May 12, 2017

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To: Environmental Protection Agency
Office of Policy Regulatory Reform
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https://www.epa.gov/laws-regulations/regulatory-reform

Re: Docket ID: EPA-HQ-OA-2017-0190
Agency: Environmental Protection Agency (EPA)
Summary: Executive Order 13777, issued 2/24/17, directs agencies to establish a Regulatory Reform Task Force to oversee the evaluation of existing regulations to make recommendations about potential repeal, replacement, or modification.
https://www.regulations.gov/docket?D=EPA-HQ-OA-2017-0190

Item 1.

April 24, 2017 EPA Public Teleconference Statement by James E. Enstrom, Ph.D., M.P.H., asking EPA to reassess and modify the National Ambient Air Quality Standard (NAAQS) for fine particulate matter (PM2.5).
https://www.epa.gov/clean-air-act-overview/oar-regulatory-reform

"My name is Dr. James E. Enstrom and I have doctoral-level training in both physics and epidemiology and for the past 44 years I have conducted high quality peer-reviewed epidemiologic research at UCLA. I am asking EPA to reassess and modify the National Ambient Air Quality Standard (NAAQS) for fine particulate matter (PM2.5).

On March 28 I published a major peer-reviewed article showing that PM2.5 is not related to total mortality or premature deaths in the United States. This null relationship, which is based on my analysis of the large 1982 American Cancer Society Cancer Prevention Study cohort, contradicts the positive relationship in the same cohort that was published in 1995 by Pope and that was the primary justification for the establishment of the PM2.5 NAAQS by EPA in 1997. The difference in findings occurred because the 1995 Pope analysis used inferior PM2.5 measurements and used only a selected portion of the available ACS data. My findings are also supported by the null findings in a 2016 article that analyzed the large national NIH AARP cohort.

My independent analysis of the otherwise still secret ACS data demonstrates the importance of basing EPA regulations on transparent and reproducible science, as required by the HONEST Act. H.R. 1340 has been approved by the House of Representatives and is awaiting action in the Senate. Since March 10 I have requested that Pope, Krewski, and the Health Effects Institute confirm my null findings and they have provided no evidence that my findings are incorrect.

Thus, EPA must immediately reassess the validity of the PM2.5 NAAQS and all regulations, such as, the Clean Power Plan, that are justified by alleged PM2.5-related premature deaths. The initial focus must be on my new findings, on the apparently incorrect findings of Pope, Krewski, and HEI, and on the extensive evidence that healthy levels of PM2.5 have already been achieved in America. EPA must not approve any further California Waivers, State Implementation Plans, or Air Quality Management Plans until this PM2.5 NAAQS reassessment has been done.

Thank you for listening to my testimony and reading my submitted comments."

Item 2.

My attached comments contain overwhelming and uncontested evidence that there is NO relationship between PM2.5 and total mortality ("premature deaths") in the American Cancer Society (ACS) Cancer Prevention Study II (CPS II) cohort. There is NO relationship in California or in the United States as a whole. Based this CPS II evidence and additional evidence that "Particulate Matter Does Not *Cause* Premature Deaths," I request EPA to completely reassess and modify the National Ambient Air Quality Standard (NAAQS) for fine particulate matter (PM2.5).

My 90-page attachment contains the following:

May 12, 2017 Enstrom Comments to EPA, Including Description of Items 1 and 2 (pages 1-3)

March 28, 2017 *Dose-Response* article by James E. Enstrom "Fine Particulate Matter and Total Mortality in Cancer Prevention Study Cohort Reanalysis" (pages 4-15)
http://journals.sagepub.com/doi/full/10.1177/1559325817693345

March 23, 2017 Heartland Twelfth International Conference on Climate Change Lecture "PM2.5 Does Not *Cause* Premature Deaths" (pages 16-35)
http://climateconferences.heartland.org/james-enstrom-iccc12/

July 19, 2016 Los Angeles County Business Federation Enstrom Summary Biography (page 36)
http://www.scientificintegrityinstitute.org/SCBCJEEB071916.pdf

April 1, 2016 *Environmental Health Perspectives* article by George D. Thurston, et al. "Ambient Particulate Matter Air Pollution Exposure and Mortality in the NIH-AARP Diet and Health Cohort" (pages 37-43)
http://ehp.niehs.nih.gov/1509676/

August 17, 2015 *Science* Perspective Manuscript "Particulate Matter Does Not *Cause* Premature Deaths" Submission and Immediate Rejection (pages 44-53)
https://www.nas.org/articles/nas_letter and https://www.nas.org/images/documents/PM2.5.pdf

December 21, 2016 US Office of Research Integrity Hohmann Email to Enstrom Regarding Alleged Research Misconduct by Jerrett et al. in 2013 *AJRCCM* Article (page 54)
http://www.scientificintegrityinstitute.org/Hohmann122116.pdf

November 11, 2016 US Office of Research Integrity Enstrom Submission of Alleged Research Misconduct by Jerrett et al. in 2013 *AJRCCM* Article (pages 55-77)
http://www.scientificintegrityinstitute.org/ORIJerrett111116.pdf

December 1, 2014 Enstrom Comments to EPA Regarding PM2.5 Justification for Clean Power Plan and PM2.5 Scientific Misconduct (pages 78-90)
http://www.scientificintegrityinstitute.org/JEECPP120114.pdf

Dose-Response:
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Fine Particulate Matter and Total Mortality in Cancer Prevention Study Cohort Reanalysis

James E. Enstrom[1]

Abstract

Background: In 1997 the US Environmental Protection Agency (EPA) established the National Ambient Air Quality Standard (NAAQS) for fine particulate matter ($PM_{2.5}$), largely because of its positive relationship to total mortality in the 1982 American Cancer Society Cancer Prevention Study (CPS II) cohort. Subsequently, EPA has used this relationship as the primary justification for many costly regulations, most recently the Clean Power Plan. An independent analysis of the CPS II data was conducted in order to test the validity of this relationship.

Methods: The original CPS II questionnaire data, including 1982 to 1988 mortality follow-up, were analyzed using Cox proportional hazards regression. Results were obtained for 292 277 participants in 85 counties with 1979-1983 EPA Inhalable Particulate Network $PM_{2.5}$ measurements, as well as for 212 370 participants in the 50 counties used in the original 1995 analysis.

