to develop a concentration-response relation for short- and long-term exposures to PM2.5 and stroke incidence. Long-term exposures to PM2.5 result in a higher risk ratio than short-term exposures, regardless of the pooling method. The evidence for short-term PM2.5-related ischemic stroke is especially strong.

Table 4. Respiratory

Authors	Title	Year Published	Journal Published	Pollutant(s) Studied	Causes of Mortality or Morbidity Considered	Geographic scope	Population studied	Study question	Statistically significant relationships?	Analysis method	Controls for factors that could obscure relationship?	Assesses potential lag between exposure and outcome?	Reports uncertainty?	Abstract
Darrow, L.A., Klein, M., Flanders, W.D., Mulholland, J.A., Tolbert, P.E., Strickland, M.J.	Air Pollution and Acute Respiratory Infections Among Children 0-4 Years of Age: an 18-Year Time-Series Study	2014	American Journal of Epidemiology	PM2.5, CO, NO2, O3	Emergency room visits for bronchitis or bronchiolitis (ICD-9: 466), pneumonia (ICD-9:480-486), upper respiratory infections (ICD-9: 460-465)	Atlanta, Georgia	Children 0-4 who visited ER for respiratory problems 1993-2010	Investigates relationships between short-term changes in ambient air pollution concentrations and emergency department visits for respiratory infections in young children	Very close, but typically not statistically significant	Used time-series analysis using Poisson generalized linear models allowing for overdispersion, estimated associations between the 3-day moving average pollutant concentration and daily counts for ER visits. First estimated associations separately for infants less than 1 and children 1-4 and then all together. Flexibly modeled shape of concentration-response function using loess smoothers in generalized additive models	Also controlled for dew point and temperature, controlled for seasonality and longer-term trends, indicators for day of week, season, holiday, and lag holiday, interactions between season and day of week. Assessed confounding by pollen concentrations. Assessed model misspecification and residual confounding by including lag negative 1. Did subanalyses estimating pollutant effects separately for different seasons using interaction terms. Ran multipollutant models and estimated joint effects of combined increase in multiple pollutants.	Used 3-day lag, but did sensitivity analysis for other lags	Yes	Upper and lower respiratory infections are common in early childhood and may be exacerbated by air pollution. We investigated short-term changes in ambient air pollutant concentrations, including speciated particulate matter less than 2.5 μm in diameter (PM2.5), in relation to emergency department (ED) visits for respiratory infections in young children. Daily counts of ED visits for bronchitis and bronchiolitis (n = 80,399), pneumonia (n = 63,359), and upper respiratory infection (URI) (n = 359,246) among children 0–4 years of age were collected from hospitals in the Atlanta, Georgia, area for the period 1993–2010. Daily pollutant measurements were combined across monitoring stations using population weighting. In Poisson generalized linear models, 3-day moving average concentrations of ozone, nitrogen dioxide, and the organic carbon fraction of particulate matter less than 2.5 μm in diameter (PM2.5) were associated with ED visits for pneumonia and URI. Ozone associations were strongest and were observed at low (cold-season) concentrations; a 1–interquartile range increase predicted a 4% increase (95% confidence interval: 2%, 6%) in visits for URI and an 8% increase (95% confidence interval: 4%, 13%) in visits for pneumonia. Rate ratios tended to be higher in the 1- to 4-year age group compared with infants. Results suggest that primary traffic pollutants, ozone, and the organic carbon fraction of PM2.5exacerbate upper and lower respiratory infections in early life, and that the carbon fraction of PM2.5 is a particularly harmful component of the ambient particulate matter mixture.
Gan, W.Q., Fitzgerald, J.M., Carlsten, C., Sadatsafavi, M., Brauer, M.	Associations of Ambient Air Pollution with Chronic Obstructive Pulmonary Disease Hospitalization and Mortality	2013	American Journal of Respiratory and Critical Care Medicine	PM2.5, NO2, NO	Chronic obstructive pulmonary disease (ICD-9: 490-492, 496, ICD-10: J40-J44)	Vancouver metropolitan area, Canada	All residents who were registered with the provincial health insurance plan, lived in the study region during 5-year exposure period, 45-85 years, no previous diagnosis of COPD	Investigates the associations of long-term exposure to elevated traffic-related air pollution and woodsmoke pollution with the risk of COPD hospitalization and mortality.		First, used a chi-square test for categorical variables and t test for continuous variables to compare baseline characteristics between cases and others. Looked at correlations between air pollutants using Spearman rank correlation. Then used Cox proportional hazards regression model to determine associations. Calculated person-days of follow-up from baseline to date of first COPD hospitalization, COPD death, or end of follow-up. Furhter examined C-R trends using natural cubic spline functions.	Controlled for age, sex, preexisting comorbid conditions, and neighborhood socioeconomic status. Comorbid conditions included asthma, diabetes, and hypertensive heart disease. Also adjusted for confounding. Performed stratified analyses to examine effect modification by age, sex, preexisting comorbid conditions, and neighborhood SES.	Used 5-year long-term exposure averages	Yes	Rationale: Ambient air pollution has been suggested as a risk factor for chronic obstructive pulmonary disease (COPD). However, there is a lack of longitudinal studies to support this assertion. Objectives: To investigate the associations of long-term exposure to elevated traffic-related air pollution and woodsmoke pollution with the risk of COPD hospitalization and mortality. Methods: This population-based cohort study included a 5-year exposure period and a 4-year follow-up period. All residents aged 45–85 years who resided in Metropolitan Vancouver, Canada, during the exposure period and did not have known COPD at baseline were included in this study (n = 467,994). Residential exposures to traffic-related air pollutants (black carbon, particulate matter <2.5 μm in aerodynamic diameter, nitrogen dioxide, and nitric oxide) and woodsmoke were estimated using land-use regression models and integrating changes in residences during the exposure period. COPD hospitalizations and deaths during the follow-up period were identified from provincial hospitalization and death registration databases. Measurements and Main Results: An interquartile range elevation in black carbon concentrations (0.97 × 10−5/m, equivalent to 0.78 μg/m3 elemental carbon) was associated with a 6% (95% confidence interval, 2–10%) increase in COPD hospitalizations and a 7% (0–13%) increase in COPD mortality after adjustment for covariates. Exposure to higher levels of woodsmoke pollution (tertile 3 vs. tertile 1) was associated with a 15% (2–29%) increase in COPD hospitalizations. There were positive exposure–response trends for these observed associations. Conclusions: Ambient air pollution, including traffic-related fine particulate pollution and woodsmoke pollution, is associated with an increased risk of COPD.

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Jones, R.R., Ozkaynak, H., Nayak, S.G., Garcia, V., Hwang, S.A., Lin, S.	Associations Between Summertime Ambient Pollutants and Respiratory Morbidity in New York City: Comparison of Results Using Ambient Concentrations Versus Predicted Exposures	2013	Journal of Exposure Science and Environmental Epidemiology	PM2.5, O3	Daily respiratory hospitalizations	New York City	Respiratory hospitalizations in New York City, 2001-2005	Evaluates associations between summertime ambient pollutants and respiratory morbidity, comparing results calculated using ambient concentrations vs. predicted exposures		Case-crossover design. Used two pollution exposure metrics: observed concentrations and predicted exposures from EPA's Stochastic Human Exposure and Dose Simulation model. **Can't see more without accessing full text.	Looked at effect modification by sociodemographic characteristics. **Can't see more without accessing full text.	Evaluates different lags, but finds strongest associations at 2- and 4-day lags	Yes	Epidemiological analyses of air quality often estimate human exposure from ambient monitoring data, potentially leading to exposure misclassification and subsequent bias in estimated health risks. To investigate this, we conducted a case-crossover study of summertime ambient ozone and fine particulate matter (PM(2.5)) levels and daily respiratory hospitalizations in New York City during 2001-2005. Comparisons were made between associations estimated using two pollutant exposure metrics: observed concentrations and predicted exposures from the EPA's Stochastic Human Exposure and Dose Simulation (SHEDS) model. Small, positive associations between interquartile range mean ozone concentrations and hospitalizations were observed and were strongest for 0-day lags (hazard ratio (HR)=1.013, 95% confidence interval (CI): 0.998, 1.029) and 3-day lags (HR=1.006, 95% CI: 0.991, 1.021); applying mean predicted ozone exposures yielded similar results. PM(2.5) was also associated with admissions, strongest at 2- and 4-day lags, with few differences between exposure metrics. Subgroup analyses support recognized sociodemographic differences in concentration-related hospitalization risk, whereas few inter-stratum variations were observed in relation to SHEDS exposures. Predicted exposures for these spatially homogenous pollutants were similar across sociodemographic strata, therefore SHEDS predictions coupled with the case-crossover design may have masked observable heterogeneity in risks. However, significant effect modification was found for subjects in the top exposure-to-concentration ratio tertiles, suggesting risks may increase as a consequence of infiltration or greater exposure to outdoor air.
Kloog, I., Coull, B.A., Zanobetti, A., Koutrakis, P., Schwartz, J.D.	Acute and Chronic Effects of Particles on Hospital Admissions in New England	2012	PLoS One	PM2.5	Hospital admissions for cardiovascular or respiratory diagnoses among the elderly (65+): respiratory (ICD-9: 460-519), cardiovascular disease (ICD-9: 390-429), stroke (ICD-9: 430-436), diabetes (ICD-9: 250)	New England: CT, ME, MA, NH, RI, VT	Medicare beneficiaries (>= 65 years)	Assess the association betweenshort term and long term PM2.5 exposure and hospital admissions among the elderly		Matched admissions counts by zip code to exposure estimates. Make use of the equivalence between Poisson regression and the piecewise constant proportional hazard model, allowing them to model the time to a hospital admission as a function of both long- and short-term exposure. Check for linearity by fitting a piecewise linear model	Controlled for temperature with the same moving average as PM2.5, age, percent minorities, median income, and percent of people with no high school education. For sensitivity analysis, analyzed other averaging periods and the addition of land use and temporal variables	For short-term exposure, used mean of same and day before, and long-term exposure calculated as the mean exposure in each zip-code. Also define short term as difference between the two-day average and the long-term average.	Yes	**Background:** Many studies have reported significant associations between exposure to PM2.5 and hospital admissions, but all have focused on the effects of short-term exposure. In addition all these studies have relied on a limited number of PM2.5 monitors in their study regions, which introduces exposure error, and excludes rural and suburban populations from locations in which monitors are not available, reducing generalizability and potentially creating selection bias. **Methods:** Using our novel prediction models for exposure combining land use regression with physical measurements (satellite aerosol optical depth) we investigated both the long and short term effects of PM2.5 exposures on hospital admissions across New-England for all residents aged 65 and older. We performed separate Poisson regression analysis for each admission type: all respiratory, cardiovascular disease (CVD), stroke and diabetes. Daily admission counts in each zip code were regressed against long and short-term PM2.5 exposure, temperature, socio-economic data and a spline of time to control for seasonal trends in baseline risk. **Results:** We observed associations between both short-term and long-term exposure to PM2.5 and hospitalization for all of the outcomes examined. In example, for respiratory diseases, for every10-µg/m3 increase in short-term PM2.5 exposure there is a 0.70 percent increase in admissions (CI = 0.35 to 0.52) while concurrently for every10-µg/m3 increase in long-term PM2.5 exposure there is a 4.22 percent increase in admissions (CI = 1.06 to 4.75). **Conclusions:** As with mortality studies, chronic exposure to particles is associated with substantially larger increases in hospital admissions than acute exposure and both can be detected simultaneously using our exposure models.

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Kloog, I., Zanobetti, A., Nordio, F., Coull, B.A., Baccarelli, A.A., Schwartz, J.	Effects of airborne fine particles on deep vein thrombosis admissions in the northeastern US	2015	Journal of Thrombosis and Haemostasis	PM2.5	Hospital admissions for deep-vein thrombosis and pulmonary embolism	Northeastern U.S. (Washington D.C., CT, ME, MA, NH, RI, VT, DE, MD, NJ, PA, VA, NY, WV)	All people >= 65	Studies whether long and short term PM2.5 exposure is associated with DVT and PE hospital admissions among the elderly across the northeastern US	Yes	Generates exposure data using spatiotemporal resolved prediction models using satellite data. For short term exposure, performed a case-crossover analysis matching on month and year and defined the hazard period as same day and day before. For long term exposure, used a Poisson proportionate hazard survival analysis, with a baseline hazard that varies for each follow-up interval	Controlled for temperature, social, economic, and housing characteristics at the zip code level. Also look at effect restricting analysis to below current EPA standards. For acute effects, the perfect matching from the case-crossover design means no confounding by other characteristics. Acknowledge possible confounding because they can't control for BMI life-style related risk factors, and possible misclassification bias.	Define short-term exposure as average of same day and day before, and define long-term as yearly moving average	Yes	**Background:** Literature relating air pollution exposure to deep vein thrombosis (DVT) and pulmonary embolism (PE), despite biological plausibility, is sparse. No comprehensive study examining associations between both short- and long-term exposure to particulate matter (PM)2.5 and DVT or PE has been published. Using a novel PM2.5 prediction model, we study whether long- and short-term PM2.5 exposure is associated with DVT and PE admissions among elderly across the northeastern United States. **Methods:** We estimated daily exposure of PM2.5 in each ZIP code. We investigated the long- and short-term effects of PM2.5 on DVT and PE hospital admissions. There were 453,413 DVT and 151,829 PE admissions in the study. For short-term exposure, we performed a case crossover analysis matching month and year and defined the hazard period as lag 01 (exposure of day of admission and previous day). For the long-term association, we used a Poisson regression. **Results:** A 10-µg m(-3) increase in short-term exposure was associated with a 0.63% increase in DVT admissions (95% confidence interval [CI] = 0.03% to 1.25%) and a 6.98% (95% CI = 5.65% to 8.33%) increase in long-term exposure admissions. For PE, the associated risks were 0.38% (95% CI = -0.68% to 1.25%) and 2.67% (95% CI = 5.65% to 8.33%). These results persisted when analyses were restricted to location-periods meeting the current Environmental Protection Agency annual standard of 12 µg m(-3) . **Conclusions:** Our findings showed that PM2.5 exposure was associated with DVT and PE hospital admissions and that current standards are not protective of this result.
Nachman, K.E., Parker, J.D.	Exposures to Fine Particulate Air Pollution and Respiratory Outcomes in Adults Using Two National Datasets: A Cross-Sectional Study	2012	Environmental Health	PM2.5	Asthma, sinusitis, chronic bronchitis	Contiguous U.S.	2002-2005 National Health Interview Survey participants, >=18	Examines the relationship between chronic exposure to fine particulate matter and the prevalence of adverse respiratory outcomes in adults on respiratory health outcomes by race/ethnicity.		Used logistic regression, controlling for confounding effects of health and socioeconomic covariates. Fitted stratified models to determine whether air pollution had different effects by race/ethnicity.	Controlled for race/ehtnicity, sex, age, BMI, smoking status, exercise status, education, urbanicity. Checked for effect modification by race/ethnicity. Did sensitivity analysis to see how results varied with urbanicity and insurance status. Acknowledge the potential for bias because subjects are reporting outcomes themselves. Also possible misclassification of outcomes and exposure.	Uses annual average pollution data	Yes	**Background:** Relationships between chronic exposures to air pollution and respiratory health outcomes have yet to be clearly articulated for adults. Recent data from nationally representative surveys suggest increasing disparity by race/ethnicity regarding asthma-related morbidity and mortality. The objectives of this study are to evaluate the relationship between annual average ambient fine particulate matter (PM2.5) concentrations and respiratory outcomes for adults using modeled air pollution and health outcome data and to examine PM2.5 sensitivity across race/ethnicity.**Methods:** Respondents from the 2002-2005 National Health Interview Survey (NHIS) were linked to annual kriged PM2.5 data from the USEPA AirData system. Logistic regression was employed to investigate increases in ambient PM2.5 concentrations and self-reported prevalence of respiratory outcomes including asthma, sinusitis and chronic bronchitis. Models included health, behavioral, demographic and resource-related covariates. Stratified analyses were conducted by race/ethnicity. **Results:** Of nearly 110,000 adult respondents, approximately 8,000 and 4,000 reported current asthma and recent attacks, respectively. Overall, odds ratios (OR) for current asthma (0.97 (95% Confidence Interval: 0.87-1.07)) and recent attacks (0.90 (0.78-1.03)) did not suggest an association with a 10 µg/m3 increase in PM2.5. Stratified analyses revealed significant associations for non-Hispanic blacks [OR = 1.73 (1.17-2.56) for current asthma and OR = 1.76 (1.07-2.91) for recent attacks] but not for Hispanics and non-Hispanic whites. Significant associations were observed overall (1.18 (1.08-1.30)) and in non-Hispanic whites (1.31 (1.18-1.46)) for sinusitis, but not for chronic bronchitis.**Conclusions:** Non-Hispanic blacks may be at increased sensitivity of asthma outcomes from PM2.5 exposure. Increased chronic PM2.5 exposures in adults may contribute to population sinusitis burdens.

