Summary of Results Showing NO Relationship Between PM2.5 and All Cause Mortality
in California Teachers Study and Health Professionals Study based on 2011 Papers
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August 6, 2011

http://ehp03.niehs.nih.gov/article/info:doi/10.1289/ehp.0901181 [free to access]

Air Pollution and Mortality: Results from the California Teachers Study
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Environmental Health Perspectives 118(3) Mar 2010
Erratum Top (June 2011)

In an article published in *Environmental Health Perspectives* (Ostro et al. 2010), we analyzed the relationships of long-term exposure to fine particulate matter (2.5 µm in aerodynamic diameter; $PM_{2.5}$) and its components with mortality in a cohort of > 100,000 active and retired female professionals participating in the California Teachers Study (CTS) cohort. We used a Cox proportional hazards model in which pollution exposure was measured as a continuous variable over the study period. Monthly average pollutant concentrations were obtained for each participant from measurements at the nearest $PM_{2.5}$ monitor within either 8 or 30 km of her geocoded residential address. Each participant was assigned a single exposure value over the follow-up period, defined as the average pollutant concentration from the beginning of the observation period (1 June 2002) to the woman's date of death, loss to follow-up, or study termination (31 July 2007). Thus, exposure assignment was dependent on the duration of follow-up for each participant.

In our article (Ostro et al. 2010), we reported associations of mortality from all causes, cardiopulmonary disease, and ischemic heart disease (IHD) with $PM_{2.5}$ mass and several of its components. However, the estimated hazard ratios (HRs) were generally higher than those reported from previous cohort studies (Dockery et al. 1993; Eftim et al. 2008; Krewski et al. 2009; Laden et al. 2006; Pope et al. 1995). Part of this difference was likely due to the nature of the exposure assignment. Most previous cohort studies have assigned the same exposure period to all study subjects, regardless of when deaths occurred. Thus, estimated exposures for some study participants in several studies occurred after their deaths. In addition, exposures have usually been assigned to participants based on their residential address at enrollment only, without taking into account exposure changes that may have occurred throughout the study period or when participants relocated. Finally, many previous studies measured exposure for only a subset of the years during which the cohort was followed. In an effort to reduce these aspects of exposure misclassification, we estimated exposures beginning prior to the cohort follow-up period, continuing to the end of the study or until the participant died or relocated out of state, incorporating updated exposure assignments when the subjects moved.

Importantly, measured concentrations of several pollutants in California declined substantially from 2002 through 2007; annual average $PM_{2.5}$, organic carbon (OC), and nitrates decreased by around 30% each. These marked decreases in ambient $PM_{2.5}$ concentrations resulted in lower

average exposure estimates for cohort members who survived to the end of our study. Thus, the exposure assigned to a participant who died at time *t* would tend to be greater for events occurring early in the observation period, compared with the long-term average exposures of the participants who comprised the remainder of the risk set (i.e., those who were still part of the cohort study at time *t* and who subsequently experienced lower ambient pollution levels).

We have reanalyzed the CTS data using time-dependent pollution metrics in which the exposure estimates for everyone remaining alive in the risk set were recalculated at the time of each death–in order to compare their average exposures up to that time with that of the individual who had died. In this way, decedents and survivors comprising the risk set had similar periods of pollution exposure, without subsequent pollution trends influencing the surviving women's exposure estimates.

As in our previous study (Ostro et al. 2010), we restricted the sample in this reanalysis to women living within 30 km of one of eight fixed-site monitors in the U.S. Environmental Protection Agency's Speciation Trend Network (STN), resulting in a study population of almost 44,000 women. Residential addresses from study enrollment forward were geocoded and linked with monthly pollutant averages at the nearest STN monitor to generate estimates of long-term exposure. We also used the same set of individual and ecological covariates in a Cox proportional hazards model as was used in the original study. Pollutants entered separately into the model included $PM_{2.5}$ mass, elemental carbon (EC), OC, sulfate, nitrate, iron, potassium, silicon, and zinc. We used data on primary cause of death from August 2002 through July 2007 to examine the relationships between pollutants and mortality from all causes and cardiopulmonary, pulmonary, and IHDs.