Results: The 1982 to 1988 relative risk (RR) of death from all causes and 95% confidence interval adjusted for age, sex, race, education, and smoking status was 1.023 (0.997-1.049) for a 10 $\mu g/m^3$ increase in $PM_{2.5}$ in 85 counties and 1.025 (0.990-1.061) in the 50 original counties. The fully adjusted RR was null in the western and eastern portions of the United States, including in areas with somewhat higher $PM_{2.5}$ levels, particularly 5 Ohio Valley states and California.

Conclusion: No significant relationship between $PM_{2.5}$ and total mortality in the CPS II cohort was found when the best available $PM_{2.5}$ data were used. The original 1995 analysis found a positive relationship by selective use of CPS II and $PM_{2.5}$ data. This independent analysis of underlying data raises serious doubts about the CPS II epidemiologic evidence supporting the $PM_{2.5}$ NAAQS. These findings provide strong justification for further independent analysis of the CPS II data.

Keywords
epidemiology, $PM_{2.5}$, deaths, CPS II, reanalysis

Introduction

In 1997 the US Environmental Protection Agency (EPA) established the National Ambient Air Quality Standard (NAAQS) for fine particulate matter ($PM_{2.5}$), largely because of its positive relationship to total mortality in the 1982 American Cancer Society (ACS) Cancer Prevention Study (CPS II) cohort, as published in 1995 by Pope et al.[1] The EPA uses this positive relationship to claim that $PM_{2.5}$ *causes* premature deaths. However, the validity of this finding was immediately challenged with detailed and well-reasoned criticism.[2-4] The relationship still remains contested and much of the original criticism has never been properly addressed, particularly the need for truly independent analysis of the CPS II data.

The EPA claim that $PM_{2.5}$ *causes* premature deaths is implausible because no etiologic mechanism has ever been established and because it involves the lifetime inhalation of only about 5 g of particles that are less than 2.5 μm in diameter.[5] The $PM_{2.5}$ mortality relationship has been further challenged because the small increased risk could be due to well-known epidemiological biases, such as, the ecological fallacy, inaccurate exposure measurements, and confounding variables like copollutants. In addition, there is extensive evidence of spatial and temporal variation in $PM_{2.5}$ mortality risk (MR) that does not support 1 national standard for $PM_{2.5}$.

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In spite of these serious problems, EPA and the major $PM_{2.5}$ investigators continue to assert that their positive findings are sufficient proof that $PM_{2.5}$ *causes* premature deaths. Their premature death claim has been used to justify many costly EPA regulations, most recently, the Clean Power Plan.[6] Indeed, 85% of the total estimated benefits of all EPA regulations have been attributed to reductions in $PM_{2.5}$-related premature deaths. With the assumed benefits of $PM_{2.5}$ reductions playing such a major role in EPA regulatory policy, it is essential that the relationship of $PM_{2.5}$ to mortality be independently verified with transparent data and reproducible findings.

In 1998, the Health Effects Institute (HEI) in Boston was commissioned to conduct a detailed reanalysis of the original Pope 1995 findings. The July 2000 HEI Reanalysis Report (HEI 2000) included "PART I: REPLICATION AND VALIDATION" and "PART II: SENSITIVITY ANALYSES."[7] The HEI Reanalysis Team lead by Daniel Krewski successfully replicated and validated the 1995 CPS II findings, but they did not analyze the CPS II data in ways that would determine whether the original results remained robust using different sources of air pollution data. For instance, none of their models used the best available $PM_{2.5}$ measurements as of 1995.

Particularly troubling is the fact that EPA and the major $PM_{2.5}$ investigators have ignored multiple null findings on the relationship between $PM_{2.5}$ and mortality in California. These null findings include my 2005 paper,[8] 2006 clarification,[9] 2012 American Statistical Society Joint Statistical Meeting Proceedings paper,[10] and 2015 International Conference on Climate Change presentation about the Clean Power Plan and $PM_{2.5}$-related cobenefits.[6] There is now overwhelming evidence of a null $PM_{2.5}$ mortality relationship in California dating back to 2000. The problems with the $PM_{2.5}$ mortality relationship have generated substantial scientific and political concern.

During 2011 to 2013, the US House Science, Space, and Technology Committee (HSSTC) repeatedly requested that EPA provide access to the underlying CPS II data, particularly since substantial Federal funding has been used for CPS II $PM_{2.5}$ mortality research and publications. On July 22, 2013, the HSSTC made a particularly detailed request to EPA that included 49 pages of letters dating back to September 22, 2011.[11] When EPA failed to provide the requested data, the HSSTC issued an August 1, 2013 subpoena to EPA for the CPS II data.[12] The ACS refused to comply with the HSSTC subpoena, as explained in an August 19, 2013 letter to EPA by Chief Medical Officer Otis W. Brawley.[13] Then, following the subpoena, ACS has refused to work with me and 3 other highly qualified investigators regarding collaborative analysis of the CPS II data.[14] Finally, HEI has refused to conduct my proposed CPS II analyses.[15] However, my recent acquisition of an original version of the CPS II data has made possible this first truly independent analysis.

Methods

Computer files containing the original 1982 ACS CPS II deidentified questionnaire data and 6-year follow-up data on deaths from September 1, 1982 through August 31, 1988, along with detailed documentation, were obtained from a source with appropriate access to these data, as explained in the "Acknowledgments." This article presents my initial analysis of the CPS II cohort and it is subject to the limitations of data and documentation that is not as complete and current as the data and documentation possessed by ACS.

The research described below is exempt from human participants or ethics approval because it involved only statistical analysis of existing deidentified data. Human participants' approval was obtained by ACS in 1982 when each individual enrolled in CPS II. Because of the epidemiologic importance of this analysis, an effort will be made to post on my Scientific Integrity Institute website a version of the CPS II data that fully preserves the confidentiality of all of participants and that contains enough information to verify my findings.

Of the 1.2 million total CPS II participants, analysis has been done on 297 592 participants residing in 85 counties in the continental United States with 1979 to 1983 EPA Inhalable Particulate Network (IPN) $PM_{2.5}$ measurements.[16,17] Among these participants, there were 18 612 total deaths from September 1, 1982 through August 31, 1988; 17 329 of these deaths (93.1%) had a known date of death. Of the 297 592 participants, 292 277 had age at entry of 30 to 99 years and sex of male [1] or female [2]. Of the 292 277 participants, 269 766 had race of white [1,2,5] or black [3,4]; education level of no or some high school [1,2], high school graduate [3], some college [4,5], college graduate [6], or graduate school [7]; and smoking status of never [1], former [5-8 for males and 3 for females], or current [2-4 for males and 2 for females]. Those participants reported to be dead [D, G, K] but without an exact date of death have been assumed to be alive in this analysis. The unconfirmed deaths were randomly distributed and did not impact relative comparisons of death in a systematic way. The computer codes for the above variables are shown in brackets.