Table 4. Respiratory

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Pride, K.R., Peel, J.L., Robinson, B.F., Busacker, A., Grandpre, J., Bisgard, K.M., Yip, F.Y., Murphy, T.D.	Association of Short-Term Exposure to Ground-Level Ozone and Respiratory Outpatient Clinic Visits in a Rural Location - Sublette County, Wyoming, 2008-2011	2015	Environmental Research	O3, PM2.5	Adverse respiratory effect, including acute bronchitis (ICD-9: 466), asthma (ICD-9: 493), chronic obstructive pulmonary disease (ICD-9: 491-492, 496), pneumonia (ICD-9: 480-486), upper respiratory tract infection (ICD-9: 460-465, 477), other respiratory (ICD-9: 786.09)	Sublette County, Wyoming	All clinic visits, 2008-2011	Evaluates the association of daily ground-level ozone concentrations and health clinic visits for respiratory disease		Executed a time-stratified case-crossover design using conditional logistic regression to compare exposure on the case-day with the weighted average of the exposure on the selected control days to estimate adjusted odds ratios. Control days were matched to cases by day of week within the same month.	Case-crossover design controls for time-invariant individual characteristics and adjusts for confounding by longer term trends and meteorological factors. Controlled for same-day temperature and humidity, with various lags. Looked for effect modification by season, and assessed a two-pollutant model including PM2.5 concentrations.			OBJECTIVE: Short-term exposure to ground-level ozone has been linked to adverse respiratory and other health effects; previous studies typically have focused on summer ground-level ozone in urban areas. During 2008-2011, Sublette County, Wyoming (population: ~10,000 persons), experienced periods of elevated ground-level ozone concentrations during the winter. This study sought to evaluate the association of daily ground-level ozone concentrations and health clinic visits for respiratory disease in this rural county. METHODS: Clinic visits for respiratory disease were ascertained from electronic billing records of the two clinics in Sublette County for January 1, 2008-December 31, 2011. A time-stratified case-crossover design, adjusted for temperature and humidity, was used to investigate associations between ground-level ozone concentrations measured at one station and clinic visits for a respiratory health concern by using an unconstrained distributed lag of 0-3 days and single-day lags of 0 day, 1 day, 2 days, and 3 days. RESULTS: The data set included 12,742 case-days and 43,285 selected control-days. The mean ground-level ozone observed was 47 ± 8 ppb. The unconstrained distributed lag of 0-3 days was consistent with a null association (adjusted odds ratio [aOR]: 1.001; 95% confidence interval [CI]: 0.990-1.012); results for lags 0, 2, and 3 days were consistent with the null. However, the results for lag 1 were indicative of a positive association; for every 10-ppb increase in the 8-h maximum average ground-level ozone, a 3.0% increase in respiratory clinic visits the following day was observed (aOR: 1.031; 95% CI: 0.994-1.069). Season modified the adverse respiratory effects: ground-level ozone was significantly associated with respiratory clinic visits during the winter months. The patterns of results from all sensitivity analyzes were consistent with the a priori model.
Rodopoulou, S., Chalbot, M.C., Samoli, E., Dubois, D.w., San Filippo, B.D., Kavouras, I.G.	Air Pollution and Hospital Emergency Room and Admissions for Cardiovascular and Respiratory Diseases in Dona Ana County, New Mexico	2014	Environmental Research	PM10, PM2.5, O3	Respiratory (ICD-9: 493, 466, 490, 491, 492, 496, 480-486, 460-465) and cardiovascular (ICD-9: 410-414, 426-427, 402, 428, 390-459)	Dona Ana County, New Mexico	Residents of Dona Ana county, estimated separately for all ages and 65+	Evaluates the association between short-term exposure to ambient PM10, PM2.5, and O3 and respiratory and cardiovascular emergency room visits and hospitalizations		Used Poisson regression models allowing for overdispersion, allowed nonlinearity by using natural splines. Remove dlong-term trends and seasonal patterns with a natural cubic regression spline for each season and year. Estimate effects separately for all ages and 65+	Controlled for long-term time trends and seasonal patterns, as well as temperature, daily humidity. Evaluated effect modification by season and tried removing days with outlier pollution. Also tried doing two day average lag.	Uses same day and day before pollution, and then two-day moving average	Yes	**Introduction:** Doña Ana County in New Mexico regularly experiences severe air pollution episodes associated with windblown dust and fires. Residents of Hispanic/Latino origin constitute the largest population group in the region. We investigated the associations of ambient particulate matter and ozone with hospital emergency room and admissions for respiratory and cardiovascular visits in adults. **Methods:** We used trajectories regression analysis to determine the local and regional components of particle mass and ozone. We applied Poisson generalized models to analyze hospital emergency room visits and admissions adjusted for pollutant levels, humidity, temperature and temporal and seasonal effects. **Results:** We found that the sources within 500km of the study area accounted for most of particle mass and ozone concentrations. Sources in Southeast Texas, Baja California and Southwest US were the most important regional contributors. Increases of cardiovascular emergency room visits were estimated for PM10 (3.1% (95% CI: -0.5 to 6.8)) and PM10-2.5 (2.8% (95% CI: -0.2 to 5.9)) for all adults during the warm period (April-September). When high PM10 (>150μg/m(3)) mass concentrations were excluded, strong effects for respiratory emergency room visits for both PM10 (3.2% (95% CI: 0.5-6.0)) and PM2.5 (5.2% (95% CI: -0.5 to 11.3)) were computed. **Conclusions:** Our analysis indicated effects of PM10, PM2.5 and O3 on emergency room visits during the April-September period in a region impacted by windblown dust and wildfires.

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Rodopoulou, S., Samoli, E., Chalbot, M.G., Kavouras, I.G.	Air Pollution and Cardiovascular and Respiratory Emergency Visits in Central Arkansas: A Time-Series Analysis	2015	Science of the Total Environment	PM2.5, O3	Emergency room visits for cardiovascular diagnoses (ICD-9: 401-459), hypertension (ICD-9: 401), hypertensive heart disease and heart failure (ICD-9: 402, 428), conduction disorders and cardiac dysrhythmias: (ICD-9: 426-427), cerebrovascular disease and stroke: (ICD-9: 430-438), respiratory diagnoses (ICD-9: 460-519), acute respiratory infections except acute bronchioloitis and bronchiolitis (ICD-9: 460-465), pneumonia (ICD-9: 480-486), asthma (ICD-9: 493), chronic obstructive pulmonary disease (ICD-9: 490-491-492-496)	Central Arkansas	Daily emergency room visits 2002-2012 among adults >=15	Studies the short-term effects of air pollution on cardiovascular and respiratory morbidity in the stroke and heart failure belt		Tallied daily hospital emergency counts and then linked these counts to lagged pollution exposure using overdispersed generalized linear Poisson regression models. Applied natural spline smooth functions to include the effect of time-varying covariates and calendar time on daily visits. Used natural cubic regression splint with 1.5 degrees of freedom for each season and year.	Controlled for temperature on day of visit, two previous days, average relative humidity with lags, dummy variables for the day of the week and holidays effect. Looked for confounding by other pollutants using two pollutant models. Also looked at effect modification by season, age, gender, and race.	Uses PM2.5 and O3 from day before visit for cardiovascular causes and on the two preceding days for respiratory causes. Experimented with other lags	Yes	**Background:** Heart disease and stroke mortality and morbidity rates in Arkansas are among the highest in the U.S. While the effect of air pollution on cardiovascular health was identified in traffic-dominated metropolitan areas, there is a lack of studies for populations with variable exposure profiles, demographic and disease characteristics. **Objective:** Determine the short-term effects of air pollution on cardiovascular and respiratory morbidity in the stroke and heart failure belt. **Methods:** We investigated the associations of fine particles and ozone with respiratory and cardiovascular emergency room visits during the 2002–2012 period for adults in Central Arkansas using Poisson generalized models adjusted for temporal, seasonal and meteorological effects. We evaluated sensitivity of the associations to mutual pollutant adjustment and effect modification patterns by sex, age, race and season. **Results:** We found effects on cardiovascular and respiratory emergencies for PM2.5 (1.52% [95% (confidence interval) CI: − 1.10%, 4.20%]; 1.45% [95%CI: − 2.64%, 5.72%] per 10 μg/m3) and O3 (0.93% [95%CI: − 0.87%, 2.76%]; 0.76 [95%CI: − 1.92%, 3.52%] per 10 ppbv) during the cold period (October–March). The effects were stronger among whites, except for the respiratory effects of O3 that were higher among Blacks/African-Americans. Effect modification patterns by age and sex differed by association. Both pollutants were associated with increases in emergency room visits for hypertension, heart failure and asthma. Effects on cardiovascular and respiratory emergencies were observed during the cold period when particulate matter was dominated by secondary nitrate and wood burning. **Conclusion:** Outdoor particulate pollution during winter had an effect on cardiovascular morbidity in central Arkansas, the region with high stroke and heart **disease incidence rates.**
Smith, G., Schoenbach, V.J., Richardson, D.B., Gammon, M.D.	Particulate Air Pollution and Susceptibility to the Development of Pulmonary Tuberculosis Disease in North Carolina: an Ecological Study	2014	International Journal of Environmental Health Research	PM2.5, PM10	Pulmonary tuberculosis	North Carolina	All residents in counties with data for PM for at least one year in 1993-2007	Examines the association between concentrations of ambient air pollutants and the rate of pulmonary tuberculosis	Yes	Used Poisson regression models to evaluate relationships between air pollution and PTB disease. Addressed possible non-linearity of the covariates using indicator variables and a scaled deviance parameter specification to account for overdispersion. Examined autocorrelation in model residuals using Durbin-Watson test. Used single pollutant models, and categorized exposure into quintiles based on the distribution of county-years of air pollution levels.	Consider covariates including age, gender, race, and year of diagnosis. First checked for effect modification by each covariate, and then included all in the model. Acknowledge the potential for misclassification due to lack of variability in air pollution data.	Uses average long-term pollution concentrations, 1993-2007 for PM10 and 1999-2007 for PM2.5	Yes	Although Mycobacterium tuberculosis is the causative agent of pulmonary tuberculosis (PTB), environmental factors may influence disease progression. Ecologic studies conducted in countries outside the USA with high levels of air pollution and PTB have suggested a link between active disease and ambient air pollution. The present investigation is the first to examine the ambient air pollution/PTB association in a country, where air pollution levels are comparatively lower. We used Poisson regression models to examine the association of outdoor air pollutants, PM10 and PM2.5 with rates of PTB in North Carolina residents during 1993–2007. Results suggest a potential association between long-term exposure to particulate matter (PM) and PTB disease. In view of the high levels of air pollution and high rates of PTB worldwide, a potential association between ambient air pollution and tuberculosis warrants further study.
Yap, P., Gilbreath, S., Garcia, C., Jareen, N., Goodrich, B.	The Influence of Socioeconomic Markers on the Association Between Fine Particulate Matter and Hospital Admissions for Respiratory Conditions Among Children	2013	American Journal of Public Health	PM2.5	Combined respiratory conditions (ICD-9: 460-519), acute respiratory infections (ICD-9: 460-466, 480-486), pneumonia (ICD-9: 480-486), and asthma (ICD-9: 493)	Central Valley and South Coast regions, California	Children aged 1-9 years	Investigates the relationships among SES, acute PM2.5 exposure and childhood morbidity		Did daily time-series analysis. Performed generalized additive Poisson regression models. Accounted for longer-term patterns in the health outcomes data using time trends and seasonality, day of the week, and smoothing splines with different lags for temperature. Ultimately used 3-day lag for PM2.5 exposure.	Looked at effect modification by single or composite area-based SES variables. Also ran stratified models on the single and composite area-based SES variables	Investigated exposure lags of 0-6 days, with 3-day lag yielding the best fit	Yes	**Objectives:** We evaluated the influence of socioeconomic status (SES) on hospital admissions for respiratory conditions associated with ambient particulate matter that is 2.5 micrometers or less in aerodynamic diameter (PM2.5) in children aged 1 to 9 years in 12 California counties, from 2000 to 2005. **Methods:** We linked daily hospital admissions for respiratory conditions (acute respiratory infections, pneumonia, and asthma) to meteorological, air pollution, and census data. **Results:** In San Diego, San Bernardino, Riverside, and Los Angeles counties, the admission rates for children associated with PM2.5 ranged from 1.03 to 1.07 for combined respiratory conditions and 1.03 to 1.08 for asthma in regions with lower SES. We observed 2 distinct patterns of the influence of the composite SES Townsend index. In lower-SES South Coast areas, PM2.5-associated hospital admission rates for all respiratory outcomes were predominantly positive whereas results in the Central Valley were variable, often tending toward the null. **Conclusions:** These distinct patterns could be attributed to the heterogeneity of regional confounders as well as the seasonal variation of emission sources of PM2.5. Composite SES is one potential factor for increasing susceptibility to air pollution.

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Atkinson, R.W., Kang, S., Anderson, H.R., Mills, I.C., Walton, H.A.	Epidemiological Time Series Studies of PM2.5 and Daily Mortality and Hospital Admissions: a Systematic Review and Meta-Analysis	2014	Thorax	PM2.5	All-cause mortality, IHD mortality, stroke mortality, COPD (excl. asthma) mortality, hospital admissions for cardiovascular and respiratory diseases: all ages: cardiovascular, respiratory, 65+ years: cardiovascular, COPD incl astha, COPD excl asthma, lower resp infection, respiratory, IHD, heart failure, cardiac, stroke, dysrhythmia; 0-14: respiratory, asthma	Worldwide, but provides estimates specific to WHO American Region A (U.S., Canada, Cuba)	For different health endpoints, considers all ages, 65+ years, 0-14 years	Assesses the evidence for associations between PM2.5 and daily mortality and hospital admissions for a range of diseases and ages using a comprehensive review and meta-analysis	Yes	Did a systematic, comprehensive review of 110 peer-reviewed time series studies published through May 2011. Within each WHO region, did a two stage meta-analysis, first pooling single-city estimates and then pooling these summary estimates with the selected multicity study estimates to get a WHO region-specific summary estimates. In WHO American Region A, had 33 total mortality studies, 31 hospital admission studies.	They assessed small study bias in single-city estimates and selected multicity estimates. They choose studies that attempt to control for confounding factors like season, lont-term temporal trends and meteorological conditions	Studies vary in the time lag they study for short-term effects, but it seems that they just combined estimates using different lags. I'm not sure about this.	Yes	**Background:** Short-term exposure to outdoor fine particulate matter (particles with a median aerodynamic diameter <2.5 μm (PM2.5)) air pollution has been associated with adverse health effects. Existing literature reviews have been limited in size and scope. **Methods:** We conducted a comprehensive, systematic review and meta-analysis of 110 peer-reviewed time series studies indexed in medical databases to May 2011 to assess the evidence for associations between PM2.5 and daily mortality and hospital admissions for a range of diseases and ages. We stratified our analyses by geographical region to determine the consistency of the evidence worldwide and investigated small study bias. **Results:** Based upon 23 estimates for all-cause mortality, a 10 μg/m3 increment in PM2.5 was associated with a 1.04% (95% CI 0.52% to 1.56%) increase in the risk of death. Worldwide, there was substantial regional variation (0.25% to 2.08%). Associations for respiratory causes of death were larger than for cardiovascular causes, 1.51% (1.01% to 2.01%) vs 0.84% (0.41% to 1.28%). Positive associations with mortality for most other causes of death and for cardiovascular and respiratory hospital admissions were also observed. We found evidence for small study bias in single-city mortality studies and in multicity studies of cardiovascular disease. **Conclusions:** The consistency of the evidence for adverse health effects of short-term exposure to PM2.5 across a range of important health outcomes and diseases supports policy measures to control PM2.5 concentrations. However, reasons for heterogeneity in effect estimates in different regions of the world require further investigation. Small study bias should also be considered in assessing and quantifying health risks from PM2.5.
Bell, M.L., Son, J.Y., Peng, R.D., Wang, Y., Dominici, F.	Brief Report: Ambient PM2.5 and Risk of Hospital Admissions: Do Risks Differ for Men and Women?	2015	Epidemiology	PM2.5	Risk of cause-specific cardiovascular and respiratory hospitalizations (I can't access full text to see specifics)	213 U.S. counties	Medicare beneficiaries (>= 65) for 1999-2000	Estimates the associations between PM2.5 exposure and risk of cause-specific cardiovascular and respiratory hospitalizations, and whether these associations differ between men and women		Use Bayesian hierarchical modeling to estimate associations.			Yes	**Background:** While strong evidence exists for associations between fine particles (PM2.5) and health, less is known about whether associations differ by sex. **Methods:** We used Bayesian hierarchical modeling to estimate associations between PM2.5, based on ambient monitors, and risk of cause-specific cardiovascular and respiratory hospitalizations for about 12.6 million Medicare beneficiaries (>65 years) residing in 213 US counties for 1999-2010. **Results:** Point estimates were higher for women than men for almost all causes of hospitalization. PM2.5 risks were higher for women than men for respiratory tract infection, cardiovascular, and heart rhythm disturbance admissions. A 10 μg/m(3) increase in same-day PM2.5 was associated with a 1.13% increased risk of heart rhythm disturbance admissions for women (95% posterior interval [PI]: 0.63%, 1.63%), and 0.03% for men (95% PI: -0.48%, 0.55%). Differences remained after stratification by age and season. **Conclusions:** Women may be more susceptible to PM2.5-related hospitalizations for some respiratory and cardiovascular causes.

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Delamater, P.L., Finley, A.O., Banerjee, S.	An Analysis of Asthma Hospitalizations, Air Pollution, and Weather Conditions in Los Angeles County, California	2012	Science of the Total Environment	CO, NO2, O3, PM10, PM2.5	Extrinsic, intrinsic, other asthma (ICD-9-CM: 493.0x, 493.1x, 493.8x)	Los Angeles County, CA	Daily hospital admissions	Examines the relationship between asthma morbidity, air pollution, and weather conditions at a county-level scale.		Generated monthly rates of asthma hospitalizations and then mean daily hospitalization rate for each month. Removed yearly trend and seasonal trends. Then experimented with a number of diferent model specifications, using Bayesian regression models with temporal random effects.	Controls for time trends and seasonality, but perhaps not other controls typically used.	Uses monthly average pollutant exposure	Yes	There is now a large body of literature supporting a linkage between exposure to air pollutants and asthma morbidity. However, the extent and significance of this relationship varies considerably between pollutants, location, scale of analysis, and analysis methods. Our primary goal is to evaluate the relationship between asthma hospitalizations, levels of ambient air pollution, and weather conditions in Los Angeles (LA) County, California, an area with a historical record of heavy air pollution. County-wide measures of carbon monoxide (CO), nitrogen dioxide (NO(2)), ozone(O(3)), particulate matter<10 µm (PM(10)), particulate matter<2.5 µm (PM(2.5)), maximum temperature, and relative humidity were collected for all months from 2001 to 2008. We then related these variables to monthly asthma hospitalization rates using Bayesian regression models with temporal random effects. We evaluated model performance using a goodness of fit criterion and predictive ability. Asthma hospitalization rates in LA County decreased between 2001 and 2008. Traffic-related pollutants, CO and NO(2), were significant and positively correlated with asthma hospitalizations. PM(2.5) also had a positive, significant association with asthma hospitalizations. PM(10), relative humidity, and maximum temperature produced mixed results, whereas O(3) was non-significant in all models. Inclusion of temporal random effects satisfies statistical model assumptions, improves model fit, and yields increased predictive accuracy and precision compared to their non-temporal counterparts. Generally, pollution levels and asthma hospitalizations decreased during the 9 year study period. Our findings also indicate that after accounting for seasonality in the data, asthma hospitalization rate has a significant positive relationship with ambient levels of CO, NO(2), and PM(2.5).
Delfino, R.J., Wu, J., Tjoa, T., Gullesserian, S.K., Nickerson, B., Gillen, D.L.	Asthma Morbidity and Ambient Air Pollution: Effect Modification by Residential Traffic-Related Air Pollution	2014	Epidemiology	PM2.5, NO2, NOx, CO, O3	"Hospital encounters" (ER visits and hospital admissions) from asthma	Orange County, CA	Subjects aged 0-18 with hospital encounters with a primary diagnosis of asthma between 2000 and 2008	Assesses the association between ambient air pollution and asthma-related hospital admissions and ER visits and investigates whether this association is modified by exposure to residential traffic-related air pollutants (NO2, NOx, CO)		Estimated long-term traffic-related NO2, NOx, CO, PM2.5 for each residence. Then evaluated associations of asthma-related hospital morbidity with air pollution exposure using a case-crossover design with conditional logistic regression. Exposures are sampled from each subject's time-varying distribution of exposure, so each person is his or her own control. Use semisymmetric bidirectional referent selection design	Case-crossover design controls for time-invariant subject characteristics, and using sufficiently narrow reference windows for controls avoids bias from seasonal confounding. To reduce serial correlation and avoid confounding from temporally adjacent exposures, did not select referent days within 7 days of exposure. Controlled for overlap bias between two sample hospitals, and controlled for within-subject correlation. Controlled for mean temperature and relative humidity over same lag period as pollutants. Tested effect modification by 6-month seasonal average residential air pollution. Addressed confounding in this analysis by doing secondary analysis to assess influence of race/ethnicity or health insurance status on differences in association with traffic-related air pollution strata	Estimates average traffic pollutant exposure for 6-month seasonal periods, and looks at PM2.5 exposure over 7 days before hospitalization, and tested other lags	Yes	**Background:** Ambient air pollution has been associated with asthma-related hospital admissions and emergency department visits (hospital encounters). We hypothesized that higher individual exposure to residential traffic-related air pollutants would enhance these associations. **Methods:** We studied 11,390 asthma-related hospital encounters among 7492 subjects 0-18 years of age living in Orange County, California. Ambient exposures were measured at regional air monitoring stations. Seasonal average traffic-related exposures (PM2.5, ultrafine particles, NOx, and CO) were estimated near subjects' geocoded residences for 6-month warm and cool seasonal periods, using dispersion models based on local traffic within 500 m radii. Associations were tested in case-crossover conditional logistic regression models adjusted for temperature and humidity. We assessed effect modification by seasonal residential traffic-related air pollution exposures above and below median dispersion-modeled exposures. Secondary analyses considered effect modification by traffic exposures within race/ethnicity and insurance group strata. **Results:** Asthma morbidity was positively associated with daily ambient O3 and PM2.5 in warm seasons and with CO, NOx, and PM2.5 in cool seasons. Associations with CO, NOx, and PM2.5 were stronger among subjects living at residences with above-median traffic-related exposures, especially in cool seasons. Secondary analyses showed no consistent differences in association, and 95% confidence intervals were wide, indicating a lack of precision for estimating these highly stratified associations. **Conclusions:** Associations of asthma with ambient air pollution were enhanced among subjects living in homes with high traffic-related air pollution. This may be because of increased susceptibility (greater asthma severity) or increased vulnerability (meteorologic amplification of local vs. correlated ambient exposures).