The results are summarized in Erratum Table 1, scaled to the interquartile range (IQR) for each pollutant. HRs were significantly attenuated from our previous results. **No associations were observed between all-cause mortality and $PM_{2.5}$ or its components.** For cardiopulmonary mortality, we observed significant associations for $PM_{2.5}$ mass, nitrate, sulfate, and silicon, with more modest associations for zinc. $PM_{2.5}$ mass and all of its components were associated with mortality from IHD, whereas none of the pollutants was associated with pulmonary mortality. This Erratum Table 1 should replace Table 5 in our previous article (Ostro et al. 2010).

Compared with our previous results (Ostro et al. 2010), these updated $PM_{2.5}$ HRs are more consistent with several other published estimates of mortality risks, which are scaled to an increment of 10 g/m^3 of long-term average $PM_{2.5}$ and summarized in Erratum Table 2. For example, relative to our revised HR of 1.19 for cardiopulmonary disease, analogous HRs from previous studies include 1.09 (95% CI, 1.03–1.16) from the American Cancer Society–Cancer Prevention II (ACS) cohort (cardiopulmonary disease; Pope et al. 2004), 1.28 (95% CI, 1.13–1.44) from the Harvard Six Cities study (cardiovascular disease; Laden et al. 2006), and 1.10 (95% CI, 0.94–1.28) from the Los Angeles subcohort of the ACS study (cardiopulmonary disease; Jerrett et al. 2005). Much higher HRs were observed in the observational study of the Women's Health Initiative cohort for cardiovascular and IHD mortality (Miller et al. 2007).

These revised results still support the existence of elevated risks of $PM_{2.5}$-associated cardiopulmonary disease and IHD, and illustrate the importance of considering the impact of

long-term pollution trends in modeling estimates of exposure.

The authors declare they have no actual or potential competing financial interests.

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Erratum Table 1. Association between mortality outcomes and $PM_{2.5}$ and its components using a 30-km buffer ($n = 43,220$).

Pollutant	IQR (µg/m³)	All-cause (ICD-10 codes, all except S–Z) ($n = 2,519$)		Cardiopulmonary (ICD-10 codes, I00–I99, J00–J98) ($n = 1,357$)		Ischemic heart disease (ICD-10 codes, I20–I25) ($n = 460$)		Pulmonary (ICD-10, codes J00–J98) ($n = 355$)	
		HR (95% CI)	p-Value	HR (95% CI)	p-Value	HR (95% CI)	p-Value	HR (95% CI)	p-Value
$PM_{2.5}$	6.1	1.03 (0.98–1.10)	0.26	1.11 (1.03–1.21)	0.01	1.31 (1.14–1.50)	<0.01	1.02 (0.87–1.19)	0.84
EC	0.65	1.02 (0.93–1.12)	0.65	1.07 (0.94–1.22)	0.28	1.46 (1.17–1.83)	<0.01	0.88 (0.68–1.15)	0.35
OC	0.84	1.00 (0.95–1.04)	0.91	1.04 (0.98–1.11)	0.19	1.13 (1.01–1.25)	0.03	0.95 (0.84–1.06)	0.35
Sulfate	2.2	1.06 (0.97–1.16)	0.18	1.14 (1.01–1.29)	0.03	1.48 (1.20–1.82)	<0.01	1.04 (0.82–1.31)	0.77
Nitrate	3.2	1.03 (0.98–1.09)	0.27	1.11 (1.03–1.19)	0.01	1.27 (1.12–1.43)	<0.01	1.04 (0.90–1.20)	0.58
Iron	0.13	1.01 (0.93–1.11)	0.77	1.05 (0.93–1.19)	0.40	1.39 (1.13–1.72)	<0.01	0.88 (0.69–1.13)	0.32
Potassium	0.07	1.01 (0.94–1.08)	0.85	1.06 (0.97–1.17)	0.22	1.27 (1.07–1.49)	<0.01	0.90 (0.74–1.09)	0.27
Silicon	0.03	1.02 (0.99–1.06)	0.22	1.05 (1.00–1.10)	0.04	1.11 (1.02–1.20)	0.01	0.98 (0.89–1.08)	0.71
Zinc	0.01	1.03 (0.96–1.11)	0.45	1.09 (0.98–1.20)	0.10	1.33 (1.12–1.58)	<0.01	0.97 (0.79–1.18)	0.74

ICD-10, *International Classification of Diseases*, 10th Revision (World Health Organization 1993). Values shown are HRs [95% confidence intervals (CIs)] and p-values scaled to the IQR of each pollutant. All models are adjusted for smoking status, total pack-years, body mass index, marital status, alcohol consumption, second-hand smoke exposure at home, dietary fat, dietary fiber, dietary calories, physical activity, menopausal status, hormone replacement therapy use, family history of myocardial infarction or stroke, blood pressure medication and aspirin use, and neighborhood contextual variables (income, income inequality, education, population size, racial composition, unemployment).