CPS II participants were entered into the master data file geographically. Since this deidentified data file does not contain home addresses, the Division number and Unit number assigned by ACS to each CPS II participant have been used to define their county of residence. For instance, ACS Division 39 represents the state of Ohio and its Unit 041 represents Jefferson County, which includes the city of Steubenville, where the IPN $PM_{2.5}$ measurements were made. In other words, most of the 575 participants in Unit 041 lived in Jefferson County as of September 1, 1982. The IPN $PM_{2.5}$ value of 29.6739 $\mu g/m^3$, based on measurements made in Steubenville, was assigned to all CPS II participants in Unit 041. This $PM_{2.5}$ value is a weighted average of 53 measurements (mean of 33.9260 $\mu g/m^3$) and 31 measurements (mean of 29.4884 $\mu g/m^3$) made during 1979 to 1982[16] and 53 measurements (mean of 27.2473 $\mu g/m^3$) and 54 measurements (mean of 28.0676 $\mu g/m^3$) made during 1983.[17] The IPN $PM_{2.5}$ data were collected only during 1979 to 1983, although some other IPN air pollution data were collected through 1984. The values for each county that includes a city with CPS II participants and IPN $PM_{2.5}$ measurements are shown in Appendix Table A1.

Table 1. Summary Characteristics of CPS II Participants in (1) Pope 1995 Table 1,[1] (2) HEI 2000 Table 24,[7] and (3) Current Analysis Based on CPS II Participants in 50 and 85 Counties.

Characteristics	Pope 1995 Table 1	HEI 2000 Table 24	Current CPS II Analysis		
			n = 50 HEI $PM_{2.5}$	n = 50 IPN $PM_{2.5}$	n = 85 IPN $PM_{2.5}$
Number of metro areas	50	50			
Number of counties	Not stated	Not stated	50	50	85
Age–sex-adjusted participants			212 370	212 370	292 277
Fully adjusted participants	295 223	298 817	195 215	195 215	269 766
Age–sex-adjusted deaths			12 518	12 518	17 231
Fully adjusted deaths	20 765	23 093	11 221	11 221	15 593
Values below are for participants in fully adjusted results					
Age at enrollment, mean years	56.6	56.6	56.66	56.66	56.64
Sex (% females)	55.9	56.4	56.72	56.72	56.61
Race (% white)	94.0	94.0	94.58	94.58	95.09
Less than high school education, %	11.3	11.3	11.71	11.71	11.71
Never smoked regularly, %			41.69	41.69	41.57
Former smoker, %			33.25	33.25	33.67
Former cigarette smoker, %	29.4	30.2	30.43	30.43	30.81
Current smoker, %			25.06	25.06	24.76
Current cigarette smoker, %	21.6	21.4	21.01	21.01	20.76
Fine particles, $\mu g/m^3$					
Average	18.2	18.2	17.99	21.37	21.16
SD	5.1	4.4	4.52	5.30	5.98
Range	9.0-33.5	9.0-33.4	9.0-33.4	10.77-29.67	10.63-42.01

Abbreviations: CPS, Cancer Prevention Study; HEI, Health Effects Institute; IPN, Inhalable Particulate Network; $PM_{2.5}$, fine particulate matter.

To make the best possible comparison with Pope 1995 and HEI 2000 results, the HEI $PM_{2.5}$ value of 23.1 $\mu g/m^3$ for Steubenville was assigned to all participants in Unit 041. This value is the median of $PM_{2.5}$ measurements made in Steubenville and is shown in HEI 2000 Appendix D "Alternative Air Pollution Data in the ACS Study."[7] Analyses were done for the 50 counties containing the original 50 cities with CPS II participants and HEI $PM_{2.5}$ values used in Pope 1995 and HEI 2000. Additional analyses were done for all 85 counties containing cities with both CPS II participants and IPN $PM_{2.5}$ data. Without explanation, Pope 1995 and HEI 2000 omitted from their analyses, 35 cities with CPS II participants and IPN $PM_{2.5}$ data. To be clear, these analyses are based on the CPS II participants assigned to each Unit (county) that included a city with IPN $PM_{2.5}$ data. The original Pope 1995 and HEI 2000 analyses were based on the CPS II participants assigned to each metropolitan area (MA) that included a city with HEI $PM_{2.5}$ data, as defined in HEI 2000 Appendix F "Definition of Metropolitan Areas in the ACS Study."[7] The MA, which was equivalent to the US Census Bureau Standard Metropolitan Statistical Area (SMSA), always included the county containing the city with the HEI $PM_{2.5}$ data and often included 1 or more additional counties.

The SAS 9.4 procedure PHREG was used to conduct Cox proportional hazards regression.[18] Relative risks (RRs) for death from all causes and 95% confidence intervals (CI) were calculated using age–sex adjustment and full adjustment (age, sex, race, education, and smoking status, as defined above). Each of the 5 adjustment variables had a strong relationship to total mortality. Race, education, and smoking status were the 3 adjustment variables that had the greatest impact on the age–sex-adjusted RR. The Pope 1995 and HEI 2000 analyses used 4 additional adjustment variables that had a lesser impact on the age–sex-adjusted RR.

In addition, county-level ecological analyses were done by comparing IPN $PM_{2.5}$ and HEI $PM_{2.5}$ values to 1980 age-adjusted white total death rates (DRs) determined by the Centers for Disease Control and Prevention (CDC) WONDER[19] and mortality risks (MRs) as shown in Figures 5 and 21 of HEI 2000.[7] Death rates are age adjusted to the 2000 US Standard Population and are expressed as annual deaths per 100 000 persons. The SAS 9.4 procedure REGRESSION was used to conduct linear regression of $PM_{2.5}$ values with DRs and MRs.