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Glad, J.A., Brink, L.L., Talbott, E.O., Lee, P.C., Xu, X., Saul, M., Rager, J.	The Relationship of Ambient Ozone and PM2.5 Levels and Asthma Emergency Department Visits: Possible Influence of Gender and Ethnicity	2012	Archives of Environmental and Occupational Health	O3, PM2.5	Emergency department visits for asthma	Pittsburgh, PA	All ED visits, 2002-2005	Investigates the relationship between ambient ozone and PM2.5 levels and asthma emergency department visits		Use a case-crossover study design	Case-crossover design will control for time-invariant individual characteristics, and look at effect modification by sex and race			An investigation of the relationship of air pollution and emergency department (ED) visits for asthma was an opportunity to assess environmental risks for asthma exacerbations in an urban population. A total of 6,979 individuals with a primary discharge diagnosis of asthma presented to 1 of 6 EDs in the Pittsburgh, Pennsylvania, area between 2002 and 2005. Using a case-crossover methodology, which controls for the effects of subject-specific covariates such as gender and race, a 2.5% increase was observed in asthma ED visits for each 10 ppb increase in the 1-hour maximum ozone level on day 2 (odds ratio [OR] = 1.025, p < .05). Particulate matter with an aerodynamic diameter ≤2.5 µm (PM2.5) had an effect both on the total population on day 1 after exposure (1.036, p < .05), and on African Americans on days 1, 2, and 3. PM2.5 had no significant effect on Caucasian Americans alone. The disparity in risk estimates by race may reflect differences in residential characteristics, exposure to ambient air pollution, or a differential effect of pollution by race.
Gleason, J.A., Fagliano, J.A.	Associations of Daily Pediatric Asthma Emergency Department Visits with Air Pollution in Newark, NJ: Utilizing Time-Series and Case-Crossover Study Designs	2015	Journal of Asthma	O3, PM2.5	Asthma	Newark, NJ	Age 3-17 with primary diagnosis of asthma during April to September, 2004-2007	Assesses the associations of ozone and PM2.5 with pediatric emergency department visits in Newark		Time-stratified case-crossover study, with bi-directional control sampling, and also time-series study design. Looked at various lags, including 1-d through 5-d, 3-d average, and 5-d average. Performed a dose-response analysis comparing the bottom 5th percentile of 3-d average lag ozone with each 5 percentile increase.	Case-crossover study should control for all time-invariant individual characteristics.	Tried different lags, with 1-d through 5-d, 3-d average, 5-d average.	Yes	**Objective:** Asthma is one of the most common chronic diseases affecting children. This study assesses the associations of ozone and fine particulate matter (PM2.5) with pediatric emergency department visits in the urban environment of Newark, NJ. Two study designs were utilized and evaluated for usability. **Methods:** We obtained daily emergency department visits among children aged 3-17 years with a primary diagnosis of asthma during April to September for 2004-2007. Both a time-stratified case-crossover study design with bi-directional control sampling and a time-series study design were utilized. Lagged effects (1-d through 5-d lag, 3-d average, and 5-d average) of ozone and PM2.5 were explored and a dose-response analysis comparing the bottom 5th percentile of 3-d average lag ozone with each 5 percentile increase was performed. **Results:** Associations of interquartile range increase in same-day ozone were similar between the time-series and case-crossover study designs (RR = 1.08, 95% CI 1.04-1.12) and (OR = 1.10, 95% CI 1.06-1.14), respectively. Similar associations were seen for 1-day lag and 3-day average lag ozone levels. PM2.5 was not associated with the outcome in either study design. Dose-response assessment indicated a statistically significant and increasing association around 50-55 ppb consistent for both study designs. **Conclusions:** Ozone was statistically positively associated with pediatric asthma ED visits in Newark, NJ. Our results were generally comparable across the time-series and case-crossover study designs, indicating both are useful to assess local air pollution impacts.
Hebbern, C., Cakmak, S.	Synoptic Weather Types and Aeroallergens Modify the Effect of Air Pollution on Hospitalisations for Asthma Hospitalisations in Canadian Cities	2015	Environmental Pollution	CO, O3, NO2, SO2, PM10, PM2.5	Hospitalizations for asthma	Ten cities across Canada	Hospitalizations for asthma April 1, 1994-March 31, 2007	Tests the association between daily changes in aeroallergens and asthma hospitalizations, contributing changes in asthma hospitalizations to individuals with susceptibility to aeroallergens	Yes (with significant effect modification by aeroallergens in particular weather types)	Used generalized additive models with stringent convergence criteria to test the association between asthma hospitalizations and individual pollutants, controlling for aeroallergens. Developed each model for days corresponding to one of seven synoptic scale eather types. Assumed that hospitalization data was Poisson-distributed. Looked at effect of each pollutant on asthma hospitalization for the day of admission and five days preceding. Then pooled data for the ten cities using a random effects model with a random intercept to account for between-city inhomogeneity.	Controlled for the presence of aeroallergens. Stratified model by weather type.	Looked at effect of each pollutant on asthma hospitalization for the day of admission and five days preceding	Yes	Pollution levels and the effect of air pollution on human health can be modified by synoptic weather type and aeroallergens. We investigated the effect modification of aeroallergens on the association between CO, O3, NO2, SO2, PM10, PM2.5 and asthma hospitalisation rates in seven synoptic weather types. We developed single air pollutant models, adjusted for the effect of aeroallergens and stratified by synoptic weather type, and pooled relative risk estimates for asthma hospitalisation in ten Canadian cities. Aeroallergens significantly modified the relative risk in 19 pollutant-weather type combinations, reducing the size and variance for each single pollutant model. However, aeroallergens did not significantly modify relative risk for any pollutant in the DT or MT weather types, or for PM10 in any weather type. Thus, there is a modifying effect of aeroallergens on the association between CO, O3, NO2, SO2, PM2.5 and asthma hospitalisations that differs under specific synoptic weather types.

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Li, T., Lin, G.	Examining the Role of Location-Specific Associations Between Ambient Air Pollutants and Adult Asthma in the United States	2013	Health and Place	PM2.5, O3	Asthma	United States	>=18 with known asthma status, from Behavioral Risk Factor Surveillance System	Assesses the association between asthma risk and ozone and PM2.5 exposure in both metropolitan and non-metropolitan areas		Used multilevel logistic regression models to account for individual-level risk factors nested within county-level risk factors. Ran both a co-pollutant model and single-pollutant model. Assessed place-specific effects by interacting different metropolitan and non-metropolitan settings with pollutant concentrations in single-pollutant models. Provides results specified for "West North Central" and "West South Central"	Ran both co-pollutant model to account for confounding and single-pollutant models. Included county-level controls for race/ethnicity, education, poverty. Included individual-level characteristics like gender, age, race/ethnicity, marital status, education, general health status, obesity status, smoking status, insurance and access to care.	Average PM2.5 exposure 2006-2009, and 2006-2009 average of annual fourth-highest daily max ozone concentration	Yes	This study examined the association between ozone and fine particulate (PM2.5) exposure and asthma risk by place of residence. We linked 412,832 adult respondents from the 2009 U.S. Behavioral Risk Factor Surveillance System to their residence counties. Observed and interpolated ozone and PM2.5 concentration data from 2006 to 2009 were used as exposures. We linked self-reported current asthma status and other individual risk factors to county-level risk factors in multilevel logistic regressions. Results indicated spatially varied asthma risks and spatially varied associations between ambient air pollution and asthma risk. Residents in counties not located within a metropolitan statistical area (MSA) and in inner ring suburbs had a relatively higher asthma risk. Positive ozone-asthma associations were detected across all spatial settings, while positive PM2.5-asthma associations were detected only in central cities of an MSA and in outer ring suburbs, indicating that residence location modified the relationship between ambient air pollution and asthma risk.
Loftus, C., Yost, M., Sampson, P., Arias, G., Torres, E., Vasquez, V.B., Bhatti, P., Karr, C	Regional PM2.5 and Asthma Morbidity in an Agricultural Community: A Panel Study	2015	Environmental Research	PM2.5	Asthma exacerbation	Washington State	School-aged children with asthma in agricultural community	Investigates the association between PM2.5 exposure and pediatric asthma exacerbation--not ideal because it's studying exacerbation rather than incidence		Followed 58 school-aged children with asthma for up to 25 months with biweekly measures of respiratory health. Performed linear regression of health outcomes on PM2.5 using generalized estimating equations with autoregressive-1 correlation structures to account for correlation among repeated measures for each subject. Asthma morbidity outcomes were measured lung function, being woken by asthma, being limited in daily activities, shortness of breath, symptoms in morning, wheezing, use of bronchodilator	Controls for subject-specific characteristics sex, age, atopy, use of inhaled corticosteroids at baseline, and BMI at baseline. Also controls for continuous adjustment variables like temperature, humidity, precip, seasonality etc. using cubic splines with 5 knots each. Checked for effect modification by atopy. Acknowledge potential bias from missing measurements and possibility of confounding from other other pollutants.	Evaluated different lags in sensitivity analysis.	Yes	**Background:** Elevated pediatric asthma morbidity has been observed in rural US communities, but the role of the ambient environment in exacerbating rural asthma is poorly understood. **Objectives:** To investigate associations between particulate matter less than 2.5 µm in diameter (PM2.5) and pediatric asthma exacerbations in an agricultural community of Washington State. **Methods:** School-aged children with asthma (n=58) were followed for up to 25 months with repeated measures of respiratory health. Asthma symptoms and quick-relief medication use were assessed biweekly through phone administered surveys (n=2023 interviews). In addition, subjects used home peak flow meters on a daily basis to measure forced expiratory volume in one second (FEV1) (n=7830 measurements). Regional PM2.5 was measured at a single air monitor located centrally in the study region. To assess relationships between PM2.5 and these outcomes we used linear regression with generalized estimating equations, adjusting for meteorological and temporal confounders. Effect modification by atopy was explored as well. **Results:** An interquartile increase (IQR) in weekly PM2.5 of 6.7 µg/m(3) was associated with an increase in reported asthma symptoms Specific symptoms including wheezing, limitation of activities, and nighttime waking displayed the strongest associations. FEV1 as a percent of predicted decreased by 0.9% (95%CI: -1.8, 0.0) for an IQR increase in PM2.5 one day prior, and by 1.4% (95%CI: -2.7, -0.2) when restricted to children with atopic asthma. **Conclusions:** This study provides evidence that PM2.5 in an agricultural setting contributes to elevated asthma morbidity. Further work on identifying and mitigating sources of PM2.5 in the area is warranted.

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Nachman, K.E., Parker, J.D.	Exposures to Fine Particulate Air Pollution and Respiratory Outcomes in Adults Using Two National Datasets: A Cross-Sectional Study	2012	Environmental Health	PM2.5	Asthma, sinusitis, chronic bronchitis	Contiguous U.S.	2002-2005 National Health Interview Survey participants, >=18	Examines the relationship between chronic exposure to fine particulate matter and the prevalence of adverse respiratory outcomes in adults		Used logistic regression, controlling for confounding effects of health and socioeconomic covariates. Fitted stratified models to determine whether air pollution had different effects on respiratory health outcomes by race/ethnicity.	Controlled for race/ehtnicity, sex, age, BMI, smoking status, exercise status, education, urbanicity. Checked for effect modification by race/ethnicity. Did sensitivity analysis to see how results varied with urbanicity and insurance status. Acknowledge the potential for bias because subjects are reporting outcomes themselves. Also possible misclassification of outcomes and exposure.	Uses annual average pollution data	Yes	**Background:** Relationships between chronic exposures to air pollution and respiratory health outcomes have yet to be clearly articulated for adults. Recent data from nationally representative surveys suggest increasing disparity by race/ethnicity regarding asthma-related morbidity and mortality. The objectives of this study are to evaluate the relationship between annual average ambient fine particulate matter (PM2.5) concentrations and respiratory outcomes for adults using modeled air pollution and health outcome data and to examine PM2.5 sensitivity across race/ethnicity.**Methods:** Respondents from the 2002-2005 National Health Interview Survey (NHIS) were linked to annual kriged PM2.5 data from the USEPA AirData system. Logistic regression was employed to investigate increases in ambient PM2.5 concentrations and self-reported prevalence of respiratory outcomes including asthma, sinusitis and chronic bronchitis. Models included health, behavioral, demographic and resource-related covariates. Stratified analyses were conducted by race/ethnicity. **Results:** Of nearly 110,000 adult respondents, approximately 8,000 and 4,000 reported current asthma and recent attacks, respectively. Overall, odds ratios (OR) for current asthma (0.97 (95% Confidence Interval: 0.87-1.07)) and recent attacks (0.90 (0.78-1.03)) did not suggest an association with a 10 µg/m3 increase in PM2.5. Stratified analyses revealed significant associations for non-Hispanic blacks [OR = 1.73 (1.17-2.56) for current asthma and OR = 1.76 (1.07-2.91) for recent attacks] but not for Hispanics and non-Hispanic whites. Significant associations were observed overall (1.18 (1.08-1.30)) and in non-Hispanic whites (1.31 (1.18-1.46)) for sinusitis, but not for chronic bronchitis.**Conclusions:** Non-Hispanic blacks may be at increased sensitivity of asthma outcomes from PM2.5 exposure. Increased chronic PM2.5 exposures in adults may contribute to population sinusitis burdens.
Pearce, J.L., Waller, L.A., Mulholland, J.A., Sarnat, S.E., Strickland, M.J., Chang, H.H., Tolbert, P.E.	Exploring Associations Between Multipollutant Day Types and Asthma Morbidity: Epidemiologic Applications of Self-Organizing Map Ambient Air Quality Classifications	2015	Environmental Health	CO, NO2, NOx, SO2, PM2.5, O3, others	Pediatric emergency department visits for asthma (ICD-9: 493.0-493.9, 786.07)	Metropolitan Atlanta	Children 5-18	Explore short-term associations between multiple pollutants and emergency department visits for pediatric asthma.		Use self-organizing map to develop categories of multipollutant day types that reflect how multipollutant combinations vary in time at the study location. Then model associations between multipollutant day types and pediatric asthma emergency department visits using case-crossover design within the framework of a Poisson generalized linear model allowing for overdispersion. Also use single-pollutant models, looking at more traditional estimates of effects of pollution on morbidity.	Controlled for confounding by year, season, month, day-of-the-week, hospital, and holidays. Looked at effect modification by those variables. Also included cubic polynomial terms for three-day averages of mean temperature and mean dew point temperature. Looked at interactions between temperature and season.	Use lag of 1 day before health outcome	Yes	Background: Recent interest in the health effects of air pollution focuses on identifying combinations of multiple pollutants that may be associated with adverse health risks. Objective: Present a methodology allowing health investigators to explore associations between categories of ambient air quality days (i.e., multipollutant day types) and adverse health. Methods: First, we applied a self-organizing map (SOM) to daily air quality data for 10 pollutants collected between January 1999 and December 2008 at a central monitoring location in Atlanta, Georgia to define a collection of multipollutant day types. Next, we conducted an epidemiologic analysis using our categories as a multipollutant metric of ambient air quality and daily counts of emergency department (ED) visits for asthma or wheeze among children aged 5 to 17 as the health endpoint. We estimated rate ratios (RR) for the association of multipollutant day types and pediatric asthma ED visits using a Poisson generalized linear model controlling for long-term, seasonal, and weekday trends and weather. Results: Using a low pollution day type as the reference level, we found significant associations of increased asthma morbidity in three of nine categories suggesting adverse effects when combinations of primary (CO, NO 2 , NO X , EC, and OC) and/or secondary (O 3 , NH 4 , SO 4) pollutants exhibited elevated concentrations (typically, occurring on dry days with low wind speed). On days with only NO 3 elevated (which tended to be relatively cool) and on days when only SO 2 was elevated (which likely reflected plume touchdowns from coal combustion point sources), estimated associations were modestly positive but confidence intervals included the null. Conclusions: We found that ED visits for pediatric asthma in Atlanta were more strongly associated with certain day types defined by multipollutant characteristics than days with low pollution levels; however, findings did not suggest that any specific combinations were more harmful than others. Relative to other health endpoints, asthma exacerbation may be driven more by total ambient pollutant