Erratum Table 1. Association between mortality outcomes and $PM_{2.5}$ and its components using a 30-km buffer ($n = 43,220$).

Erratum Table 2. Comparative HRs (95% CIs) associated with a 10-µg/m³ change in long-term exposure to $PM_{2.5}$ in several cohort studies conducted in the United States.

Authors	Exposure assessment	All causes	Cardiovascular	Cardiopulmonary	IHD
Ostro et al. (this report)	From 1 year prior to follow-up until event (either death or end of study), time-dependent	1.06 (0.96–1.16)[a]		1.19 (1.05–1.36)[a]	1.55 (1.24–1.93)[a]
Ostro et al. (2010)	From 2 months prior to study through event month	1.84 (1.66–2.05)[a]		2.05 (1.80–2.36)[a]	2.89 (2.27–3.67)[a]
Pope et al. (2002, 2004)	Four years prior to or at start of follow-up and 2 years after end of follow-up	1.06 (1.02–1.11)	1.12 (1.08–1.15)	1.09 (1.03–1.16)	
Laden et al. (2006)	Multiyear average concurrent with follow-up	1.16 (1.07–1.26)	1.28 (1.13–1.44)		
Miller et al. (2007)	One year in middle of follow-up		1.76 (1.25–2.47)[a]		2.21 (1.17–4.16)[a]
Jerrett et al. (2005)	One year at end of follow-up	1.15 (1.03–1.29)		1.10 (0.94–1.28)	1.32 (1.05–1.66)
Eftim et al. (2008)	Three-year average concurrent with follow-up	1.21 (1.15–1.27)			
Chen et al. (2005)	Four-year moving average prior to event				1.42 (1.06–1.90)[a]
Puett et al (2009)	One year prior to event	1.26 (1.02–1.54)[a]			2.02 (1.07–3.78)[a]

HRs are scaled to 10-µg/m³ change in $PM_{2.5}$, in contrast to Table 1, in which HRs are scaled to the pollutant interquartile range.
[a]Women only.

Erratum Table 2. Comparative HRs (95% CIs) associated with a 10- µg/m³ change in long-term exposure to $PM_{2.5}$ in several cohort studies conducted in the United States.

Long-term Exposure to Air Pollution and Cardiorespiratory Disease in the California Teachers Study Cohort

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Results
Table 3 summarizes the estimated HRs for incident MI and stroke, as well as for mortality from all causes, and from cardiovascular, cerebrovascular, and nonmalignant respiratory diseases, ischemic heart disease (IHD), and lung cancer, per 10 $\mu g/m^3$ increment of the long-term average concentrations of PM2.5 and PM10. Although most HR point estimates for PM2.5 were greater than unity, only that for IHD mortality was significantly elevated (HR = 1.20, 95% C.I. 1.02-1.41).

Discussion
Several other long-term air pollution studies have found associations of PM2.5 with increased risk of all-cause mortality, and larger risks with either cardiopulmonary or cardiovascular disease. **We found no associations with all-cause mortality in any analysis** except for NOx and SO2, and these results were based on few events. Although our results are different from those of several other U.S. cohorts, they are generally consistent with the recent Dutch study by Beelen et al., who reported no significant increases in all cause or cardiovascular mortality associated with measured PM2.5 (12).

Several prior California-specific studies of air pollutant exposure and mortality have produced mixed results. Enstrom found essentially no relationship between exposure to fine PM and all-cause mortality among elderly California participants in the ACS CPS I from 1973-2002, although the relative risk (RR) for the 20,210 women was slightly elevated (RR = 1.027, 95% CI 1.005 - 1.050) (14). . . . In an analysis of the ACS CPS II data for 22,905 Los Angeles residents, Jerrett et al. (6) reported that a 10 $\mu g/m^3$ increase in PM2.5 was associated with HRs of 1.11 (95% CI = 0.99 – 1.25) for all-cause and 1.25 (95% CI = 0.99 - 1.59) for IHD mortality, using a model with 44 individual-level and parsimonious contextual covariates. In a more recent

analysis of these data using land use regression, these estimates were only slightly greater (13).