Appendix Table A1 lists the 50 original cities used in Pope 1995 and HEI 2000 and includes city, county, state, ACS Division and Unit numbers, Federal Information Processing Standards (FIPS) code, IPN average $PM_{2.5}$ level, HEI median $PM_{2.5}$ level, 1980 DR, and HEI MR. Appendix Table A1 also lists similar information for the 35 additional cities with CPS II participants and IPN $PM_{2.5}$ data. However, HEI $PM_{2.5}$ and HEI MR data are not available for these 35 cities.

Results

Table 1 shows basic demographic characteristics for the CPS II participants, as stated in Pope 1995,[1] HEI 2000,[7] and this current analysis. There is excellent agreement on age, sex, race, education, and smoking status. However, the IPN $PM_{2.5}$ averages are generally about 20% higher than the HEI $PM_{2.5}$ medians, although the differences range from +78% to −28%.

Table 2. Age–Sex-Adjusted and Fully Adjusted Relative Risk of Death From All Causes (RR and 95% CI) From September 1, 1982 Through August 31, 1988 Associated With Change of 10 μg/m^3 Increase in $PM_{2.5}$ for CPS II Participants Residing in 50 and 85 Counties in the Continental United States With 1979 to 1983 IPN $PM_{2.5}$ Measurements.[a]

$PM_{2.5}$ Years and Source	Number of Counties	Number of Participants	Number of Deaths	RR	95% CI Lower Upper	Average $PM_{2.5}$
Age–sex adjusted RR for the continental United States						
1979-1983 IPN	85	292 277	17 321	1.038	(1.014-1.063)	21.16
1979-1983 IPN	50	212 370	12 518	1.046	(1.013-1.081)	21.36
1979-1983 HEI	50	212 370	12 518	1.121	(1.078-1.166)	17.99
Fully adjusted RR for the continental United States						
1979-1983 IPN	85	269 766	15 593	1.023	(0.997-1.049)	21.15
1979-1983 IPN	50	195 215	11 221	1.025	(0.990-1.061)	21.36
1979-1983 HEI	50	195 215	11 221	1.082	(1.039-1.128)	17.99
Age–sex adjusted RR for Ohio Valley States (IN, KY, OH, PA, WV)						
1979-1983 IPN	17	56 979	3649	1.126	(1.011-1.255)	25.51
1979-1983 IPN	12	45 303	2942	1.079	(0.951-1.225)	25.76
1979-1983 HEI	12	45 303	2942	1.153	(1.027-1.296)	22.02
Fully adjusted RR for Ohio Valley states (IN, KY, OH, PA, WV)						
1979-1983 IPN	17	53 026	3293	1.096	(0.978-1.228)	25.51
1979-1983 IPN	12	42 174	2652	1.050	(0.918-1.201)	25.75
1979-1983 HEI	12	42 174	2652	1.111	(0.983-1.256)	22.02
Age–sex adjusted RR for states other than the Ohio Valley states						
1979-1983 IPN	68	235 298	13 672	0.999	(0.973-1.027)	20.11
1979-1983 IPN	38	167 067	9576	0.983	(0.946-1.021)	20.18
1979-1983 HEI	38	167 067	9576	1.045	(0.997-1.096)	16.90
Fully adjusted RR for states other than the Ohio Valley states						
1979-1983 IPN	68	216 740	12 300	0.994	(0.967-1.023)	20.09
1979-1983 IPN	38	153 041	8569	0.975	(0.936-1.015)	20.15
1979-1983 HEI	38	153 041	8569	1.025	(0.975-1.078)	16.89

Abbreviations: CI, confidence interval; CPS, Cancer Prevention Study; HEI, Health Effects Institute; IPN, Inhalable Particulate Network; $PM_{2.5}$, particulate matter.
[a]Analysis includes continental United States, 5 Ohio Valley states, and remainder of the states. Appendix Table A1 lists the 85 cities and counties with $PM_{2.5}$ measurements.

Table 2 shows that during 1982 to 1988, there was no significant relationship between IPN $PM_{2.5}$ and total mortality in the entire United States. The fully adjusted RR and 95% CI was 1.023 (0.997-1.049) for a 10 μg/m^3 increase in $PM_{2.5}$ in all 85 counties and 1.025 (0.990-1.061) in the 50 original counties. Indeed, the fully adjusted RR was not significant in any area of the United States, such as, the states west of the Mississippi River, the states east of the Mississippi River, the 5 Ohio Valley states (Indiana, Kentucky, Ohio, Pennsylvania, and West Virginia), and the states other than the Ohio Valley states. The age–sex-adjusted and fully adjusted RRs in the states other than the Ohio Valley states are all consistent with no relationship and most are very close to 1.00. The slightly positive age–sex-adjusted RRs for the entire United States and the Ohio Valley states became statistically consistent with no relationship after controlling for the 3 confounding variables of race, education, and smoking status.

However, the fully adjusted RR for the entire United States was 1.082 (1.039-1.128) when based on the HEI $PM_{2.5}$ values in 50 counties. This RR agrees quite well with the fully adjusted RR of 1.067 (1.037-1.099) for 1982 to 1989, which is shown in Table 34 of the June 2009 HEI Extended Follow-up Research Report (HEI 2009).[20] Thus, the positive nationwide RRs in the CPS II cohort depend upon the use of HEI $PM_{2.5}$ values. The nationwide RRs are consistent with no effect when based on IPN $PM_{2.5}$ values. The findings in Table 2 clearly demonstrate the large influence of $PM_{2.5}$ values and geography on the RRs.

Table 3 shows that the fully adjusted RR in California was 0.992 (0.954-1.032) when based on IPN $PM_{2.5}$ values in all 11 California counties. This null finding is consistent with the 15 other findings of a null relationship in California, all of which are shown in Appendix Table B1. However, when the RR is based on the 4 California counties used in Pope 1995 and HEI 2000, there is a significant inverse relationship. The fully adjusted RR is 0.879 (0.805-0.960) when based on the IPN $PM_{2.5}$ values and is 0.870 (0.788-0.960) when based on the HEI $PM_{2.5}$ values. This significant inverse relationship is in exact agreement with the finding of a special analysis of the CPS II cohort done for HEI by Krewski in 2010, which yielded a fully adjusted RR of 0.872 (0.805-0.944) during 1982 to 1989 in California when based on HEI $PM_{2.5}$ values.[21] In this instance, the California RRs are clearly dependent upon the number of counties used.