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Pride, K.R., Peel, J.L., Robinson, B.F., Busacker, A., Grandpre, J., Bisgard, K.M., Yip, F.Y., Murphy, T.D.	Association of Short-Term Exposure to Ground-Level Ozone and Respiratory Outpatient Clinic Visits in a Rural Location - Sublette County, Wyoming, 2008-2011	2015	Environmental Research	O3, PM2.5	Adverse respiratory effect, including acute bronchitis (ICD-9: 466), asthma (ICD-9: 493), chronic obstructive pulmonary disease (ICD-9: 491-492, 496), pneumonia (ICD-9: 480-486), upper respiratory tract infection (ICD-9: 460-465, 477), other respiratory (ICD-9: 786.09)	Sublette County, Wyoming	All clinic visits, 2008-2011	Evaluates the association of daily ground-level ozone concentrations and health clinic visits for respiratory disease		Executed a time-stratified case-crossover design using conditional logistic regression to compare exposure on the case-day with the weighted average of the exposure on the selected control days to estimate adjusted odds ratios. Control days were matched to cases by day of week within the same month.	Case-crossover design controls for time-invariant individual characteristics and adjusts for confounding by longer term trends and meteorological factors. Controlled for same-day temperature and humidity, with various lags. Looked for effect modification by season, and assessed a two-pollutant model including PM2.5 concentrations.			OBJECTIVE: Short-term exposure to ground-level ozone has been linked to adverse respiratory and other health effects; previous studies typically have focused on summer ground-level ozone in urban areas. During 2008-2011, Sublette County, Wyoming (population: ~10,000 persons), experienced periods of elevated ground-level ozone concentrations during the winter. This study sought to evaluate the association of daily ground-level ozone concentrations and health clinic visits for respiratory disease in this rural county. METHODS: Clinic visits for respiratory disease were ascertained from electronic billing records of the two clinics in Sublette County for January 1, 2008-December 31, 2011. A time-stratified case-crossover design, adjusted for temperature and humidity, was used to investigate associations between ground-level ozone concentrations measured at one station and clinic visits for a respiratory health concern by using an unconstrained distributed lag of 0-3 days and single-day lags of 0 day, 1 day, 2 days, and 3 days. RESULTS: The data set included 12,742 case-days and 43,285 selected control-days. The mean ground-level ozone observed was 47 ± 8 ppb. The unconstrained distributed lag of 0-3 days was consistent with a null association (adjusted odds ratio [aOR]: 1.001; 95% confidence interval [CI]: 0.990-1.012); results for lags 0, 2, and 3 days were consistent with the null. However, the results for lag 1 were indicative of a positive association; for every 10-ppb increase in the 8-h maximum average ground-level ozone, a 3.0% increase in respiratory clinic visits the following day was observed (aOR: 1.031; 95% CI: 0.994-1.069). Season modified the adverse respiratory effects: ground-level ozone was significantly associated with respiratory clinic visits during the winter months. The patterns of results from all sensitivity analyzes were consistent with the a priori model.
Rodopoulou, S., Samoli, E., Chalbot, M.G., Kavouras, I.G.	Air Pollution and Cardiovascular and Respiratory Emergency Visits in Central Arkansas: A Time-Series Analysis	2015	Science of the Total Environment	PM2.5, O3	Emergency room visits for cardiovascular diagnoses (ICD-9: 401-459), hypertension (ICD-9: 401), hypertensive heart disease and heart failure (ICD-9: 402, 428), conduction disorders and cardiac dysrhythmias: (ICD-9: 426-427), cerebrovascular disease and stroke: (ICD-9: 430-438), respiratory diagnoses (ICD-9: 460-519), acute respiratory infections except acute bronchioloitis and bronchiolitis (ICD-9: 460-465), pneumonia (ICD-9: 480-486), asthma (ICD-9: 493), chronic obstructive pulmonary disease (ICD-9: 490-491-492-496)	Central Arkansas	Daily emergency room visits 2002-2012 among adults >=15	Studies the short-term effects of air pollution on cardiovascular and respiratory morbidity in the stroke and heart failure belt		Tallied daily hospital emergency counts and then linked these counts to lagged pollution exposure using overdispersed generalized linear Poisson regression models. Applied natural spline smooth functions to include the effect of time-varying covariates and calendar time on daily visits. Used natural cubic regression splint with 1.5 degrees of freedom for each season and year.	Controlled for temperature on day of visit, two previous days, average relative humidity with lags, dummy variables for the day of the week and holidays effect. Looked for confounding by other pollutants using two pollutant models. Also looked at effect modification by season, age, gender, and race.	Uses PM2.5 and O3 from day before visit for cardiovascular causes and on the two preceding days for respiratory causes. Experimented with other lags	Yes	**Background:** Heart disease and stroke mortality and morbidity rates in Arkansas are among the highest in the U.S. While the effect of air pollution on cardiovascular health was identified in traffic-dominated metropolitan areas, there is a lack of studies for populations with variable exposure profiles, demographic and disease characteristics. **Objective:** Determine the short-term effects of air pollution on cardiovascular and respiratory morbidity in the stroke and heart failure belt. **Methods:** We investigated the associations of fine particles and ozone with respiratory and cardiovascular emergency room visits during the 2002–2012 period for adults in Central Arkansas using Poisson generalized models adjusted for temporal, seasonal and meteorological effects. We evaluated sensitivity of the associations to mutual pollutant adjustment and effect modification patterns by sex, age, race and season. **Results:** We found effects on cardiovascular and respiratory emergencies for PM2.5 (1.52% [95% (confidence interval) CI: − 1.10%, 4.20%]; 1.45% [95%CI: − 2.64%, 5.72%] per 10 μg/m3) and O3 (0.93% [95%CI: − 0.87%, 2.76%]; 0.76 [95%CI: − 1.92%, 3.52%] per 10 ppbv) during the cold period (October–March). The effects were stronger among whites, except for the respiratory effects of O3 that were higher among Blacks/African-Americans. Effect modification patterns by age and sex differed by association. Both pollutants were associated with increases in emergency room visits for hypertension, heart failure and asthma. Effects on cardiovascular and respiratory emergencies were observed during the cold period when particulate matter was dominated by secondary nitrate and wood burning. **Conclusion:** Outdoor particulate pollution during winter had an effect on cardiovascular morbidity in central Arkansas, the region with high stroke and hear**t disease incidence rates.**

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Sacks, J.D., Rappold, A.G., Davis, J.A., Richardson, D.B., Waller, A.E., Luben, T.J.	Influence of Urbanicity and County Characteristics on the Association Between Ozone and Asthma Emergency Department Visits in North Carolina	2014	Environmental Health Perspectives	O3, PM2.5	ED visits for asthma (ICD-9: 493.0-493.9)	North Carolina	All ED visits	Examines the association between estimates of short-term O3 exposures and asthma ED visits in North Carolina		Used a time-stratified case-crossover approach, where referent days were selected as the same day of the wek within the same month and year as the case day. Used a conditional logistic regression model.	Controlled for weather confounding by including same-day mean temperature and mean dew point temperature with natural splines and 4 degrees of freedom. Looked at a copollutant model with PM2.5 to look for confounding, and also tried stratifying on days where PM2.5 concentrations were relatively high or low. Looked at effect modification by urbanicity and health factor.			BACKGROUND: Air pollution epidemiologic studies, often conducted in large metropolitan areas because of proximity to regulatory monitors, are limited in their ability to examine potential associations between air pollution exposures and health effects in rural locations. METHODS: Using a time-stratified case-crossover framework, we examined associations between asthma emergency department (ED) visits in North Carolina (2006-2008), collected by a surveillance system, and short-term ozone (O3) exposures using predicted concentrations from the Community Multiscale Air Quality (CMAQ) model. We estimated associations by county groupings based on four urbanicity classifications (representative of county size and urban proximity) and county health. RESULTS: O3 was associated with asthma ED visits in all-year and warm season (April-October) analyses [odds ratio (OR) = 1.019; 95% CI: 0.998, 1.040; OR = 1.020; 95% CI: 0.997, 1.044, respectively, for a 20-ppb increase in lag 0-2 days O3]. The association was strongest in Less Urbanized counties, with no evidence of a positive association in Rural counties. Associations were similar when adjusted for fine particulate matter in copollutant models. Associations were stronger for children (5-17 years of age) compared with other age groups, and for individuals living in counties identified with poorer health status compared with counties that had the highest health rankings, although estimated associations for these subgroups had larger uncertainty. CONCLUSIONS: Associations between short-term O3 exposures and asthma ED visits differed by overall county health and urbanicity, with stronger associations in Less Urbanized counties, and no positive association in Rural counties. Results also suggest that children are at increased risk of O3-related respiratory effects.
Sarnat, J.A., Sarnat, S.E., Flanders, W.D., Chang, H.H., Mulholland, J., Baxter, L., Isakov, V., Ozkaynak, H.	Spatiotemporally Resolved Air Exchange Rate as a Modifier of Acute Air Pollution-Related Morbidity in Atlanta	2013	Journal of Exposure Science and Environmental Epidemiology	CO, NOx, PM2.5, O3	Emergency department visits for asthma and wheeze	Atlanta, GA metropolitan area	All emergency department visits, Jan 1999-Dec 2002	Examines air exchange rates as an effect modifier of associations between several urban air pollutants and corresponding emergency department visits for asthma and wheeze			Looks at effect modification by air exchange rates.			Epidemiological studies frequently use central site concentrations as surrogates of exposure to air pollutants. Variability in air pollutant infiltration due to differential air exchange rates (AERs) is potentially a major factor affecting the relationship between central site concentrations and actual exposure, and may thus influence observed health risk estimates. In this analysis, we examined AER as an effect modifier of associations between several urban air pollutants and corresponding emergency department (ED) visits for asthma and wheeze during a 4-year study period (January 1999-December 2002) for a 186 ZIP code area in metro Atlanta. We found positive associations for the interaction between AER and pollution on asthma ED visits for both carbon monoxide (CO) and nitrogen oxides (NO(x)), indicating significant or near-significant effect modification by AER on the pollutant risk-ratio estimates. In contrast, the interaction term between particulate matter (PM)(2.5) and AER on asthma ED visits was negative and significant. However, alternative distributional tertile analyses showed PM(2.5) and AER epidemiological model results to be similar to those found for NOx and CO (namely, increasing risk ratios (RRs) with increasing AERs when ambient PM(2.5) concentrations were below the highest tertile of their distribution). Despite the fact that ozone (O(3)) was a strong independent predictor of asthma ED visits in our main analysis, we found no O(3)-AER effect modification. To our knowledge, our findings for CO, NOx, and PM(2.5) are the first to provide an indication of short-term (i.e., daily) effect modification of multiple air pollution-related risk associations with daily changes in AER. Although limited to one outcome category in a single large urban locale, the findings suggest that the use of relatively simple and easy-to-derive AER surrogates may reflect intraurban differences in short-term exposures to pollutants of ambient origin.

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Sheffield, P.E., Zhao, J., Shmool, J.L.C., Clougherty, J.E.	Ambient Ozone Exposure and Children's Acute Asthma in New York City: A Case-Crossover Analysis	2015	Environmental Health	O3, PM2.5, NO2	ED visits and hospitalization for asthma (ICD-9: 493)	New York City	Children age 5-17, 2005-2011	Explores the association of childhood asthma morbidity with ambient ozone, with modifications by child age and sex		Used conditional logistic regression with time-stratified referent sampling in case-crossover design. Chose control days bidirectionally, matching by day of week in the same month and year. Conducted time-series analysis using Poisson regression to compare results with the case-crossover model. Also explored ozone's functional form, and played with different lag periods.	Looked for differential effects across age and sex subgroups and also modeled interactive effects between ozone, sex, and age for individuals. Case control design controls for time-invariant individual characteristics and day of week and season. Control for weather using smooth function of current-day minimum temperature and relative humidity.			Background: Childhood asthma morbidity has been associated with ambient ozone in case-crossover studies. Varying effects of ozone by child age and sex, however, have been less explored. Methods: This study evaluates associations between ozone exposure and asthma emergency department visits and hospitalizations among boys and girls aged 5-17 years in New York City for the 2005-2011 warm season period. Time-stratified case-crossover analysis was conducted and, for comparison, time-series analysis controlling for season, day-of-week, same-day and delayed effects of temperature and relative humidity were also performed. Results: We found associations between ambient ozone levels and childhood asthma emergency department visits and hospitalizations in New York City, although the relationships varied among boys and girls and by age group. For an increase of interquartile range (0.013 ppm) in ozone, there was a 2.9-8.4% increased risk for boys and 5.4-6.5% for girls in asthma emergency department visits; and 8.2% increased risk for girls in hospitalizations. Among girls, we observed stronger associations among older children (10-13 and 14-17 year age groups). We did not observe significant modification by age for boys. Boys exhibited a more prompt response (lag day 1) to ozone than did girls (lag day 3), but significant associations for girls were retained longer, through lag day 6. Conclusions: Our study indicates significant variance in associations between short-term ozone concentrations and asthma events by child sex and age. Differences in ozone response for boys and girls, before and after puberty, may point towards both social (gendered) and biological (sex-linked) sources of effect modification.
Strickland, M.J., Klein, M., Flanders, W.D., Chang, H.H., Mulholland, J.A., Tolbert, P.E., Darrow, L.A.	Modification of the Effect of Ambient Air Pollution on Pediatric Asthma Emergency Visits: Susceptible Subpopulations	2014	Epidemiology	PM10, PM2.5, CO, NO2, O3	Pediatric emergency visits for asthma or wheeze	Atlanta, Georgia	Children 2-16 from Jan 2002-June 2010	Assesses the extent to which different subgroups of children are susceptible to the effect of ambient air pollution on pediatric asthma emergency visits		Calculated population-weighted daily average concentrations for 1-hour maximum CO and NO2, 8-hour maximum O3, and 24-hour PM10, PM2.5, and PM2.5 constituents. Estimate dPoisson time-series models to estimate rate ratios for associations between 3-day moving average pollutant concentrations and daily ED visit counts. Stratified analysis by preterm delivery, term low birth weight, maternal race, Medicaid status, maternal education, maternal smoking, delivery method, and history of bronchiolitis ED visit	Evaluated effect modification by a number of factors, including preterm delivery, term low birth weight, maternal race, Medicaid status, maternal education, maternal smoking, delivery method, history of bronchiolitis ED visit	Use 3-day moving average pollutant concentrations	Yes	**Background:** Children may have differing susceptibility to ambient air pollution concentrations depending on various background characteristics of the children. **Methods:** Using emergency department (ED) data linked with birth records from Atlanta, Georgia, we identified ED visits for asthma or wheeze among children 2 to 16 years of age from 1 January 2002 through 30 June 2010 (n = 109,758). We stratified by preterm delivery, term low birth weight, maternal race, Medicaid status, maternal education, maternal smoking, delivery method, and history of a bronchiolitis ED visit. Population-weighted daily average concentrations were calculated for 1-hour maximum carbon monoxide and nitrogen dioxide; 8-hour maximum ozone; and 24-hour average particulate matter less than 10 microns in diameter, particulate matter less than 2.5 microns in diameter (PM2.5), and the PM2.5 components sulfate, nitrate, ammonium, elemental carbon, and organic carbon, using measurements from stationary monitors. Poisson time-series models were used to estimate rate ratios for associations between 3-day moving average pollutant concentrations and daily ED visit counts and to investigate effect-measure modification by the stratification factors. **Results:** Associations between pollutant concentrations and asthma exacerbations were larger among children born preterm and among children born to African American mothers. Stratification by race and preterm status together suggested that both factors affected susceptibility. The largest estimated effect size (for an interquartile range increase in pollution) was observed for ozone among preterm births to African American mothers: rate ratio = 1.138 (95% confidence interval = 1.077-1.203). In contrast, the rate ratio for the ozone association among full-term births to mothers of other races was 1.025 (0.970-1.083). **Conclusions:** Results support the hypothesis that children vary in their susceptibility to ambient air pollutants.

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Wendt, J.K., Symanski, E., Stock, T.H., Chan, W., Du., X.L.	Association of Short-Term Increases in Ambient Air Pollution and Timing of Initial Asthma Diagnosis Among Medicaid-Enrolled Children in a Metropolitan Area	2014	Environmental Research	O3, NO2, PM2.5	Diagnosis of new-onset asthma	Harris County, Texas	Incident asthma cases among Medicaid-enrolled children between 2005-2007	Investigates whether short-term increases in O3, NO2, and PM2.5 levels were related to timing of initial diagnosis in children with asthma		Used a time-stratified, case-crossover design. Specified forty 28-day strata, matching each asthma case-day with the three referent dates in the pre-defined strata that were the same weekday. Ran conditional logistic regression to estimate Ors for each exposure metric and pollutant. Ran various lags and average cumulative exposures, and tested for non-linearity of effect using restricted cubic splines.	Case-crossover design allowed them to control for person-level factors and design also controlled for time-dependent exposures. Adjusted for temperature, mean relative humidity, and all aeroallergen variables. Also ran both single and co-pollutant models. Stratified analysis by age group, gender, race, and season.	Considered various lags and average cumulative exposures, with single-day values lagged 1 through 5 days, cumulative values averaged over 2 day through 6 days	Yes	**Objective:** We investigated associations of short-term changes in ambient ozone (O3), fine particulate matter (PM2.5) and nitrogen dioxide (NO2) concentrations and the timing of new-onset asthma, using a large, high-risk population in an area with historically high ozone levels. **Methods:** The study population included 18,289 incident asthma cases identified among Medicaid-enrolled children in Harris County Texas between 2005-2007, using Medicaid Analytic Extract enrollment and claims files. We used a time-stratified case-crossover design and conditional logistic regression to assess the effect of increased short-term pollutant concentrations on the timing of asthma onset. **Results:** Each 10 ppb increase in ozone was significantly associated with new-onset asthma during the warm season (May-October), with the strongest association seen when a 6-day cumulative average period was used as the exposure metric (odds ratio [OR]=1.05, 95% confidence interval [CI], 1.02-1.08). Similar results were seen for NO2 and PM2.5 (OR=1.07, 95% CI, 1.03-1.11 and OR=1.12, 95% CI, 1.03-1.22, respectively), and PM2.5 also had significant effects in the cold season (November-April), 5-day cumulative lag (OR=1.11. 95% CI, 1.00-1.22). Significantly increased ORs for O3 and NO2 during the warm season persisted in co-pollutant models including PM2.5. Race and age at diagnosis modified associations between ozone and onset of asthma. **Conclusion:** Our results indicate that among children in this low-income urban population who developed asthma, their initial date of diagnosis was more likely to occur following periods of higher short-term ambient pollutant levels.
Winquist, A., Kirrane, E., Klein, M., Strickland, M., Darrow, L.A., Sarnat, S.E., Gass, K., Mulholland, J., Russell, A., Tolbert, P.	Joint Effects of Ambient Air Pollutants on Pediatric Asthma Emergency Department Visits in Atlanta, 1998-2004	2014	Epidemiology	PM2.5, O3, NO2, SO2	Pediatric asthma emergency department visits	Atlanta, Georgia	Pediatric asthma emergency department visits 1998-2004	Investigated joint effects of multiple pollutants on pediatric asthma emergency department visits		Selected combinations of pollutants that were representative of oxidant gases and secondary, traffic, power plant, and criteria pollutants. Assessed joint effects using multipollutant Poisson generalized linear models. Calculated rate ratios for the combined effect of an interquartile range increment in each pollutant's concentration.	Controlled analysis for time trends, meteorology, and daily nonasthma upper respiratory emergency department visit counts.		Yes	**Background:** Because ambient air pollution exposure occurs as mixtures, consideration of joint effects of multiple pollutants may advance our understanding of the health effects of air pollution. **Methods:** We assessed the joint effect of air pollutants on pediatric asthma emergency department visits in Atlanta during 1998-2004. We selected combinations of pollutants that were representative of oxidant gases and secondary, traffic, power plant, and criteria pollutants, constructed using combinations of criteria pollutants and fine particulate matter (PM2.5) components. Joint effects were assessed using multipollutant Poisson generalized linear models controlling for time trends, meteorology, and daily nonasthma upper respiratory emergency department visit counts. Rate ratios (RRs) were calculated for the combined effect of an interquartile range increment in each pollutant's concentration. **Results:** Increases in all of the selected pollutant combinations were associated with increases in warm-season pediatric asthma emergency department visits (eg, joint-effect RR = 1.13 [95% confidence interval = 1.06-1.21] for criteria pollutants, including ozone, carbon monoxide, nitrogen dioxide, sulfur dioxide, and PM2.5). Cold-season joint effects from models without nonlinear effects were generally weaker than warm-season effects. Joint-effect estimates from multipollutant models were often smaller than estimates based on single-pollutant models, due to control for confounding. Compared with models without interactions, joint-effect estimates from models including first-order pollutant interactions were largely similar. There was evidence of nonlinear cold-season effects. **Conclusions:** Our analyses illustrate how consideration of joint effects can add to our understanding of health effects of multipollutant exposures and also illustrate some of the complexities involved in calculating and interpreting joint effects of multiple pollutants.