Although we found no relationship of PM2.5 with all-cause mortality, the association between a 10 **μ**g/m3 increase in PM2.5 and increased risk of fatal IHD (HR = 1.20, 95% CI 1.02 - 1.41) was of similar magnitude to that reported by Jerrett et al. (6).

TABLE 3. HAZARD RATIOS FOR MORTALITY AND FOR INCIDENT MI AND STROKE, PER 10 μg/m3 INCREMENT OF PM2.5 (2000-2005) AND PM10 (1996-2005) FOR THE CALIFORNIA TEACHERS STUDY COHORT

	PM2.5		PM10	
Outcome	# events N	HR (95% CI)	# events N	HR* (95% CI)
All-cause mortality	**4,147 73,489**	**1.01 (0.95, 1.09)**	4,694 61,181	1.00 (0.97, 1.04)
Cardiovascular mortality	1,630 73,489	1.07 (0.95, 1.19)	1,863 61,181	1.03 (0.98, 1.08)

* Models adjusted for age, race, smoking status, total pack-years, BMI, marital status, alcohol consumption, second-hand smoke exposure at home, dietary fat, dietary fiber, dietary calories, physical activity, menopausal status, hormone therapy use, family history of MI or stroke, blood pressure medication and aspirin use; and contextual variables (income, income inequality, education, population size, racial composition, and unemployment). Exposure period for PM2.5: March 1999-December 2005; cohort follow-up period: March 2000-December 2005. Exposure period for PM10: June 1996-December 2005; cohort follow-up period: June 1997- December 2005. MI = myocardial infarction; NM = nonmalignant; IHD = ischemic heart disease; HR = hazard ratio; CI = confidence interval

Enstrom Note: This paper clearly finds NO relationship between PM2.5 and all-cause mortality, as shown in Table 3: **HR = 1.01 (0.95 - 1.09)**. These results contradict the LARGE HR ~ 1.8 for all cause mortality in CTS, as presented in Jerrett slide 26 in Sacramento, CA on February 26, 2010 (http://www.scientificintegrityinstitute.org/carbjerrett022610.pdf).

Particulate Matter Exposures, Mortality and Cardiovascular Disease in the Health Professionals Follow-up Study

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Abstract
Background: The association of all cause mortality and cardiovascular outcomes with air pollution exposures has been well established in the literature. The number of studies examining chronic exposures in cohorts is growing, with more recent studies conducted among women finding risk estimates of greater magnitude. Questions remain regarding gender differences in the relationship of chronic particulate matter exposures with mortality and cardiovascular outcomes.

Objectives: The current study explored these associations in the male Health Professionals Follow-Up Study prospective cohort.

Methods: The same spatio-temporal exposure estimation models, and similar outcomes and biennially updated covariates were used as those previously applied in the female Nurses' Health Study cohort. Results: Among 17,545 men residing in the Northeastern and Midwestern US, there were 2,813 deaths, including 746 cases of fatal coronary heart disease (CHD). **An interquartile range change (4 μg/m3) in average PM2.5 exposure in the 12 previous months was not associated with all cause mortality (HR: 0.94; 95%CI: 0.87,1.00) or fatal CHD (HR: 0.99; 95%CI: 0.87,1.13) in fully adjusted models.** Findings were similar for separate models of PM10 and PM10-2.5 exposures and for co-pollutant models.

Conclusions: **Among this cohort of men with high socioeconomic status, living in the Midwestern and Northeastern US, the results did not support an association of chronic particulate matter exposures with all cause mortality and cardiovascular outcomes in models with time-varying covariates.** Whether these findings suggest gender differences in susceptibility or the protective impact of healthier lifestyles and higher socioeconomic status requires additional investigation.

Table 2: Hazard ratios and 95% CIs for associations of an interquartile range change in average predicted particulate matter exposure adjusting for covariates
PM2.5 (interquartile range=4 μg/m3)

Outcome	Cases	Person Years	Basic Model[a]	Full Model[b]
All Cause Mortality	2,813	220,552	**0.96 (0.90,1.03)**	**0.94 (0.87,1.00)**
Fatal CHD	746	220,562	1.01 (0.89,1.15)	0.99 (0.87,1.13)
Total CVD	1,661	212,649	1.02 (0.94,1.11)	1.01 (0.93,1.10)