Table 4 shows that the ecological analysis based on linear regression is quite consistent with the proportional hazard regression results in Tables 2 and 3, in spite of the fact that the regression results are not fully adjusted. Using 1980 age-adjusted white total DRs versus HEI $PM_{2.5}$ values in 50 counties, linear regression yielded a regression coefficient of 6.96 (standard error [SE] = 1.85) that was statistically significant at the 95% confidence level. Pope 1995 reported a significant regression coefficient for 50 cities of 8.0 (SE = 1.4). However, this positive coefficient is

Table 3. Age–Sex-Adjusted and Fully Adjusted Relative Risk of Death From All Causes (RR and 95% CI) From September 1, 1982 Through August 31, 1988 Associated With 10 $\mu g/m^3$ Increase in $PM_{2.5}$ for California CPS II Participants Living in 4 and 11 Counties With 1979 to 1983 IPN $PM_{2.5}$ Measurements.[a]

$PM_{2.5}$ Years and Source	Number of Counties	Number of Participants	Number of Deaths	RR	95% CI of RR Lower Upper	Average $PM_{2.5}$
Age–sex adjusted RR for California during 1982 to 1988						
1979-1983 IPN	11	66 615	3856	1.005	(0.968-1.043)	24.08
1979-1983 IPN	4	40 527	2146	0.904	(0.831-0.983)	24.90
1979-1983 HEI	4	40 527	2146	0.894	(0.817-0.986)	18.83
Fully adjusted (age, sex, race, education, and smoking status) RR for California during 1982 to 1988						
1979-1983 IPN	11	60 521	3512	0.992	(0.954-1.032)	24.11
1979-1983 IPN	4	36 201	1939	0.879	(0.805-0.960)	25.01
1979-1983 HEI	4	36 201	1939	0.870	(0.788-0.960)	18.91
Fully adjusted (44 confounders) RR for California during 1982 to 1989 as per Krewski[21]						
"Same" Standard Cox Model 1979-1983 HEI	4	40 408		0.872	(0.805-0.944)	~19
"Different" Standard Cox Model 1979-1983 HEI	4	38 925		0.893	(0.823-0.969)	~19

Abbreviations: CI, confidence interval; CPS, Cancer Prevention Study; HEI, Health Effects Institute; IPN, Inhalable Particulate Network; $PM_{2.5}$, particulate matter.
[a]Also, fully adjusted RR for California participants in 4 counties from September 1, 1982 through December 31, 1989 as calculated by Krewski.[21]

Table 4. Linear Regression Results for 1979 to 1983 IPN $PM_{2.5}$ and 1979 to 1983 HEI $PM_{2.5}$ Versus 1980 Age-Adjusted White Total Death Rate (DR) for 85 Counties With IPN $PM_{2.5}$ Data and for 50 HEI 2000 Counties With IPN $PM_{2.5}$ and HEI $PM_{2.5}$ data.

DR or MR, $PM_{2.5}$ Years and Source	Number of Counties	DR or MR Intercept	DR or MR Slope	95% CI of DR or MR Slope Lower	Upper	*P* Value
Entire continental United States						
DR and 1979-1983 IPN	85	892.68	6.8331	3.8483	9.8180	0.0000
DR and 1979-1983 HEI	50	910.92	6.9557	3.2452	10.6662	0.0004
MR and 1979-1983 IPN	50	0.6821	0.0102	0.0044	0.0160	0.0009
MR and 1979-1983 HEI	50	0.6754	0.0121	0.0068	0.0173	0.0000
Ohio Valley states (IN, KY, OH, PA, and WV)						
DR and 1979-1983 IPN	17	941.77	6.0705	−0.0730	12.2139	0.0524
DR and 1979-1983 HEI	12	1067.29	1.3235	−7.3460	9.9930	0.7408
MR and 1979-1983 IPN	12	0.8153	0.0077	−0.0054	0.0208	0.2202
MR and 1979-1983 HEI	12	0.9628	0.0020	−0.0080	0.0121	0.6608
States other than the Ohio Valley states						
DR and 1979-1983 IPN	68	921.45	4.8639	0.9093	8.8186	0.0167
DR and 1979-1983 HEI	38	934.66	4.8940	−0.4337	10.2218	0.0706
MR and 1979-1983 IPN	38	0.8111	0.0020	−0.0054	0.0094	0.5891
MR and 1979-1983 HEI	38	0.7334	0.0072	0.0000	0.0144	0.0491
States west of the Mississippi river						
DR and 1979-1983 IPN	36	920.10	4.0155	−0.9396	8.9706	0.1088
DR and 1979-1983 HEI	22	930.11	4.1726	−5.2015	13.5468	0.3642
MR and 1979-1983 IPN	22	0.8663	−0.0025	−0.0162	0.0112	0.7067
MR and 1979-1983 HEI	22	0.6413	0.0134	−0.0018	0.0285	0.0807
California						
DR and 1979-1983 IPN	11	921.71	3.6516	−1.8230	9.1262	0.1656
DR and 1979-1983 HEI	4	992.50	1.9664	−46.6929	50.6256	0.8780
MR and 1979-1983 IPN	4	0.9529	−0.0074	−0.0600	0.0453	0.6072
MR and 1979-1983 HEI	4	0.8336	−0.0021	−0.0618	0.0576	0.8935

Abbreviations: CI, confidence interval; HEI, Health Effects Institute; IPN, Inhalable Particulate Network; MR, mortality risk; $PM_{2.5}$, particulate matter.
[a]Linear regression results are also shown for 1979 to 1983 IPN $PM_{2.5}$ and 1979 to 1983 HEI $PM_{2.5}$ versus MR for the 50 "cities" (metropolitan areas) in figures 5 and 21 in HEI 2000.

misleading because both DRs and $PM_{2.5}$ levels are higher in the East than in the West. Regional regression analyses did not generally yield significant regression coefficients. Specifically, there were no significant regression coefficients for California, the 5 Ohio Valley states, or all states west of the Mississippi River. These findings reinforce the CPS II cohort evidence of statistically insignificant $PM_{2.5}$ MR throughout the United States.

Conclusion

This independent analysis of the CPS II cohort found that there was no significant relationship between $PM_{2.5}$ and death from all causes during 1982 to 1988, when the best available $PM_{2.5}$ measurements were used for the 50 original counties and for all 85 counties with $PM_{2.5}$ data and CPS II participants. However, a positive relationship was found when the HEI $PM_{2.5}$ measurements were used for the 50 original counties, consistent with the findings in Pope 1995 and HEI 2000. This null and positive evidence demonstrates that the $PM_{2.5}$ mortality relationship is not robust and is quite sensitive to the $PM_{2.5}$ data and CPS II participants used in the analysis.