Table 4. Respiratory

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Authors	Title	Year Published	Journal Published	Pollutant(s) Studied	Causes of Mortality or Morbidity Considered	Geographic scope	Population studied	Study question	Statistically significant relationships?	Analysis method	Controls for factors that could obscure relationship?	Assesses potential lag between exposure and outcome?	Reports uncertainty?	Abstract
Yap, P., Gilbreath, S., Garcia, C., Jareen, N., Goodrich, B.	The Influence of Socioeconomic Markers on the Association Between Fine Particulate Matter and Hospital Admissions for Respiratory Conditions Among Children	2013	American Journal of Public Health	PM2.5	Combined respiratory conditions (ICD-9: 460-519), acute respiratory infections (ICD-9: 460-466, 480-486), pneumonia (ICD-9: 480-486), and asthma (ICD-9: 493)	Central Valley and South Coast regions, California	Children aged 1-9 years	Investigates the relationships among SES, acute PM2.5 exposure and childhood morbidity		Did daily time-series analysis. Performed generalized additive Poisson regression models. Accounted for longer-term patterns in the health outcomes data using time trends and seasonality, day of the week, and smoothing splines with different lags for temperature. Ultimately used 3-day lag for PM2.5 exposure.	Looked at effect modification by single or composite area-based SES variables. Also ran stratified models on the single and composite area-based SES variables	Investigated exposure lags of 0-6 days, with 3-day lag yielding the best fit	Yes	**Objectives:** We evaluated the influence of socioeconomic status (SES) on hospital admissions for respiratory conditions associated with ambient particulate matter that is 2.5 micrometers or less in aerodynamic diameter (PM2.5) in children aged 1 to 9 years in 12 California counties, from 2000 to 2005. **Methods:** We linked daily hospital admissions for respiratory conditions (acute respiratory infections, pneumonia, and asthma) to meteorological, air pollution, and census data. **Results:** In San Diego, San Bernardino, Riverside, and Los Angeles counties, the admission rates for children associated with PM2.5 ranged from 1.03 to 1.07 for combined respiratory conditions and 1.03 to 1.08 for asthma in regions with lower SES. We observed 2 distinct patterns of the influence of the composite SES Townsend index. In lower-SES South Coast areas, PM2.5-associated hospital admission rates for all respiratory outcomes were predominantly positive whereas results in the Central Valley were variable, often tending toward the null. **Conclusions:** These distinct patterns could be attributed to the heterogeneity of regional confounders as well as the seasonal variation of emission sources of PM2.5. Composite SES is one potential factor for increasing susceptibility to air pollution.
Young, M.T., Sandler, D.P., DeRoo, L.A., Vedal, S., Kaufman, J.D., London, S.J.	Ambient Air Pollution Exposure and Incident Adult Asthma in a Nationwide Cohort of U.S. Women	2014	American Journal of Respiratory and Critical Care Medicine	PM2.5, NO2	Development of asthma and incident respiratory symptoms	United States	Sister Study cohort (sisters of women with breast cancer enrolled 2003-2009)	Assesses the effect of long-term exposure to PM2.5 on adult incident asthma	Yes (for incident wheeze and almost for incident asthma, not with cough)	Estimated annual average PM2.5 and NO2 concentration at participants' addresses using a national land-use/kriging model incorporating roadway information. Evaluate outcomes at follow-up between 2008 and 2012, including incident self-reported wheeze, chronic cough, and doctor-diagnosed asthma in women without baseline symptoms		Uses average ambient PM2.5 and NO2 concentrations from 2006	Yes	**Rationale:** Limited prior data suggest an association between traffic-related air pollution and incident asthma in adults. No published studies assess the effect of long-term exposures to particulate matter less than 2.5 μm in diameter (PM2.5) on adult incident asthma. **Objectives:** To estimate the association between ambient air pollution exposures (PM2.5 and nitrogen dioxide, NO2) and development of asthma and incident respiratory symptoms. **Methods:** The Sister Study is a U.S. cohort study of risk factors for breast cancer and other health outcomes (n = 50,884) in sisters of women with breast cancer (enrollment, 2003-2009). Annual average (2006) ambient PM2.5 and NO2 concentrations were estimated at participants' addresses, using a national land-use/kriging model incorporating roadway information. Outcomes at follow-up (2008-2012) included incident self-reported wheeze, chronic cough, and doctor-diagnosed asthma in women without baseline symptoms. **Measurements and Main Results:** Adjusted analyses included 254 incident cases of asthma, 1,023 of wheeze, and 1,559 of chronic cough. For an interquartile range (IQR) difference (3.6 μg/m(3)) in estimated PM2.5 exposure, the adjusted odds ratio (aOR) was 1.20 (95% confidence interval [CI] = 0.99-1.46, P = 0.063) for incident asthma and 1.14 (95% CI = 1.04-1.26, P = 0.008) for incident wheeze. For NO2, there was evidence for an association with incident wheeze (aOR = 1.08, 95% CI = 1.00-1.17, P = 0.048 per IQR of 5.8 ppb). Neither pollutant was significantly associated with incident cough (PM2.5: aOR = 0.95, 95% CI = 0.88-1.03, P = 0.194; NO2: aOR = 1.00, 95% CI = 0.93-1.07, P = 0.939). **Conclusions:** Results suggest that PM2.5 exposure increases the risk of developing asthma and that PM2.5 and NO2 increase the risk of developing wheeze, the cardinal symptom of asthma, in adult women.

Table 5. Other

Authors	Title	Year Published	Journal Published	Pollutant(s) Studied	Causes of Mortality or Morbidity Considered	Geographic scope	Population studied	Study question	Statistically significant relationships?	Analysis method	Controls for factors that could obscure relationship?	Assesses potential lag between exposure and outcome?	Reports uncertainty?	Abstract
Becerra, T.A., Wilhelm, M., Olsen, J., Cockburn, M., Ritz, B.	Ambient Air Pollution and Autism in Los Angeles County, California	2013	Environmental Health Perspectives	CO, NO2, O3, PM10, PM2.5	Autism Disorder	Los Angeles County, CA	Children born 1995-2006 to mothers living in LA County at time of giving birth	Examines associations between measured and modeled exposures to prenatal air pollution and autism in children		First calculated Pearson's correlation coefficients to examine relations between various pollutant measures. Then looked at associations between air pollution exposure and odds of AD diagnosis using one- and two-pollutant models.	Adjusted for maternal age, maternal place of birth, race/ethnicity, and education, type of birth, parity, insurance type, gestational age at birth. Also excluded control for gestational age, since that might be a step on the causal pathway. Looks at potential confounding by co-pollutant exposure.	Estimated pollutant exposure for full pregnancy and for each trimester	Yes	Background: The prevalence of autistic disorder (AD), a serious developmental condition, has risen dramatically over the past two decades, but high-quality population-based research addressing etiology is limited. Objectives: We studied the influence of exposures to traffic-related air pollution during pregnancy on the development of autism using data from air monitoring stations and a land use regression (LUR) model to estimate exposures. Methods: Children of mothers who gave birth in Los Angeles, California, who were diagnosed with a primary AD diagnosis at 3–5 years of age during 1998–2009 were identified through the California Department of Developmental Services and linked to 1995–2006 California birth certificates. For 7,603 children with autism and 10 controls per case matched by sex, birth year, and minimum gestational age, birth addresses were mapped and linked to the nearest air monitoring station and a LUR model. We used conditional logistic regression, adjusting for maternal and perinatal characteristics including indicators of SES. Results: Per interquartile range (IQR) increase, we estimated a 12–15% relative increase in odds of autism for ozone [odds ratio (OR) = 1.12, 95% CI: 1.06, 1.19; per 11.54-ppb increase] and particulate matter ≤ 2.5 μm (OR = 1.15; 95% CI: 1.06, 1.24; per 4.68-μg/m3 increase) when mutually adjusting for both pollutants. Furthermore, we estimated 3–9% relative increases in odds per IQR increase for LUR-based nitric oxide and nitrogen dioxide exposure estimates. LUR-based associations were strongest for children of mothers with less than a high school education. Conclusion: Measured and estimated exposures from ambient pollutant monitors and LUR model suggest associations between autism and prenatal air pollution exposure, mostly related to traffic sources.
Raz, R., Roberts, A.L., Lyall, K., Hart, J.E., Just, A.C., Laden, F., Weisskopf, M.G.	Autism Spectrum Disorder and Particulate Matter Air Pollution Before, During, and After Pregnancy: A Nested Case-Control Analysis Within the Nurses' Health Study II Cohort	2015	Environmental Health Perspectives	PM2.5	Incidence of Autism Spectrum Disorders	United States	Offspring of participants in Nurses' Health Study II, who were female nurses 25-43 years old when recruited in 1989	Explores the association between Autism spectrum disorders and exposure to PM before, during, and after pregnancy	Yes	Used logistic regression models to estimate odds ratios of ASD by PM exposures modeled both using PM quartiles as continuous variables in separate models. Looked at exposures to different PM size fractions in separate models, and also together in a single model. To examine temporal specificity, considered associations between exposure during 9 months before pregnancy, during pregnancy, and 9 months after birth. Time periods considered separately and then in a single model.	Reduced misclassification bias by doing separate analyses for exposures assigned assuming the nurse was at the earlier address during the whole period or at the later address for nurses who moved between questionnaries. Also tried limiting to nurses whose addresses were the same to reduce misclassification bias. Examined associations stratified by sex of the child.	Looks at exposure 9 months pre-pregnancy, during pregnancy, and 9 months following birth	Yes	**Background:** Autism spectrum disorder (ASD) is a developmental disorder with increasing prevalence worldwide, yet has unclear etiology. **Objective:** We explored the association between maternal exposure to particulate matter (PM) air pollution and odds of ASD in her child. **Methods:** We conducted a nested case–control study of participants in the Nurses' Health Study II (NHS II), a prospective cohort of 116,430 U.S. female nurses recruited in 1989, followed by biennial mailed questionnaires. Subjects were NHS II participants' children born 1990–2002 with ASD (n = 245), and children without ASD (n = 1,522) randomly selected using frequency matching for birth years. Diagnosis of ASD was based on maternal report, which was validated against the Autism Diagnostic Interview-Revised in a subset. Monthly averages of PM with diameters ≤ 2.5 μm (PM2.5) and 2.5–10 μm (PM10–2.5) were predicted from a spatiotemporal model for the continental United States and linked to residential addresses. **Results:** PM2.5 exposure during pregnancy was associated with increased odds of ASD, with an adjusted odds ratio (OR) for ASD per interquartile range (IQR) higher PM2.5 (4.42 μg/m3) of 1.57 (95% CI: 1.22, 2.03) among women with the same address before and after pregnancy (160 cases, 986 controls). Associations with PM2.5 exposure 9 months before or after the pregnancy were weaker in independent models and null when all three time periods were included, whereas the association with the 9 months of pregnancy remained (OR = 1.63; 95% CI: 1.08, 2.47). The association between ASD and PM2.5 was stronger for exposure during the third trimester (OR = 1.42 per IQR increase in PM2.5; 95% CI: 1.09, 1.86) than during the first two trimesters (ORs = 1.06 and 1.00) when mutually adjusted. There was little association between PM10–2.5 and ASD. **Conclusions:** Higher maternal exposure to PM2.5 during pregnancy, particularly the third trimester, was associated with greater odds of a child having ASD.

Table 5. Other

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Talbott, E.O., Arena, V.C., Rager, J.R., Clougherty, J.E., Michanowicz, D.R., Sharma, R.K., Stacy, S.L.	Fine Particulate Matter and the Risk of Autism Spectrum Disorde	2015	Environmental Research	PM2.5	Autism spectrum disorder	Southwestern PA	Children born 2005-2009	Investigates the association between prenatal and early childhood exposure to fine particulate matter and risk for childhood ASD	Yes (exposure during postnatal year two, cumulative exposure for pre-pregnancy through pregnancy)	Did a population-based case-control study, using controls for ASD cases matched to cases on birth year, gender, and race. Used multiple logistic regression, performing separate logistic regression models for exposure during several critical prenatal and postnatal time periods.	Adjusted analysis for maternal age, maternal education, maternal race, and maternal smoking. Acknowledge potential for misclassification bias of PM2.5 exposure due to differential PM2.5 exposures outside of the home.	Average and cumulative exposure estimates computed for key developmental time periods of three months prior to LMP, trimesters of pregnancy, and first and second year of life	Yes	The causes of autism spectrum disorder (ASD) are not well known. Recent investigations have suggested that air pollution, including PM2.5, may play a role in the onset of this condition. The objective of the present work was to investigate the association between prenatal and early childhood exposure to fine particulate matter (PM2.5) and risk for childhood ASD. A population-based case-control study was conducted in children born between January 1, 2005 and December 31, 2009 in six counties in Southwestern Pennsylvania. ASD cases were recruited from specialty autism clinics, local pediatric practices, and school-based special needs services. ASD cases were children who scored 15 or above on the Social Communication Questionnaire (SCQ) and had written documentation of an ASD diagnosis. Controls were children without ASD recruited from a random sample of births from the Pennsylvania state birth registry and frequency matched to cases on birth year, gender, and race. A total of 217 cases and 226 controls were interviewed. A land use regression (LUR) model was used to create person- and time-specific PM2.5 estimates for individual (pre-pregnancy, trimesters one through three, pregnancy, years one and two of life) and cumulative (starting from pre-pregnancy) key developmental time periods. Logistic regression was used to investigate the association between estimated exposure to PM2.5 during key developmental time periods and risk of ASD, adjusting for mother's age, education, race, and smoking. Adjusted odds ratios (AOR) were elevated for specific pregnancy and postnatal intervals (pre-pregnancy, pregnancy, and year one), and postnatal year two was significant, (AOR=1.45, 95% CI=1.01–2.08). We also examined the effect of cumulative pregnancy periods; noting that starting with pre-pregnancy through pregnancy, the adjusted odds ratios are in the 1.46–1.51 range and significant for pre-pregnancy through year 2 (OR=1.51, 95% CI=1.01–2.26). Our data indicate that both prenatal and postnatal exposures to PM2.5 are associated with increased risk of ASD. Future research should include multiple
Volk, H.E., Lurmann, F., Penfold, B., Hertz-Picciotto, I., McConnell, R.	Traffic-Related Air Pollution, Particulate Matter, and Autism	2013	JAMA Psychiatry	NO2, PM2.5, PM10	Autism spectrum disorder	California	Participants in CHARGE study, between 24-60 months at time of recruitment, born in CA	Estimates the association between autism risk and exposure to mixture or traffic-related pollutants, NO2, PM2.5, PM10	Yes	Calculated Spearman correlation coefficients between TRP estimates and regional pollution measures for pregnancy and first year of life. Then, used logistic regression to examine the association between exposure to traffic-related air pollution and autism risk. Fitted models of autism risk as a function of TRP exposure levels from all raod types separately for each time period, with categories of exposure based on quartiles of TRP distribution and continuous variables for other pollutants. When possible, examined both in the same model.	Adjusted models for children's gender and ethnicity, maximum education level of parents, maternal age, maternal smoking during pregnancy. Also adjusted by urban vs. rural. Acknowledge the potential for confounding if proximity to diagnosing physicians or treatment centers was associated with exposure.	Uses long-term exposure, with average exposure during first year of life and during gestational period	Yes	**Context:** Autism is a heterogeneous disorder with genetic and environmental factors likely contributing to its origins. Examination of hazardous pollutants has suggested the importance of air toxics in the etiology of autism, yet little research has examined its association with local levels of air pollution using residence-specific exposure assignments. **Objective:** To examine the relationship between traffic-related air pollution, air quality, and autism. **Design:** This population-based case-control study includes data obtained from children with autism and control children with typical development who were enrolled in the Childhood Autism Risks from Genetics and the Environment study in California. The mother's address from the birth certificate and addresses reported from a residential history questionnaire were used to estimate exposure for each trimester of pregnancy and first year of life. Traffic-related air pollution was assigned to each location using a line-source air-quality dispersion model. Regional air pollutant measures were based on the Environmental Protection Agency's Air Quality System data. Logistic regression models compared estimated and measured pollutant levels for children with autism and for control children with typical development. **Setting:** Case-control study from California. **Participants:** A total of 279 children with autism and a total of 245 control children with typical development. **Main Outcome Measures:** Crude and multivariable adjusted odds ratios (AORs) for autism. **Results:** Children with autism were more likely to live at residences that had the highest quartile of exposure to traffic-related air pollution, during gestation (AOR, 1.98 [95% CI, 1.20-3.31]) and during the first year of life (AOR, 3.10 [95% CI, 1.76-5.57]), compared with control children. Regional exposure measures of nitrogen dioxide and particulate matter less than 2.5 and 10 μm in diameter (PM2.5 and PM10) were also associated with autism during gestation (exposure to nitrogen dioxide: AOR, 1.81 [95% CI, 1.37-3.09]; exposure to PM2.5: AOR, 2.08 [95% CI, 1.93-2.25]; exposure to PM10: AOR, 2.17 [95% CI, 1.49-3.16) and during the first year of life

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Balti, E.V., Echouffo-Tcheugui, J.B., Yako, Y.Y., Kengne, A.P.	Air Pollution and Risk of Type 2 Diabetes Mellitus: a Systematic Review and Meta-Analysis	2014	Diabetes Research and Clinical Practice	NO2, Nox, PM2.5, PM10, PM10-2.5	Type 2 diabetes mellitus	6 of 10 studies are in the US or Canada. Others are in Europe	All studies assessed adult	Investigates whether exposure to relatively high levels of air pollution is associated with diabetes occurrence	Yes	Looked for cross-sectional, case-control, and cohort studies repoting a quantitative measure of the association between exposure to air pollution and risk of T2DM, only studies using humans but no language restrictions. Pooled estimates using random-effects meta-analysis, and assessed heterogeneity using I-squared test. Ultimately used 10 studies	Most studies used single-pollutant mdoels, so they don't take into account potential interaction between pollutants. Controls commonly included were age, sex, BMI, smoking. Possible misclassification of diabetes diagnoses. Acknowledges potential for bias from heterogeneity in assessment strategies used to assess exposure.	Looks at long-term exposure studies, but none look at lifetime exposure	Yes	**Aim:** Whether exposure to relatively high levels of air pollution is associated with diabetes occurrence remains unclear. We sought to assess and quantify the association between exposure to major air pollutants and risk of type 2 diabetes. **Methods:** PubMed and EMBASE databases (through September 2013) were searched using a combination of terms related to exposure to gaseous (NO2 and NOx) or particulate matter pollutants (PM2.5, PM10 and PM10-2.5) and type 2 diabetes. Descriptive and quantitative information were extracted from selected studies. We used random-effects models meta-analysis to derive overall risk estimates per type of pollutant. **Results:** We included ten studies (five cross-sectional and five prospective), assessing the effects of air pollutants on the occurrence of diabetes. In prospective investigations, the overall effect on diabetes occurrence was significant for both NO2 (adjusted hazard ratio [HR], 1.13; 95% confidence interval [95%CI], 1.01-1.22; p < 0.001; I(2) = 36.4%, pheterogeneity = 0.208) and PM2.5 (HR, 1.11; 95%CI, 1.03-1.20; p < 0.001; I(2) = 0.0%, pheterogeneity = 0.827). Odds ratios were reported by two cross-sectional studies which revealed similar associations between both NO2 and PM2.5 with type 2 diabetes. Across studies, risk estimates were generally adjusted for age, gender, body mass index and cigarette smoking. **Conclusions:** Available evidence supports a prospective association of main air pollutants with an increased risk for type 2 diabetes. This finding may have implications for population-based strategies to reduce diabetes risk.
Chen, H., Burnett, R.T., Kwong, J.C., Villeneuve, P.J., Golberg, M.S., Brook, R.D., van Donkelaar, A., Jerrett, M., Martin, R.V., Brook, J.R., Copes, R.	Risk of Incident Diabetes in Relation to Long-Term Exposure to Fine Particulate Matter in Ontario, Canada	2013	Environmental Health Perspectives	PM2.5	Diabetes (ICD-9: 250, ICD-10: E10-E14)	Ontario, Canada	Respondents to five health surveys between 1996-2005 who at the time were >=35, registered with provincial health insurance, free of diabetes, Canadian-born	Assesses whether long-term exposure to ambient PM2.5 Is associated with incident diabetes	Yes	Used satellite-based estimates of surface concentrations of PM2.5. Then used a stratified Cox proportional hazards model with strata dfined as single-year age groups, cycle of survey, and region (south/north). Outcome was incident diagnosis date. Assumed linearity, but checked this assumption by using natural cubic splines with two or three degrees of freedom.	Adjusted analysis for sex, marital status, educatino, household income adequacy, race/ethnicity, BMI, physical activity, smoking, drinking, diet, urban residency, hypertension at baseline, area-level unemployment, education, mean household income. In separate analyses also controlled for comorbidities like congestive heart failure. Investigated potential effect modification by age, sex, BMI, education, race/ethnicity, household income adequacy, phsical activity, smoking, and comorbidities	Uses six-year average PM2.5 levels, 2001-2006	Yes	**Background:** Laboratory studies suggest that fine particulate matter (≤ 2.5 μm in diameter; PM2.5) can activate pathophysiological responses that may induce insulin resistance and type 2 diabetes. However, epidemiological evidence relating PM2.5 and diabetes is sparse, particularly for incident diabetes. **Objectives:** We conducted a population-based cohort study to determine whether long-term exposure to ambient PM2.5 is associated with incident diabetes. **Methods:** We assembled a cohort of 62,012 nondiabetic adults who lived in Ontario, Canada, and completed one of five population-based health surveys between 1996 and 2005. Follow-up extended until 31 December 2010. Incident diabetes diagnosed between 1996 and 2010 was ascertained using the Ontario Diabetes Database, a validated registry of persons diagnosed with diabetes (sensitivity = 86%, specificity = 97%). Six-year average concentrations of PM2.5 at the postal codes of baseline residences were derived from satellite observations. We used Cox proportional hazards models to estimate the associations, adjusting for various individual-level risk factors and contextual covariates such as smoking, body mass index, physical activity, and neighborhood-level household income. We also conducted multiple sensitivity analyses. In addition, we examined effect modification for selected comorbidities and sociodemographic characteristics. **Results:** There were 6,310 incident cases of diabetes over 484,644 total person-years of follow-up. The adjusted hazard ratio for a 10-μg/m3 increase in PM2.5 was 1.11 (95% CI: 1.02, 1.21). Estimated associations were comparable among all sensitivity analyses. We did not find strong evidence of effect modification by comorbidities or sociodemographic covariates. **Conclusions:** This study suggests that long-term exposure to PM2.5 may contribute to the development of diabetes.