Furthermore, the following statement on page 80 of HEI 2000 raises serious doubts about the quality of the air pollution data used in Pope 1995 and HEI 2000: "AUDIT OF AIR QUALITY DATA. The ACS study was not originally designed as an air pollution study. The air quality monitoring data used for the ACS analyses came from various sources, some of which are now technologically difficult to access. Documentation of the statistical reduction procedures has been lost. Summary statistics for different groups of standard metropolitan statistical areas had been derived by different investigators. These data sources do not indicate whether the tabulated values refer to all or a subset of monitors in a region or whether they represent means or medians."[7]

The Pope 1995 and HEI 2000 analyses were based on 50 median $PM_{2.5}$ values shown in Appendix A of the 1988 Brookhaven National Laboratory Report 52122 by Lipfert et al.[22] These analyses did not use or cite the high quality and widely known EPA IPN $PM_{2.5}$ data in spite of the fact that these data have been available in 2 detailed EPA reports since 1986.[16,17] Lipfert informed HEI about the IPN data in 1998: "During the early stages of the Reanalysis Project, I notified HEI and the reanalysis contractors of the availability of an updated version of the IPN data from EPA, which they apparently obtained. This version includes more locations and a slightly longer period of time. It does not appear that the newer IPN data are listed in Appendix G, and it is thus not possible to confirm if SMSA assignments were made properly."[23]

Thus, the HEI Reanalysis Team failed to properly "evaluate the sensitivity of the original findings to the indicators of exposure to fine particle air pollution used by the Original Investigators" and failed to select "all participants who lived within each MA for which data on sulfate or fine particle pollution were available."[7] Furthermore, HEI 2009 did not use these data even though the investigators were aware of my 2005 null $PM_{2.5}$ mortality findings in California,[8] which were based on the IPN data for 11 California counties, instead of the 4 California counties used in Pope 1995 and HEI 2000. Indeed, HEI 2009 did not cite my 2005 findings, in spite of my personal discussion of these findings with Pope, Jerrett, and Burnett on July 11, 2008.[24] Finally, HEI 2009 did not acknowledge or address my 2006 concerns about the geographic variation in $PM_{2.5}$ MR clearly shown in HEI 2000 Figure 21,[7] which is included here as Appendix Figure C1. HEI 2009 entirely avoided the issue of geographic variation in $PM_{2.5}$ MR and omitted the equivalent to HEI 2000 Figure 21.

Since 2002, HEI has repeatedly refused to provide the city-specific $PM_{2.5}$-related MR for the 50 cities included in HEI 2000 Figure 21.[15] I estimated these MRs in 2010 based on visual measurements of HEI 2000 Figure 5, and my estimates are shown in Appendix Table A1.[25] Figure 21 and its MRs represented early evidence that there was no $PM_{2.5}$-related MR in California. Appendix Table B1 shows the now overwhelming 2000 to 2016 evidence from 6 different cohorts that there is no relationship between $PM_{2.5}$ and total mortality in California. Indeed, the weighted average RR of the latest results from the 6 California cohorts is RR = 0.999 (0.988-1.010).[26]

The authors of the CPS II $PM_{2.5}$ mortality publications, which began with Pope 1995, have faced original criticism,[2-4] my criticism,[6-10,14,15] and the criticism of the HSSTC and its subpoena.[11-13] Now, my null findings represent a direct challenge to the positive findings of Pope 1995. All of this criticism is relevant to the EPA claim that $PM_{2.5}$ has a *causal* relationship to total mortality. The authors of Pope 1995, HEI 2000, and HEI 2009 need to promptly address my findings, as well as the earlier criticism. Then, they need to cooperate with critics on transparent air pollution epidemiology analyses of the CPS II cohort data.

Also, major scientific journals like the *New England Journal of Medicine* (*NEJM*) and *Science,* which have consistently written about the positive relationship between $PM_{2.5}$ and total mortality, need to publish evidence of no relationship when strong null evidence is submitted to them. In 2015, *Science* immediately rejected without peer reviewing 3 versions of strong evidence that $PM_{2.5}$ does not *cause* premature deaths.[5] In 2016, *Science* immediately rejected without peer reviewing this article. Indeed, this article was rejected by *NEJM*, *Science*, and 5 other major journals, as described in a detailed compilation of relevant correspondence.[27] Most troubling is the rejection by the *American Journal of Respiratory and Clinical Care Medicine*, which has published Pope 1995 and several other $PM_{2.5}$ mortality articles based on the CPS II cohort data.

In summary, the null CPS II $PM_{2.5}$ mortality findings in this article directly challenge the original positive Pope 1995 findings, and they raise serious doubts about the CPS II epidemiologic evidence supporting the $PM_{2.5}$ NAAQS. These findings demonstrate the importance of independent and transparent analysis of underlying data. Finally, these findings provide strong justification for further independent analysis of CPS II cohort data.

Appendix A

Table A1. List of the 85 Counties Containing the 50 Cities Used in Pope 1995, HEI 2000, and This Analysis, as well as the 35 Additional Cities Used Only in This Analysis.[a]