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Coogan, P.F., White, L.F., Jerrett, M., Brook, R.D., Su, J.G., Seto, E., Burnett, R., Palmer, J.R. Rosenberg, L.	Air Pollution and Incidence of Hypertension and Diabetes Mellitus in Black Women in Los Angeles	2012	Circulation	PM2.5, NOx	Incident hypertension, diabetes	Los Angeles	Participants in the Black Women's Health Study, free from hypertension and diabetes at 1995 baseline	Assesses the risks of incident hyperension and diabetes associated with eposure to PM2.5 and NOx	Very close to significant for PM2.5 in single pollutant model	Used Cox proportional hazards models to estimate incidence rate ratios associated with increases in pollutant concentrations. Calculated person-time from start of follow-up in 1995 until occurrence of hypertension or diabetes, loss to follow-up, moving from study aea, death, or end of follow-up. Used both single and co-pollutant models.	Adjusted IRRs for both hypertension and diabetes by age, BMI, years of education, household income, number of people supported by household income, smoking status, alcohol consumption, hours per week of vigorous exercise, and neighborhood SES score. Adjusted hypertension IRRs with neighborhood noise level. Analyzed co-pollutant models, and looked at interactions of noise with both pollutants in hypertension analysis.	Look at long-term exposure, annual values	Yes	**Background:** Evidence suggests that longer-term exposure to air pollutants over years confers higher risks of cardiovascular morbidity and mortality than shorter term exposure. One explanation is that cumulative adverse effects that develop over longer durations lead to the genesis of chronic disease. Preliminary epidemiological and clinical evidence suggest that air pollution may contribute to the development hypertension and type 2 diabetes. **Methods and Results:** We used Cox proportional hazards models to assess incidence rate ratios (IRRs) and 95% confidence intervals (CI) for incident hypertension and diabetes associated with exposure to fine particulate matter (PM2.5) and nitrogen oxides (NOx) in a cohort of African American women living in Los Angeles. Pollutant levels were estimated at participant residential addresses with land use regression models (NOx) and interpolation from monitoring station measurements (PM2.5). Over follow-up from 1995-2005, 531 incident cases of hypertension and 183 incident cases of diabetes occurred. When pollutants were analyzed separately, the IRR for hypertension for a 10 µg/m3 increase in PM2.5 was 1.48 (95% CI 0.95-2.31) and the IRR for the interquartile range (12.4 parts per billion) of NOx was 1.14 (95% CI 1.03-1.25). The corresponding IRRs for diabetes were 1.63 (95% CI 0.78-3.44) and 1.25 (95% CI 1.07-1.46). When both pollutants were included in the same model, the IRRs for PM2.5 were attenuated and the IRRs for NOx were essentially unchanged for both outcomes. **Conclusions:** Our results suggest that exposure to air pollutants, especially traffic-related pollutants, may increase the risk of type 2 diabetes and possibly of hypertension.
Kloog, I., Coull, B.A., Zanobetti, A., Koutrakis, P., Schwartz, J.D.	Acute and Chronic Effects of Particles on Hospital Admissions in New England	2012	PLoS One	PM2.5	Hospital admissions for cardiovascular or respiratory diagnoses among the elderly (65+): respiratory (ICD-9: 460-519), cardiovascular disease (ICD-9: 390-429), stroke (ICD-9: 430-436), diabetes (ICD-9: 250)	New England: CT, ME, MA, NH, RI, VT	Medicare beneficiaries (>= 65 years)	Assess the association betweenshort term and long term PM2.5 exposure and hospital admissions among the elderly		Matched admissions counts by zip code to exposure estimates. Make use of the equivalence between Poisson regression and the piecewise constant proportional hazard model, allowing them to model the time to a hospital admission as a function of both long- and short-term exposure. Check for linearity by fitting a piecewise linear model	Controlled for temperature with the same moving average as PM2.5, age, percent minorities, median income, and percent of people with no high school education. For sensitivity analysis, analyzed other averaging periods and the addition of land use and temporal variables	For short-term exposure, used mean of same and day before, and long-term exposure calculated as the mean exposure in each zip code. Also define short term as difference between the two-day average and the long-term average.	Yes	**Background:** Many studies have reported significant associations between exposure to PM2.5 and hospital admissions, but all have focused on the effects of short-term exposure. In addition all these studies have relied on a limited number of PM2.5 monitors in their study regions, which introduces exposure error, and excludes rural and suburban populations from locations in which monitors are not available, reducing generalizability and potentially creating selection bias. **Methods:** Using our novel prediction models for exposure combining land use regression with physical measurements (satellite aerosol optical depth) we investigated both the long and short term effects of PM2.5 exposures on hospital admissions across New-England for all residents aged 65 and older. We performed separate Poisson regression analysis for each admission type: all respiratory, cardiovascular disease (CVD), stroke and diabetes. Daily admission counts in each zip code were regressed against long and short-term PM2.5 exposure, temperature, socio-economic data and a spline of time to control for seasonal trends in baseline risk. **Results:** We observed associations between both short-term and long-term exposure to PM2.5 and hospitalization for all of the outcomes examined. In example, for respiratory diseases, for every10-µg/m3 increase in short-term PM2.5 exposure there is a 0.70 percent increase in admissions (CI = 0.35 to 0.52) while concurrently for every10-µg/m3 increase in long-term PM2.5 exposure there is a 4.22 percent increase in admissions (CI = 1.06 to 4.75). **Conclusions:** As with mortality studies, chronic exposure to particles is associated with substantially larger increases in hospital admissions than acute exposure and both can be detected simultaneously using our exposure models.

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Chen, H., Burnett, R.T., Kwong, J.C., Villeneuve, P.J., Goldberg, M.S., Brook, R.D., van Donkelaar, A., Jerrett, M., Martin, R.V., Kopp, A., Brook, J.R., Copes, R.	Spatial Association Between Ambient Fine Particulate Matter and Incident Hypertension	2014	Circulation	PM2.5	Incident hypertension (ICD-9: 401-405, ICD-10: I10-I13 or I15 after 2002)	Ontario, Canada	Respondents to the 1996/1997 National Population Health Survey and the 2000/2001, 2003, and 2005 cycles of the Canadian Community Health Survey who were nonhypertensive at the time	Assessed the association between long-term exposure to ambient PM2.5 and incident hypertension	Yes	Derived estimates of ground-level PM2.5 concentrations from satellite observations, and used 6-year mean concentration. Estimated a stratified Cox proportional hazards model with strata defined as single-year age groups, cycle of survey, and region. Cox model was time-varying and modeled time-weighted exposure since cohort entry until the event.	Controlled for covariates like age, sex, marital status, race/ethnicity, education, smoking status, alcohol consumption, daily consumption of fruits and vegetables, physical activity, residency, household income adequacy, indicator variable to classify Ontario into regions. Did sensitivity analysis considering mean annual exposures for other time windows, restricting analysis to participants who had lived at baseline address for at least 5 years before enrollment, restricting to southern Ontario, included linear term for time, and others. Checked for effect modification by age, sex, and comorbidities, and fitted Cox model with frailty term to allow for possibility of spatial dependence	Used 6-year average PM2.5 concentration	Yes	**Background:** Laboratory studies suggest that exposure to fine particulate matter (≤2.5 μm in diameter) (PM2.5) can trigger a combination of pathophysiological responses that may induce the development of hypertension. However, epidemiological evidence relating PM2.5 and hypertension is sparse. We thus conducted a population-based cohort study to determine whether exposure to ambient PM2.5 is associated with incident hypertension. **Methods and Results:** We assembled a cohort of 35 303 nonhypertensive adults from Ontario, Canada, who responded to 1 of 4 population-based health surveys between 1996 and 2005 and were followed up until December 31, 2010. Incident diagnoses of hypertension were ascertained from the Ontario Hypertension Database, a validated registry of persons diagnosed with hypertension in Ontario (sensitivity=72%, specificity=95%). Estimates of long-term exposure to PM2.5 at participants' postal-code residences were derived from satellite observations. We used Cox proportional hazards models, adjusting for various individual and contextual risk factors including body mass index, smoking, physical activity, and neighbourhood-level unemployment rates. We conducted various sensitivity analyses to assess the robustness of the effect estimate, such as investigating several time windows of exposure and controlling for potential changes in the risk of hypertension over time. Between 1996 and 2010, we identified 8649 incident cases of hypertension and 2296 deaths. For every 10-μg/m(3) increase of PM2.5, the adjusted hazard ratio of incident hypertension was 1.13 (95% confidence interval, 1.05-1.22). Estimated associations were comparable among all sensitivity analyses. **Conclusions:** This study supports an association between PM2.5 and incident hypertension.
Coogan, P.F., White, L.F., Jerrett, M., Brook, R.D., Su, J.G., Seto, E., Burnett, R., Palmer, J.R. Rosenberg, L.	Air Pollution and Incidence of Hypertension and Diabetes Mellitus in Black Women in Los Angeles	2012	Circulation	PM2.5, NOx	Incident hypertension, diabetes	Los Angeles	Participants in the Black Women's Health Study, free from hypertension and diabetes at 1995 baseline	Assesses the risks of incident hyperension and diabetes associated with eposure to PM2.5 and NOx	Very close to significant for PM2.5 in single pollutant model	Used Cox proportional hazards models to estimate incidence rate ratios associated with increases in pollutant concentrations. Calculated person-time from start of follow-up in 1995 until occurrence of hypertension or diabetes, loss to follow-up, moving from study aea, death, or end of follow-up. Used both single and co-pollutant models.	Adjusted IRRs for both hypertension and diabetes by age, BMI, years of education, household income, number of people supported by household income, smoking status, alcohol consumption, hours per week of vigorous exercise, and neighborhood SES score. Adjusted hypertension IRRs with neighborhood noise level. Analyzed co-pollutant models, and looked at interactions of noise with both pollutants in hypertension analysis.	Look at long-term exposure, annual values	Yes	**Background:** Evidence suggests that longer-term exposure to air pollutants over years confers higher risks of cardiovascular morbidity and mortality than shorter term exposure. One explanation is that cumulative adverse effects that develop over longer durations lead to the genesis of chronic disease. Preliminary epidemiological and clinical evidence suggest that air pollution may contribute to the development hypertension and type 2 diabetes. **Methods and Results:** We used Cox proportional hazards models to assess incidence rate ratios (IRRs) and 95% confidence intervals (CI) for incident hypertension and diabetes associated with exposure to fine particulate matter (PM2.5) and nitrogen oxides (NOx) in a cohort of African American women living in Los Angeles. Pollutant levels were estimated at participant residential addresses with land use regression models (NOx) and interpolation from monitoring station measurements (PM2.5). Over follow-up from 1995-2005, 531 incident cases of hypertension and 183 incident cases of diabetes occurred. When pollutants were analyzed separately, the IRR for hypertension for a 10 μg/m3 increase in PM2.5 was 1.48 (95% CI 0.95-2.31) and the IRR for the interquartile range (12.4 parts per billion) of NOx was 1.14 (95% CI 1.03-1.25). The corresponding IRRs for diabetes were 1.63 (95% CI 0.78-3.44) and 1.25 (95% CI 1.07-1.46). When both pollutants were included in the same model, the IRRs for PM2.5 were attenuated and the IRRs for NOx were essentially unchanged for both outcomes. **Conclusions:** Our results suggest that exposure to air pollutants, especially traffic-related pollutants, may increase the risk of type 2 diabetes and possibly of hypertension.

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Rodopoulou, S., Samoli, E., Chalbot, M.G., Kavouras, I.G.	Air Pollution and Cardiovascular and Respiratory Emergency Visits in Central Arkansas: A Time-Series Analysis	2015	Science of the Total Environment	PM2.5, O3	Emergency room visits for cardiovascular diagnoses (ICD-9: 401-459), hypertension (ICD-9: 401), hypertensive heart disease and heart failure (ICD-9: 402, 428), conduction disorders and cardiac dysrhythmias: (ICD-9: 426-427), cerebrovascular disease and stroke: (ICD-9: 430-438), respiratory diagnoses (ICD-9: 460-519), acute respiratory infections except acute bronchioloitis and bronchiolitis (ICD-9: 460-465), pneumonia (ICD-9: 480-486), asthma (ICD-9: 493), chronic obstructive pulmonary disease (ICD-9: 490-491-492-496)	Central Arkansas	Daily emergency room visits 2002-2012 among adults >=15	Studies the short-term effects of air pollution on cardiovascular and respiratory morbidity in the stroke and heart failure belt		Tallied daily hospital emergency counts and then linked these counts to lagged pollution exposure using overdispersed generalized linear Poisson regression models. Applied natural spline smooth functions to include the effect of time-varying covariates and calendar time on daily visits. Used natural cubic regression splint with 1.5 degrees of freedom for each season and year.	Controlled for temperature on day of visit, two previous days, average relative humidity with lags, dummy variables for the day of the week and holidays effect. Looked for confounding by other pollutants using two pollutant models. Also looked at effect modification by season, age, gender, and race.	Uses PM2.5 and O3 from day before visit for cardiovascular causes and on the two preceding days for respiratory causes. Experimented with other lags	Yes	**Background:** Heart disease and stroke mortality and morbidity rates in Arkansas are among the highest in the U.S. While the effect of air pollution on cardiovascular health was identified in traffic-dominated metropolitan areas, there is a lack of studies for populations with variable exposure profiles, demographic and disease characteristics. **Objective:** Determine the short-term effects of air pollution on cardiovascular and respiratory morbidity in the stroke and heart failure belt. **Methods:** We investigated the associations of fine particles and ozone with respiratory and cardiovascular emergency room visits during the 2002–2012 period for adults in Central Arkansas using Poisson generalized models adjusted for temporal, seasonal and meteorological effects. We evaluated sensitivity of the associations to mutual pollutant adjustment and effect modification patterns by sex, age, race and season. **Results:** We found effects on cardiovascular and respiratory emergencies for PM2.5 (1.52% [95% (confidence interval) CI: − 1.10%, 4.20%]; 1.45% [95%CI: − 2.64%, 5.72%] per 10 μg/m3) and O3 (0.93% [95%CI: − 0.87%, 2.76%]; 0.76 [95%CI: − 1.92%, 3.52%] per 10 ppbv) during the cold period (October–March). The effects were stronger among whites, except for the respiratory effects of O3 that were higher among Blacks/African-Americans. Effect modification patterns by age and sex differed by association. Both pollutants were associated with increases in emergency room visits for hypertension, heart failure and asthma. Effects on cardiovascular and respiratory emergencies were observed during the cold period when particulate matter was dominated by secondary nitrate and wood burning. **Conclusion:** Outdoor particulate pollution during winter had an effect on cardiovascular morbidity in central Arkansas, the region with high stroke and hear**t disease incidence rates.**
Bernatsky, S., Smargiassi, A., Johnson, M., Kaplan, G.G., Barnabe, C., Svenson, L., Brand, A., Bertazzon, S., Hudson, M., Clarke, A.E., Fortin, P.R., Edworthy, S., Belisle, P., Joseph, L.	Fine Particulate Air Pollution, Nitrogen Dioxide, and Systemic Autoimmune Rheumatic Disease in Calgary, Alberta	2015	Environmental Research	NO2, PM2.5	Systemic autoimmune rheumatic diseases (SARDs) (ICD-10: M32.1, M32.8-32.9, M33-M34, M35.0, M35.8-35.9, M36.0)	Calgary, Alberta	Residents of Calgary	Examines associations between air pollution and SARDS at a fine spatial scale.	Yes	Estimated air pollution exposure using land use regression models. Used case definitions in a Bayesian hierarchical latent class regression models to esimate the probability that each resident was a SARD case, and then summed individual level probability to get the estimated number of cases in each area. Then used Bayesian logistic regression model that estimated odds ratios adjusted for NO2 and PM2.5 pollutant models.	Adjusted for neighborhood income, age, sex, and an interaction between age and sex. Also stratified by First-Nations and non-First-Nations subgroups. Acknowledges potential for mis-classification of pollutant exposure.	Assessed long-term exposure using two-week summer and winter measurements from 2010 and 2011	Yes	**Objective:** To estimate the association between fine particulate (PM2.5) and nitrogen dioxide (NO2) pollution and systemic autoimmune rheumatic diseases (SARDs). **Methods:** Associations between ambient air pollution (PM2.5 and NO2) and SARDs were assessed using land-use regression models for Calgary, Alberta and administrative health data (1993–2007). SARD case definitions were based on ≥2 physician claims, or ≥1 rheumatology billing code; or ≥1 hospitalization code (for systemic lupus, Sjogren's Syndrome, scleroderma, polymyositis, dermatomyositis, or undifferentiated connective tissue disease). Bayesian hierarchical latent class regression models estimated the probability that each resident was a SARD case, based on these case definitions. The sum of individual level probabilities provided the estimated number of cases in each area. The latent class model included terms for age, sex, and an interaction term between age and sex. Bayesian logistic regression models were used to generate adjusted odds ratios (OR) for NO2 and PM2.5. pollutant models, adjusting for neighbourhood income, age, sex, and an interaction between age and sex. We also examined models stratified for First-Nations (FN) and non-FN subgroups. **Results:** Residents that were female and/or aged >45 had a greater probability of being a SARD case, with the highest OR estimates for older females. Independently, the odds of being a SARDs case increased with PM2.5 levels, but the results were inconclusive for NO2. The results stratified by FN and non-FN groups were not distinctly different. **Conclusion:** In this urban Canadian sample, adjusting for demographics, exposure to PM2.5 was associated with an increased risk of SARDs. The results for NO2 were inconclusive.