State	ACS Div-Unit	FIPS Code	IPN/HEI County Containing IPN/HEI City	IPN/HEI City With $PM_{2.5}$ Measurements	1979-1983 IPN $PM_{2.5}$, $\mu g/m^3$, (Weighted Average)	1979-1983 HEI $PM_{2.5}$, $\mu g/m^3$ (Median)	1980 Age-Adj White Death Rate (DR)	HEI Figure 5 Mortality Risk (MR)
AL	01037	01073	Jefferson	Birmingham	25.6016	24.5	1025.3	0.760
AL	01049	01097	Mobile	Mobile	22.0296	20.9	1067.2	0.950
AZ	03700	04013	Maricopa	Phoenix	15.7790	15.2	953.0	0.855
AR	04071	05119	Pulaski	Little Rock	20.5773	17.8	1059.4	0.870
CA	06001	06001	Alameda	Livermore	14.3882		1016.6	
CA	06002	06007	Butte	Chico	15.4525		962.5	
CA	06003	06013	Contra Costa	Richmond	13.9197		937.1	
CA	06004	06019	Fresno	Fresno	18.3731	10.3	1001.4	0.680
CA	06008	06029	Kern	Bakersfield	30.8628		1119.3	
CA	06051	06037	Los Angeles	Los Angeles	28.2239	21.8	1035.1	0.760
CA	06019	06065	Riverside	Rubidoux	42.0117		1013.9	
CA	06020	06073	San Diego	San Diego	18.9189		943.7	
CA	06021	06075	San Francisco	San Francisco	16.3522	12.2	1123.1	0.890
CA	06025	06083	Santa Barbara	Lompoc	10.6277		892.8	
CA	06026	06085	Santa Clara	San Jose	17.7884	12.4	921.9	0.885
CO	07004	08031	Denver	Denver	10.7675	16.1	967.3	0.925
CO	07047	08069	Larimer	Fort Collins	11.1226		810.5	
CO	07008	08101	Pueblo	Pueblo	10.9155		1024.1	
CT	08001	09003	Hartford	Hartford	18.3949	14.8	952.0	0.845
CT	08004	09005	Litchfield	Litchfield	11.6502		941.5	
DE	09002	10001	Kent	Dover	19.5280		959.4	
DE	09004	10003	New Castle	Wilmington	20.3743		1053.7	
DC	10001	11001	Dist Columbia	Washington	25.9289	22.5	993.2	0.850
FL	11044	12057	Hillsborough	Tampa	13.7337	11.4	1021.8	0.845
GA	12027	13051	Chatham	Savannah	17.8127		1029.6	
GA	12062	13121	Fulton	Atlanta	22.5688	20.3	1063.5	0.840
ID	13001	16001	ADA	Boise	18.0052	12.1	892.6	0.600
IL	14089	17031	Cook	Chicago	25.1019	21.0	1076.3	0.945
IL	14098	17197	Will	Braidwood	17.1851		1054.0	
IN	15045	18089	Lake	Gary	27.4759	25.2	1129.8	0.995
IN	15049	18097	Marion	Indianapolis	23.0925	21.1	1041.2	0.970
KS	17287	20173	Sedgwick	Wichita	15.0222	13.6	953.4	0.890
KS	17289	20177	Shawnee	Topeka	11.7518	10.3	933.7	0.830
KY	18010	21019	Boyd	Ashland	37.7700		1184.6	
KY	18055	21111	Jefferson	Louisville	24.2134		1095.7	
MD	21106	24510	Baltimore City	Baltimore	21.6922		1237.8	
MD	21101	24031	Montgomery	Rockville	20.2009		881.9	
MA	22105	25013	Hampden	Springfield	17.5682		1025.3	
MA	22136	25027	Worcester	Worcester	16.2641		1014.6	
MN	25001	27053	Hennepin	Minneapolis	15.5172	13.7	905.3	0.815
MN	25150	27123	Ramsey	St Paul	15.5823		935.7	
MS	26086	28049	Hinds	Jackson	18.1339	15.7	1087.4	0.930
MO	27001	29095	Jackson	Kansas City	17.8488		1090.3	
MT	28009	30063	Missoula	Missoula	17.6212		938.0	
MT	28011	30093	Silver Bow	Butte	16.0405		1299.5	
NE	30028	31055	Douglas	Omaha	15.2760	13.1	991.0	0.880
NV	31101	32031	Washoe	Reno	13.1184	11.8	1049.5	0.670
NJ	33004	34007	Camden	Camden	20.9523		1146.9	
NJ	33007	34013	Essex	Livingston	16.4775		1072.7	
NJ	33009	34017	Hudson	Jersey City	19.9121	17.3	1172.6	0.810
NM	34201	35001	Bernalillo	Albuquerque	12.8865	9.0	1014.7	0.710
NY	36014	36029	Erie	Buffalo	25.1623	23.5	1085.6	0.960
NY	35001	36061	New York	New York City	23.9064		1090.4	
NC	37033	37063	Durham	Durham	19.4092	16.8	1039.2	1.000

(continued)

Table A1. (continued)

State	ACS Div-Unit	FIPS Code	IPN/HEI County Containing IPN/HEI City	IPN/HEI City With $PM_{2.5}$ Measurements	1979-1983 IPN $PM_{2.5}$, $\mu g/m^3$, (Weighted Average)	1979-1983 HEI $PM_{2.5}$, $\mu g/m^3$ (Median)	1980 Age-Adj White Death Rate (DR)	HEI Figure 5 Mortality Risk (MR)
NC	37064	37119	Mecklenburg	Charlotte	24.1214	22.6	932.8	0.835
OH	39009	39017	Butler	Middletown	25.1789		1108.3	
OH	39018	39035	Cuyahoga	Cleveland	28.4120	24.6	1089.1	0.980
OH	39031	39061	Hamilton	Cincinnati	24.9979	23.1	1095.2	0.980
OH	39041	39081	Jefferson	Steubenville	29.6739	23.1	1058.6	1.145
OH	39050	39099	Mahoning	Youngstown	22.9404	20.2	1058.4	1.060
OH	39057	39113	Montgomery	Dayton	20.8120	18.8	1039.5	0.980
OH	39077	39153	Summit	Akron	25.9864	24.6	1064.0	1.060
OK	40055	40109	Oklahoma	Oklahoma City	14.9767	15.9	1050.4	0.985
OR	41019	41039	Lane	Eugene	17.1653		885.5	
OR	41026	41051	Multnomah	Portland	16.3537	14.7	1060.8	0.830
PA	42101	42003	Allegheny	Pittsburgh	29.1043	17.9	1115.6	1.005
PA	42443	42095	Northampton	Bethlehem	19.5265		998.6	
PA	43002	42101	Philadelphia	Philadelphia	24.0704	21.4	1211.0	0.910
RI	45001	44007	Providence	Providence	14.2341	12.9	1006.1	0.890
SC	46016	45019	Charleston	Charleston	16.1635		1023.5	
TN	51019	47037	Davidson	Nashville	21.8944	20.5	981.9	0.845
TN	51088	47065	Hamilton	Chattanooga	18.2433	16.6	1087.9	0.840
TX	52811	48113	Dallas	Dallas	18.7594	16.5	1024.9	0.850
TX	52859	48141	El Paso	El Paso	16.9021	15.7	903.5	0.910
TX	52882	48201	Harris	Houston	18.0421	13.4	1025.7	0.700
UT	53024	49035	Salt Lake	Salt Lake City	16.6590	15.4	954.3	1.025
VA	55024	51059	Fairfax	Fairfax	19.5425		925.7	
VA	55002	51710	Norfolk City	Norfolk	19.5500	16.9	1139.3	0.910
WA	56017	53033	King	Seattle	14.9121	11.9	943.6	0.780
WA	56032	53063	Spokane	Spokane	13.5200	9.4	959.2	0.810
WV	58130	54029	Hancock	Weirton	25.9181		1094.8	
WV	58207	54039	Kanawha	Charleston	21.9511	20.1	1149.5	1.005
WV	58117	54069	Ohio	Wheeling	23.9840	33.4	1117.5	1.020
WI	59005	55009	Brown	Green Bay	20.5462		931.0	
WI	59052	55105	Rock	Beloit	19.8584		1019.4	