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De Roos, A.J., Koehoorn, M., Tamburic, L., Davies, H.W., Brauer, M.	Proximity to Traffic, Ambient Air Pollution, and Community Noise in Relation to Incident Rheumatoid Arthritis	2014	Environmental Health Perspectives	PM2.5, NO2, NO	Rheumatoid arthritis (ICD-9: 714)	Vancouver, Victoria, Canada	Residents age 45-84, registered with Canadian health insurance plan	Investigates proximity to traffic, ambient air pollution, and community noise as risk factors for rheumatoid arthritis	No (only for proximity to traffic)	Estimated individual exposure using land-use regression. Used a nested case-control design to evaluate risk in relation to a consistent window of exposure. Cases were diagnosed with RA, and matched ten controls per case by age and sex. Generated odds ratios from conditional logistic regression models, accounting for the age- and sex-matched design.	Controlled for traffic and other pollutants (black carbon, etc.), which should address some confounding by other pollutants. Adjusted analysis for potential confuonding by neigborhood-level SES, tried excluding people who moved during the exposure period. Also tried different specification of concentration-response function. The study's population-based sample should reduce selection bias.	Used average exposure for 5-year period before index date	Yes	**Background:** The risk of rheumatoid arthritis (RA) has been associated with living near traffic; however, there is evidence suggesting that air pollution may not be responsible for this association. Noise, another traffic-generated exposure, has not been studied as a risk factor for RA. **Objectives:** We investigated proximity to traffic, ambient air pollution, and community noise in relation to RA in the Vancouver and Victoria regions of British Columbia, Canada. **Methods:** Cases and controls were identified in a cohort of adults that was assembled using health insurance registration records. Incident RA cases from 1999 through 2002 were identified by diagnostic codes in combination with prescriptions and type of physician (e.g., rheumatologist). Controls were matched to RA cases by age and sex. Environmental exposures were assigned to each member of the study population by their residential postal code(s). We estimated relative risks using conditional logistic regression, with additional adjustment for median income at the postal code. **Results:** RA incidence was increased with proximity to traffic, with an odds ratio (OR) of 1.37 (95% CI: 1.11, 1.68) for residence ≤ 50 m from a highway compared with residence > 150 m away. We found no association with traffic-related exposures such as PM2.5, nitrogen oxides, or noise. Ground-level ozone, which was highest in suburban areas, was associated with an increased risk of RA (OR = 1.26; 95% CI: 1.18, 1.36 per interquartile range increase). **Conclusions:** Our study confirms a previously observed association of RA risk with proximity to traffic and suggests that neither noise levels nor traffic-related air pollutants are responsible for this relationship. Additional investigation of neighborhood and individual correlates of residence near roadways may provide new insight into risk factors for RA.
Hart, J.E., Kallberg, H., Laden, F., Costenbader, K.H., Yanosky, J.D., Klareskog, Alfredsson, L., Karlson, E.W.	Ambient Air Pollution Exposures and Risk of Rheumatoid Arthritis in the Nurses' Health Study	2014	Arthritis Care Research	PM10, PM2.5, SO2, NO2	Rheumatoid arthritis	United States	Nurses' Health Study participants, with no history of RA or other connective tissue disease at baseine in 1976	Considers the possible association between air pollution and risks of rheumatoid arthritis		Used time-varying Cox proportional hazards models with each air pollutant in a separate model. Person-time accrued from baseine until diagnosis of RA, loss to follow-up, date of death, or end of follow-up. Stratified all models by age in months and calendar year.	Controlled for age, race, age at menarche, parity, total months of lactation, current menopausal status, menopausal hormone use, oral contraceptive use, physical activity, and BMI. Controlled for smoking and individual level SES using education levels. Also included census tract-level median income and house value. Looked at effect modification by age in months and calendar year. Also looked at effect modification by SES and smoking status, as well as by census region.	Looked at time-varying annual exposure the 6th- and 10th-year prior to each questionnaire cycle. Also looked at time-varying cumulative average exposure during the follow-up period	Yes	Objective: Environmental factors may play a role in the development of rheumatoid arthritis (RA), and we have previously observed increased RA risk among women living closer to major roads (a source of air pollution). We examined whether long-term exposures to specific air pollutants were associated with RA risk among women in the Nurses' Health Study. Methods: The Nurses' Health Study (NHS) is a large cohort of U.S. female nurses followed prospectively every two years since 1976. We studied 111,425 NHS participants with information on air pollution exposures as well as data concerning other lifestyle and behavioral exposures and disease outcomes. Outdoor levels of different size fractions of particulate matter (PM10 and PM2.5) and gaseous pollutants (SO2 and NO2) were predicted for all available residential addresses using monitoring data from the USEPA. We examined the association of time-varying exposures, 6 and 10 years before each questionnaire cycle, and cumulative average exposure with the risks of RA, seronegative (rheumatoid factor [RF] and anti–citrullinated peptide antibodies [ACPA]) RA, and seropositive RA. Results: Over the 3,019,424 years of follow-up, 858 incident RA cases were validated by medical record review by two board-certified rheumatologists. Overall, we found no evidence of increased risks of RA, seronegative or seropositive RA, with exposure to the different pollutants, and little evidence of effect modification by socioeconomic status or smoking status, geographic region, or calendar period. Conclusion: In this group of socioeconomically-advantaged middle-aged and elderly women, adult exposures to air pollution were not associated with an increased RA risk.

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Hu, H., Dailey, A.B., Kan, H., Xu, X.	The Effect of Atmospheric Particulate Matter on Survival of Breast Cancer Among U.S. Females	2013	Breast Cancer Research and Treatment	PM10, PM2.5	Survival of breast cancer, with breast cancer defined as ICD-O-3:C500-506, 508-509	California	All incident female breast cancer cases 1999-2009	Investigates the effect of long-term exposure to ambient particulate matter on breast cancer survival	Yes (with significant effect modification by cancer stage)	Performed descriptive statistics tests to compare the distributions of categorical variables among different exposure levels of both PM10 and PM2.5, and created survival curves using Kaplan-Meier life table analyses. Used log-rank tests to test significance of the difference of survival among three groups for both pollutants. Estimated marginal Cox proportional hazard models. Used marginal approach for county-level analysis and used maximum partial likelihood estimates of regression parameters and a robust sandwich covariance matrix estimate to account for dependence among subjects within counties	Estimated effect modification by cancer stage and pollution exposure. Adjusted for individual-level information, including demographics and cancer characteristics. Also considered year diagnosed as a potential confounder. Minimize confounders by just looking within California, but can't control for differences in types of healthcare, culture, dietary habits, individual-level SES, smoking, and alcohol consumption. Did sensitivity analysis including census tract-level SES characteristics. Acknowledge possible exposure misclassification etc.	Monthly average exposure during survival period	Yes	Short-term effects of ambient particulate matter (PM) on cardiopulmonary morbidity and mortality have been consistently documented. However, no study has investigated its long-term effects on breast cancer survival. We selected all female breast cancer cases (n = 255,128) available in the California Surveillance Epidemiology and End Results cancer data. These cases were linked to 1999-2009 California county-level PM daily monitoring data. We examined the effect of PM on breast cancer survival. Results from Kaplan-Meier survival analysis show that female breast cancer cases living in areas with higher levels of PM10 and PM2.5 had a significant shorter survival than those living in areas with lower exposures ($p < 0.0001$). The results from marginal cox proportional hazards models suggest that exposure to higher PM10 (HR 1.13, 95 % CI 1.02-1.25, per 10 µg/m(3)) or PM2.5 (HR 1.86, 95 % CI 1.12-3.10, per 5 µg/m(3)) was significantly associated with early mortality among female breast cancer cases after adjusting for individual-level covariates such as demographic factors, cancer stage and year diagnosed, and county-level covariates such as socioeconomic status and accessibility to medical resources. Interactions between cancer stage and PM were also observed; the effect of PM on survival was more pronounced among individuals diagnosed with early stage cancers. This study suggests that exposure to high levels of PM may have deleterious effects on the length of survival from breast cancer, particularly among women diagnosed with early stage cancers. The findings from this study warrant further investigation.
Hystad, P., Demers, P.A., Johnson, K.C., Carpiano, R.M., Brauer, M.	Long-term Residential Exposure to Air Pollution and Lung Cancer Risk	2013	Epidemiology	PM2.5, NO2, O3	Lung cancer	Eight Canadian provinces	Lung cancer cases 1994 to 1997	Investigates the relationship between lung cancer incidence and long-term exposure to ambient air pollution and proximity to major roads using hierarchical logistic regression models, also doing subanalysis in urban centers.	Close for PM2.5	Developed spatiotemporal models for Canada to estimate annual residential exposure to PM2.5, NO2, and O3 over 20-year exposure period. Then compared incident lung cancer cases with population controls	Case-control design should control for some key individual characteristics	Evaluates average over 20-year exposure period	Yes	**Background:** There is accumulating evidence that air pollution causes lung cancer. Still, questions remain about exposure misclassification, the components of air pollution responsible, and the histological subtypes of lung cancer that might be produced. **Methods:** We investigated lung cancer incidence in relation to long-term exposure to three ambient air pollutants and proximity to major roads, using a Canadian population-based case-control study. We compared 2,390 incident, histologically confirmed lung cancer cases with 3,507 population controls in eight Canadian provinces from 1994 to 1997. We developed spatiotemporal models for the whole country to estimate annual residential exposure to fine particulate matter (PM2.5), nitrogen dioxide (NO2), and ozone (O3) over a 20-year exposure period. We carried out a subanalysis in urban centers, using exposures derived from fixed-site air pollution monitors, and also examined traffic proximity measures. Hierarchical logistic regression models incorporated a comprehensive set of individual and geographic covariates. **Results:** The increase in lung cancer incidence (expressed as fully adjusted odds ratios [ORs]) was 1.29 (95% confidence interval = 0.95-1.76) with a ten-unit increase in PM2.5 (µg/m), 1.11 (1.00-1.24) with a ten-unit increase in NO2 (ppb), and 1.09 (0.85-1.39) with a ten-unit increase in O3 (ppb). The urban monitor-based subanalyses generally supported the national results, with larger associations for NO2 (OR = 1.34; 1.07-1.69) per 10 ppb increase. No dose-response trends were observed, and no clear relationships were found for specific histological cancer subtypes. There was the suggestion of increased risk among those living within 100 m of highways, but not among those living near major roads. **Conclusions:** Lung cancer incidence in this Canadian study was increased most strongly with NO2 and PM2.5 exposure. Further investigation is needed into possible effects of O3 on development of lung cancer.

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Kaplan, G.G., Szyszkowicz, M., Fichna, J., Rowe, B.H., Porada, E., Vincent, R., Madsen, K., Ghosh, S., Storr, M.	Non-Specific Abdominal Pain and Air Pollution: A Novel Association	2012	PLoS One	O3, NO2, SO2, CO, PM10, PM2.5	Emergency department visit for non-specific abdominal pain (ICD-9: 789.0x)	Edmonton and Montreal, Canada	Patients served at emergency departments for 5 Edmonton hospitals, 1992-2002, second population served at ED in Montreal (>=15)	Investigates whether acute exposure to air pollutants is associated with emergency department visits for non-specific abdominal pain	Yes	Used a case-crossover design, time-stratified, where referent period is chosen to match on day of week, month, and year. Used a conditional logistic regression to model the air pollutants, with 6 components for natural splines for temperature and relative humidity. Stratified by age, and tried different lags for exposure. Also did a controlled experiment with male Swiss albino mice.	Case-crossover design limits confounding from time-independent individual risk factors, and matching of control to cases controls for the influence of day of week. Control for possible nonlinear effects of temperature and humidity. Looked at effect modification by age and sex.	Used same day, 1-day lag, and 2-day lag	Yes	Background: We studied whether short-term exposure to air pollution was associated with non-specific abdominal pain in epidemiologic and animal studies. Methods: patients visiting the emergency department with non-specific abdominal pain were identified in Edmonton (1992 to 2002, n = 95,173) and Montreal (1997 to 2002, n = 25,852). We calculated the daily concentrations for ozone (O3), nitrogen dioxide (NO2), sulfur dioxide (SO2), carbon monoxide (CO), and particles <10 (PM10) or <2.5 (PM2.5) μm. A case crossover study design was used to estimate the odds ratio (OR) and 95% confidence interval (CI) associated with an increase in the interquartile range of the air pollutants. We investigated differential effects by age and sex. Mice were gavaged with urban particle extracts. In animal models, colonic motility was tested, and visceral abdominal pain was measured using a writhing test, and behavioral response to oil of mustard and neostigmine. Motility and pain was measured acutely (1.5 hours after gavage) and chronically (7-days and 21-days after gavage). Results: Emergency department visits for non-specific abdominal pain were primarily by women between the ages of 15–24 years. Individuals aged 15 to 24 years were at increased risk of non-specific abdominal pain in Edmonton (same day CO: OR = 1.04, 95% CI = 1.02–1.06; and NO2: OR = 1.06, 95% CI = 1.03–1.09). The risk of air pollution among 15–24 year olds in Montreal was significantly positive (same day CO: OR = 1.11, 95% CI = 1.05–1.17; NO2: OR = 1.09, 95% CI = 1.01–1.16; SO2: OR = 1.17, 95% CI = 1.10–1.25; PM2.5: OR = 1.09, 95% CI = 1.04–1.15). Abdominal pain was increased by an acute gavage of pollution extract but not to chronic exposure to pollutants. Colonic transit was delayed following chronic but not acute exposure with the pollutants. Conclusions: Epidemiological and animal data suggest that short-term exposure to air pollution may trigger non-specific abdominal pain in young individuals.
Kaplan, G.G., Tanyingoh, D., Dixon, E., Johnson, M., Wheeler, A.J., Myers, R.P., Bertazzon, S., Saini, V., Madsen, K., Ghosh, S., Villeneuve, P.J.	Ambient Ozone Concentrations and the Risk of Perforated and Nonperforated Appendicitis: A Multicity Case-Crossover Study	2013	Environmental Health Perspectives	O3, NO2, PM2.5	Incident cases of appendicitis (ICD-10-CA: K35.9, K35.0, K35.1)	12 Canadian cities	All inpatient discharges, 2004, 2008	Estimates associations between short-term ambient O3 concentrations and appendicitis across multiple Canadian cities		Used a time-stratified case-crossover design, comparing air pollution on the case day to exposure on a series of regerent days. Cases and controls are matched by day of the week and month-year. Did a conditional logistic regression to get city-specific estimates, and then pooled them using a random effects meta-analysis.	Time-invariant factors are controlled by case-control design. Should also control for any time-variant individual factors that don't vary within a month. Looked at potential confounding by other pollutants using two-pollutant models adjusted for NO2 or PM2.5. Also look at effect modification by age, sex, season, and appendicitis phenotype			Background: Environmental determinants of appendicitis are poorly understood. Past work suggests that air pollution may increase the risk of appendicitis. Objectives: We investigated whether ambient ground-level ozone (O3) concentrations were associated with appendicitis and whether these associations varied between perforated and nonperforated appendicitis. Methods: We based this time-stratified case-crossover study on 35,811 patients hospitalized with appendicitis from 2004 to 2008 in 12 Canadian cities. Data from a national network of fixed-site monitors were used to calculate daily maximum O3 concentrations for each city. Conditional logistic regression was used to estimate city-specific odds ratios (ORs) relative to an interquartile range (IQR) increase in O3 adjusted for temperature and relative humidity. A random-effects meta-analysis was used to derive a pooled risk estimate. Stratified analyses were used to estimate associations separately for perforated and nonperforated appendicitis. Results: Overall, a 16-ppb increase in the 7-day cumulative average daily maximum O3 concentration was associated with all appendicitis cases across the 12 cities (pooled OR = 1.07; 95% CI: 1.02, 1.13). The association was stronger among patients presenting with perforated appendicitis for the 7-day average (pooled OR = 1.22; 95% CI: 1.09, 1.36) when compared with the corresponding estimate for nonperforated appendicitis [7-day average (pooled OR = 1.02, 95% CI: 0.95, 1.09)]. Heterogeneity was not statistically significant across cities for either perforated or nonperforated appendicitis (p > 0.20). Conclusions: Higher levels of ambient O3 exposure may increase the risk of perforated appendicitis.

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Kioumourtzoglou, M., Schwartz, J.D., Weisskopf, M.G., Melly, S.J., Wang, Y., Dominici, F., Zanobetti, A.	Long-term PM2.5 Exposure and Neurological Hospital Admissions in the Northeastern United States	2015	Environmental Health Perspectives	PM2.5	Admissions for Parkinson's disease (ICD-9: 332), Alzheimer's disease (ICD-9: 331.0), dementia (ICD-9: 290), congestive heart failure (ICD-9: 428), myocardial infarction (ICD-9: 410), chronic obstructive pulmonary disease (ICD-9: 490-492, 494-496), diabetes (ICD-9: 250)	Northeastern U.S. (50 cities in CT, DE, DC, ME, MD, MA, NH, NJ, NY, PA, RI, VT)	Medicare enrollees (>= 65 years) 1999-2000	Assesses the potential impact of long-term PM2.5 exposure on event time, defined as time to the first admission for dementia, Alzheimer's or Parkinson's	Yes (for all outcomes)	Ran separate models for PD, Ad, and dementia. Fit time-varying Cox proportional hazards models separately in each city. Used city-wide annual PM2.5 concentrations as time-varying exposure of interest, as well as a term for calendar year. Fit city-specific models to avoid confounding by factors varying across cities. After making city-specific estimates, pooled them together in a second stage using a random effects meta-analysis. Assess whether the association between PM2.5 and neurological admissions is nonlinear.	Control for confounding by things that vary across cities, and control for year-to-year variations in cause-specific admissions in each city adjusting for calendar year--Should eliminate all confounding by covariates that vary across cities and by covariates whose long-term trends coincide with trends in PM2.5 within cities. Adjust for previous admissions for CHF, COPD, MI, or diabetes and # days spent in the intensive and coronary care units. Adjust for median income, and stratify models by age, gender, race, and year of follow-up. Assess potential effect modification by gender.	Looked at long-term exposure as annual averages	Yes	**Background:** Long-term exposure to fine particles (PM2.5) has been consistently linked to heart and lung disease. Recently there has been increased interest to examine the effects of air pollution on the nervous system, with evidence showing potentially harmful effects on neurodegeneration. Our objective was to assess the potential impact of long-term PM2.5 exposure on event time, defined as time to the first admission for dementia, Alzheimer's or Parkinson's diseases (AD and PD, respectively) in an elderly population across the Northeastern US. **Methods:** We estimated the effects of PM2.5 on first hospital admission for dementia, AD and PD, among all Medicare enrollees >64 years in 50 northeastern US cities (1999–2010). For each outcome, we first ran a Cox proportional hazards model in each city, adjusting for prior cardiopulmonary-related hospitalizations and year, and stratified by follow-up time, age, gender and race. We then pooled the city-specific estimates together by employing a random effects meta-regression. **Results:** We followed approximately 10 million subjects and observed significant associations of long-term PM2.5 city-wide exposure on all three outcomes. Specifically, we estimated a HR of 1.08; 95% CI: 1.05, 1.11 for dementia, 1.15; 95% CI: 1.11, 1.19 for AD and 1.08; 95% CI: 1.04, 1.12 for PD admissions per 1 μg/m3 of increase in annual PM2.5 concentrations. **Conclusions:** To our knowledge, this is the first study to examine the relationship between longterm exposure to PM2.5 and time to the first hospitalization for the most common neurodegenerative diseases. We found strong evidence of an association for all three outcomes. Our findings provide the basis for more studies, as the implications to public health can be crucial.
Kirrane, E.F., Bowman, C., Davis, J.A., Hoppin, J.A., Blair, A., Chen, H., Patel, M.M., Sandler, D.P., Tanner, C.M., Vinikoor-Imler, L., Ward, M.H., Luben, T.J., Kamel, F.	Associations of Ozone and PM2.5 Concentrations with Parkinson's Disease Among Participants in the Agricultural Health Study	2015	Journal of Occupational and Environmental Medicine	O3, PM2.5	Incidence of self-reported, doctor-diagnosed Parkinson's disease	North Carolina and Iowa	U.S. Agricultural Health Study cohort	Estimates associations of ozone and fine particulate matter with Parkinson's disease among farmers in NC and Iowa	Yes (in North Carolina)	Derived surrogates of long-term exposure using daily predicted pollutant concentrations, and linked these to participants' geocoded addresses. Uses logistic regression to determine the associations between these pollutants and incidence of Parkinson's disease.	Acknowledges the possibility of confounding and a poor grasp of the temporal aspects of the estimated relationship	Uses "long-term exposure," but seems to be based on daily concentrations	Yes	**Objective:** This study describes associations of ozone and fine particulate matter with Parkinson's disease observed among farmers in North Carolina and Iowa. **Methods:** We used logistic regression to determine the associations of these pollutants with self-reported, doctor-diagnosed Parkinson's disease. Daily predicted pollutant concentrations were used to derive surrogates of long-term exposure and link them to study participants' geocoded addresses. **Results:** We observed positive associations of Parkinson's disease with ozone (odds ratio = 1.39; 95% CI: 0.98 to 1.98) and fine particulate matter (odds ratio = 1.34; 95% CI: 0.93 to 1.93) in North Carolina but not in Iowa. **Conclusions:** The plausibility of an effect of ambient concentrations of these pollutants on Parkinson's disease risk is supported by experimental data demonstrating damage to dopaminergic neurons at relevant concentrations. Additional studies are needed to address uncertainties related to confounding and to examine temporal aspects of the associations we observed.
Mahalingaiah, S., Hart, J.E., Laden, F., Aschengrau, A., Missmer, S.A.	Air Pollution Exposures During Adulthood and Risk of Endometriosis in the Nurses' Health Study II	2014	Environmental Health Perspectives	PM2.5, PM10	Endometriosis	United States	Participants in the Nurses' Health Study, no diagnosis of endometriosis before 1993	Evaluate the association of exposure to traffic-related exhaust and PM during adulthood with the incidence of endometriosis	No	Estimated time-varying Cox proportional hazard models, with person-time accruing from September 1993 to first diagnosis, hysterectomy, menopause, loss to follow-up, cancer diagnosis, date of death, or end of follow-up. For effect modifications, performed time-varying stratified models. Also used multiplicative interaction terms. Presents region-specific estimates, with "West" as one region.	Controlled for traffic-related pollutants using distance to nearest road. Examined possible confounding by age, race/ethnicity, age at menarche, smoking status, BMI, oral contraception use, infertility, ever performed rotating shift work, region, area-level SES. Examined effect mofidication by parity, overweight/obese, smoking status, age at menarche, infertility, and rotating shift work. Also performed models stratified by region of the country.	Used average air pollution in prior 2 calendar years, average air pollution in prior 4 calendar years, and cumulative average exposure	Yes	**Background:** Particulate matter and proximity to large roadways may promote disease mechanisms, including systemic inflammation, hormonal alteration, and vascular proliferation, that may contribute to the development and severity of endometriosis. **Objective:** Our goal was to determine the association of air pollution exposures during adulthood, including distance to road, particulate matter < 2.5 μm, between 2.5 and 10 μm, and < 10 μm, (PM2.5, PM10–2.5, PM10), and timing of exposure with risk of endometriosis in the Nurses' Health Study II. **Methods**: Proximity to major roadways and outdoor levels of PM2.5, PM10–2.5, and PM10 were determined for all residential addresses from 1993 to 2007. Multivariable-adjusted time-varying Cox proportional hazard models were used to estimate the relation between these air pollution exposures and endometriosis risk. **Results:** Among 84,060 women, 2,486 incident cases of surgically confirmed endometriosis were identified over 710,230 person-years of follow-up. There was no evidence of an association between endometriosis risk and distance to road or exposure to PM2.5, PM10–2.5, or PM10 averaged over follow-up or during the previous 2- or 4-year period. **Conclusions:** Traffic and air pollution exposures during adulthood were not associated with incident endometriosis in this cohort of women.

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Mahalingaiah, S., Hart, J.E., Laden, F., Terry, K.L., Boynton-Jarrett, R., Aschengrau, A., Missmer, S.A.	Air Pollution and Risk of Uterine Leiomyomata	2014	Epidemiology	PM2.5, PM10	Incidence of uterine leiomyomata	United States	Participants in Nurses' Health Study II, premenopausal, without diagnosis of cancer or prevalent uterine leiomyomata	Estimates the association between air pollution exposure and the occurrence of uterine leiomyomata, a hormonally sensitive tumor of the uterus	Yes (for 2-year average, cumulative average, and almost for 4-year average)	Used distance to road as a proxy for traffic exposure and included PM2.5 exposure to estimate time-varing Cox proportional hazards models. Used cubic splines to test for linearity of al continuous exposures. Estimated separate baseline hazards for age in months and calendar year in the Cox models	Controlled for potential confounders at individual level, including age, race, smoking status, BMI, parity, diagnosis of infertility, age at first birth, age at last birth, etc. Also considered adjustment for region, and looked at effect modification by age. Acknowledges potential for exposure misclassification from using ambient exposures as a proxy for personal exposures.	Used chronic exposure from moving 2-year average, moving 4-year average, and time-varying cumulative average	Yes	**Background:** Air pollution, particularly from vehicle exhaust, has been shown to influence hormonal activity. However, it is unknown whether air pollution exposure is associated with the occurrence of uterine leiomyomata, a hormonally sensitive tumor of the uterus. **Methods:** For 85,251 women 25-42 years of age at enrollment in the Nurses' Health Study II, we examined proximity to major roadways and outdoor levels of particulate matter less than 10 microns (PM10) or 2.5 microns (PM2.5) or between 10 and 2.5 microns (PM10-2.5) in diameter for all residential addresses from September 1989 to May 2007. To be eligible for this analysis, a woman had to be alive and respond to questionnaires, premenopausal with an intact uterus, and without diagnoses of cancer or prevalent uterine leiomyomata. Incidence of ultrasound- or hysterectomy-confirmed uterine leiomyomata and covariates were reported on biennial questionnaires sent through May 2007. Multivariable time-varying Cox proportional hazard models were used to estimate the relationship between distance to road or PM exposures and uterine leiomyomata risk. **Results:** During 837,573 person-years of follow-up, there were 7760 incident cases of uterine leiomyomata. Living close to a major road and exposures to PM10 or PM10-2.5 were not associated with an increased risk of uterine leiomyomata. However, each 10 µg/m increase in 2-year average, 4-year average, or cumulative average PM2.5 was associated with an adjusted hazard ratio of 1.08 (95% confidence interval = 1.00-1.17), 1.09 (0.99-1.19), and 1.11 (1.03-1.19), respectively. **Conclusions:** Chronic exposure to PM2.5 may be associated with a modest increased risk of uterine leiomyomata.
Palacios, N., Fitzgerald, K.C., Hart, J.E., Weisskopf, M.G., Schwarzschild, M.A., Ascherio, A., Laden, F.	Particulate Matter and Risk of Parkinson Disease in a Large Prospective Study of Women	2014	Environmental Health	PM10, PM2.5, PM10-2.5	Risk of Parkinson's Disease	United States	Participants in the Nurses' Health Study	Assesses the association between exposure to particulate matter air pollution and risk of Parkinson's disease	No	Estimated Cox proportional hazards models with age as the time scale. Calculated person-months of follow-up from baseline to the end of follow-up (June 30, 2008), death, or date of PD diagnosis, whichever occurred first.	Adjusted analysis for age in months, region of the United States, pack years smoking, smoking status, population density, caffeine consumption, use of ibuprofen. Controlled for census tract-level income and housing value. Did other analyses stratified by smoking, caffeine intake and ubiprofen use. Acknowledge possibility of misclassification of exposure	Use cumulative exposure over 2 years before diagnosis, and tested sensitivity for 5-year lag	Yes	**Background:** Exposure to air pollution has been implicated in a number of adverse health outcomes and the effect of particulate matter (PM) on the brain is beginning to be recognized. Yet, no prospective study has examined the association between PM and risk of Parkinson Disease. Thus, our goal was assess if exposure to particulate matter air pollution is related to risk of Parkinson's disease (PD) in the Nurses' Health Study (NHS), a large prospective cohort of women. **Methods:** Cumulative average exposure to different size fractions of PM up to 2 years before the onset of PD, was estimated using a spatio-temporal model by linking each individual's places of residence throughout the study with location-specific air pollution levels. We prospectively followed 115,767 women in the NHS, identified 508 incident PD cases and used multivariable Cox proportional hazards models to estimate the risk of PD associated with each size fraction of PM independently. **Results:** In models adjusted for age in months, smoking, region, population density, caffeine and ibuprofen intake, we observed no statistically significant associations between exposure to air pollution and PD risk. The relative risk (RR) comparing the top quartile to the bottom quartile of PM exposure was 1.03 (95% Confidence Intervals (CI): 0.78, 1.37) for PM10 (≤ 10 microns in diameter), 1.10 (95% CI: 0.83, 1.45) for PM2.5 (≤ 2.5 microns in diameter), and 0.93 (95% CI: 0.69, 1.26) for PM10–2.5 (2.5 to 10 microns in diameter). **Conclusions:** In this study, we found no evidence that exposure to air pollution is a risk factor for PD.

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Power, M.C., Kiomourtzoglou, M.A., Hart, J.E., Okereke, O.I., Laden, F., Weisskopf, M.G.	The Relation Between Past Exposure to Fine Particulate Air Pollution and Prevalent Anxiety: Observational Cohort Study	2015	British Medical Journal	PM2.5, PM10	Meaningfully high symptoms of anxiety, defined as a score of 6 points or greater on the phobic anxiety subscale of Crown-Crisp index	Contiguous U.S.	Participants in the Nurses' Health Study with data for both PM2.5 exposure and anxiety symptoms	Evaluates association between past exposure to PM2.5 and prevalent high symptoms of anxiety	Yes (for multiple averaging periods)	Used spatiotemporal prediction models to estimate monthly exposure to PM10 and PM2.5 from January 1988 onward, with at least a zip-code level geocoding match for each participant. Used separate logistic regression models to estimate the association between each exposure and high anxiety symptoms. Used splines to evaluate shape of the dose-response curve, and use both fifths of exposure indicators and linear terms. To determine which exposure periods are most relevant, consider mutually adjusted models with different exposure periods	Controlled for potential confounders including calendar month of questionnaire, educational attainment, spouse's educational attainment, age, age squared, marital status, employment status, physical activity, residential census tract level characteristics, region of residence, residence within MSA, and social support. Do sensitivity analysis with other individual level covariates that are not expected to be confounders, like alcohol consumption, BMI, and try various sample restrictions. Test for effect modification by residence with MSA and U.S. census region, prevalent reactive airway disease, atrial fibrillation, heart failure, or multiple major medical conditions at time of anxiety assessment, age, and earlier anxiety assessment	Try different exposure periods, using either 1988-2003 and past one month or past 12 months and past one month exposures	Yes	**Objective:** To determine whether higher past exposure to particulate air pollution is associated with prevalent high symptoms of anxiety. **Design:** Observational cohort study. **Setting:** Nurses' Health Study. **Main outcome measures:** Meaningfully high symptoms of anxiety, defined as a score of 6 points or greater on the phobic anxiety subscale of the Crown-Crisp index, administered in 2004. **Results:** The 71 271 eligible women were aged between 57 and 85 years (mean 70 years) at the time of assessment of anxiety symptoms, with a prevalence of high anxiety symptoms of 15%. Exposure to particulate matter was characterized using estimated average exposure to particulate matter <2.5 µm in diameter (PM2.5) and 2.5 to 10 µm in diameter (PM2.5-10) in the one month, three months, six months, one year, and 15 years prior to assessment of anxiety symptoms, and residential distance to the nearest major road two years prior to assessment. Significantly increased odds of high anxiety symptoms were observed with higher exposure to PM2.5 for multiple averaging periods (for example, odds ratio per 10 µg/m3 increase in prior one month average PM2.5: 1.12, 95% confidence interval 1.06 to 1.19; in prior 12 month average PM2.5: 1.15, 1.06 to 1.26). Models including multiple exposure windows suggested short term averaging periods were more relevant than long term averaging periods. There was no association between anxiety and exposure to PM2.5-10. Residential proximity to major roads was not related to anxiety symptoms in a dose dependent manner. **Conclusions:** Exposure to fine particulate matter (PM2.5) was associated with high symptoms of anxiety, with more recent exposures potentially more relevant than more distant exposures. Research evaluating whether reductions in exposure to ambient PM2.5 would reduce the population level burden of clinically relevant symptoms of anxiety is warranted.
Wang, Y., Eliot, M.N., Koutrakis, P., Gryparis, A., Schwartz, J.D., Coull, B.A., Mittleman, M.A., Milberg, W.P., Lipsitz, L.A., Wellenius, G.A.	Ambient Air Pollution and Depressive Symptoms in Older Adults: Results From the MOBILIZE Boston Study	2014	Environmental Health Perspectives	PM2.5, BC, UFP, sulfates, O3, CO, NO, NO2	Depressive symptoms (>= 16 on Center for Epidemiological Studies Depression Scale)	Boston, MA	Participants in MOBILIZE Boston Study >=65	Evaluates the association of both long-term exposure to traffic pollution and short-term exposure to ambient air pollution with the presence of depressive symptoms	No	Used generalized estimating equations with a logit link function and an exchangeable correlation matrix to study association between long-term exposure to traffic pollution and depressive symptoms. Used similar approach to evaluate association between mean ambient air pollution levels and presence of depressive symptoms.	In traffic estimates, adjusted for age, sex, race/ethnicity, visit, season, day of week, household income, education, and neighborhood SES. Also tried adjusting for BMI, physical activity, alcohol consumption, smoking, diabetes mellitus, hypertension, hyperlipidermia, and use of antidepressant medication. In ambient air pollution models, adjusted for age, sex, race/ethnicity, bisit, ambient and dew point temperatures, barometric pressure, day of week, season, and long-term temporal trends. Considered effect modificaiton by season. Acknowledge possibility of selection bias. Multi-pollutant models should control for confounding by other pollutants.	Assesses mean ambient air pollution levels in preceding 2 weeks	Yes	**Background**: Exposure to ambient air pollution, particularly from traffic, has been associated with adverse cognitive outcomes, but the association with depressive symptoms remains unclear. **Objectives:** We investigated the association between exposure to ambient air and traffic pollution and the presence of depressive symptoms among 732 Boston-area adults ≥ 65 years of age (78.1 ± 5.5 years, mean ± SD). **Methods:** We assessed depressive symptoms during home interviews using the Revised Center for Epidemiological Studies Depression Scale (CESD-R). We estimated residential distance to the nearest major roadway as a marker of long-term exposure to traffic pollution and assessed short-term exposure to ambient fine particulate matter (PM2.5), sulfates, black carbon (BC), ultrafine particles, and gaseous pollutants, averaged over the 2 weeks preceding each assessment. We used generalized estimating equations to estimate the odds ratio (OR) of a CESD-R score ≥ 16 associated with exposure, adjusting for potential confounders. In sensitivity analyses, we considered CESD-R score as a continuous outcome and mean annual residential BC as an alternate marker of long-term exposure to traffic pollution. **Results:** We found no evidence of a positive association between depressive symptoms and long-term exposure to traffic pollution or short-term changes in pollutant levels. For example, we found an OR of CESD-R score ≥ 16 of 0.67 (95% CI: 0.46, 0.98) per interquartile range (3.4 µg/m3) increase in PM2.5 over the 2 weeks preceding assessment. **Conclusions:** We found no evidence suggesting that ambient air pollution is associated with depressive symptoms among older adults living in a metropolitan area in attainment of current U.S. regulatory standards.

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Winters, N., goldberg, M.S., Hystad, P., Villeneuve, P.J., Johnson, K.C.	Exposure to Ambient Air Pollution in Canada and the Risk of Adult Leukemia	2015	Science of the Total Environment	NO2, PM2.5	Incident leukemia, subtypes are acute myeloid leukemia, chronic myeloid leukemia, and chronic lymphocytic leukemia	Canada (except New Brunswick and Quebec)	Full population	Assesses the association between leukemia and NO2 and PM2.5	No	Uses data from a population-based case-control study conducted in Canada in 1994-1997, where cases are people with incident leukemia. Conducted analysis on all types of leukemia combined and subtypes where numbers are sufficient. Performed unconditional logistic regression to estimate odds ratios and confidence intervals. Did not assume linear response, but rather used natural cubic spline smoothers with varying degrees of freedom	Adusted analysis with five-year age groups, gender, and province. Controlled for exposure to benzene and ionizing radiation, active cigarette smoking, BMI. Also considered total household income, education. Did sensitivity analysis for just using subjects with granular residential information, compared association for subjects who lived in rural vs. urban areas. Caution that there may be selection bias and misclassification bias.	Used long-term exposure, average of all annual means at all residences where subject lived between 1975 and 1994	Yes	There is a paucity of studies investigating adult leukemia and air pollution. To address this gap, we analyzed data from a Canadian population-based case-control study conducted in 1994-1997. Cases were 1064 adults with incident leukemia and controls were 5039 healthy adults. We used data from satellites and fixed-site monitoring stations to estimate residential concentrations of NO2 and fine particulate matter (PM2.5) for the period prior to diagnosis, starting in 1975 and ending in 1994. We modeled the average annual exposure of each subject. Odds ratios (OR) and their 95% confidence intervals (CI) were estimated using logistic regression, adjusted for age, gender, province, smoking, education, body mass index, income, and self-reported exposures to ionizing radiation and benzene. We found an 'n-shaped' response function between exposure to NO2 and all forms of leukemia: from the tenth percentile to the median (4.51 to 14.66ppb), the OR was 1.20; 95% CI: 0.97-1.48 and from the 75th percentile to the 90th (22.75 to 29.7ppb), the OR was 0.79; 95% CI 0.68-0.93. For PM2.5 we found a response function consistent with a linear model, with an OR per 10µg/m(3) of 0.97 (95% CI 0.75-1.26). For chronic lymphocytic leukemia we found response functions that were consistent with a simple linear model, with an OR per 5ppb of NO2 of 0.93 (95% CI 0.86-1.00) and an OR per 10µg/m(3) of PM2.5 of 0.62 (95% CI 0.42-0.93). In summary, for chronic lymphocytic leukemia we found no evidence of an association with air pollution and with all forms of leukemia we found weak evidence of an association only at low concentrations of NO2. It is possible that these inconsistent results may have arisen because of unaccounted urban/rural differences or possibly from a selection effect, especially among controls.