[a]Each location includes State, ACS Division Unit number, Federal Information Processing Standards (FIPS) code, IPN/HEI county, IPN/HEI city with $PM_{2.5}$ measurements, 1979-1983 IPN average $PM_{2.5}$ level, 1979-1983 HEI median $PM_{2.5}$ level, 1980 age-adjusted white county total death rate (annual deaths per 100 000), and HEI 2000 figure 5 mortality risk for HEI city (metropolitan area). List also includes 35 additional counties containing cities with IPN $PM_{2.5}$ data used in this analysis. These 35 counties do not have HEI $PM_{2.5}$ data.

Appendix B

Table B1. Epidemiologic Cohort Studies of $PM_{2.5}$ and Total Mortality in California, 2000 to 2016: Relative Risk of Death From All Causes (RR and 95% CI) Associated With Increase of 10 $\mu g/m^3$ in $PM_{2.5}$ (http://scientificintegrityinstitute.org/NoPMDeaths081516.pdf).

Krewski 2000 and 2010[a,b]	CA CPS II Cohort	N = 40 408	RR = 0.872 (0.805-0.944)	1982-1989
(N = [18 000 M + 22 408 F]; 4 MSAs; 1979-1983 $PM_{2.5}$; 44 covariates)				
McDonnell 2000[c]	CA AHSMOG Cohort	N ~ 3800	RR ~ 1.00 (0.95-1.05)	1977-1992
(N ~ [1347 M + 2422 F]; SC&SD&SF AB; M RR = 1.09 (0.98-1.21) & F RR ~ 0.98 (0.92-1.03))				
Jerrett 2005[d]	CPS II Cohort in LA Basin	N = 22 905	RR = 1.11 (0.99-1.25)	1982-2000
(N = 22 905 M and F; 267 zip code areas; 1999-2000 $PM_{2.5}$; 44 cov + max confounders)				
Enstrom 2005[e]	CA CPS I Cohort	N = 35 783	RR = 1.039 (1.010-1.069)	1973-1982
(N = [15 573 M + 20 210 F]; 11 counties; 1979-1983 $PM_{2.5}$)			RR = 0.997 (0.978-1.016)	1983-2002
Enstrom 2006[f]	CA CPS I Cohort	N = 35 783	RR = 1.061 (1.017-1.106)	1973-1982
(N = [15 573 M + 20 210 F]; 11 counties; 1979-1983 and 1999-2001 $PM_{2.5}$)			RR = 0.995 (0.968-1.024)	1983-2002
Zeger 2008[g]	MCAPS Cohort "West"	N = 3 100 000	RR = 0.989 (0.970-1.008)	2000-2005
(N = [1.5 M M + 1.6 M F]; Medicare enrollees in CA + OR + WA (CA = 73%); 2000-2005 $PM_{2.5}$)				

(continued)

Table B1. (continued)

Jerrett 2010[h]	CA CPS II Cohort	N = 77 767	RR ~ 0.994 (0.965-1.025)	1982-2000
(N = [34 367 M + 43 400 F]; 54 counties; 2000 $PM_{2.5}$; KRG ZIP; 20 ind cov + 7 eco var; slide 12)				
Krewski 2010[b] (2009)	CA CPS II Cohort			
(4 MSAs; 1979-1983 $PM_{2.5}$; 44 cov)		N = 40 408	RR = 0.960 (0.920-1.002)	1982-2000
(7 MSAs; 1999-2000 $PM_{2.5}$; 44 cov)		N = 50 930	RR = 0.968 (0.916-1.022)	1982-2000
Jerrett 2011[i]	CA CPS II Cohort	N = 73 609	RR = 0.994 (0.965-1.024)	1982-2000
(N = [32 509 M + 41 100 F]; 54 counties; 2000 $PM_{2.5}$; KRG ZIP Model; 20 ind cov + 7 eco var; Table 28)				
Jerrett 2011[i]	CA CPS II Cohort	N = 73 609	RR = 1.002 (0.992-1.012)	1982-2000
(N = [32 509 M + 41 100 F]; 54 counties; 2000 $PM_{2.5}$; Nine Model Ave; 20 ic + 7 ev; Figure 22 and Tables 27-32)				
Lipsett 2011[j]	CA Teachers Cohort	N = 73 489	RR = 1.01 (0.95-1.09)	2000-2005
(N = [73 489 F]; 2000-2005 $PM_{2.5}$)				
Ostro 2011[k]	CA Teachers Cohort	N = 43 220	RR = 1.06 (0.96-1.16)	2002-2007
(N = [43 220 F]; 2002-2007 $PM_{2.5}$)				
Jerrett 2013[l]	CA CPS II Cohort	N = 73 711	RR = 1.060 (1.003-1.120)	1982-2000
(N = [~32 550 M + ~41 161 F]; 54 counties; 2000 $PM_{2.5}$; LUR Conurb Model; 42 ind cov + 7 eco var + 5 metro; Table 6)				
Jerrett 2013[l]	CA CPS II Cohort	N = 73 711	RR = 1.028 (0.957-1.104)	1982-2000
(Same parameters and model as above, except including co-pollutants NO_2 and Ozone; Table 5)				
Ostro 2015[m]	CA Teachers Cohort	N = 101 884	RR = 1.01 (0.98-1.05)	2001-2007
(N = [101 881 F]; 2002-2007 $PM_{2.5}$) (all natural causes of death)				
Thurston 2016[n]	CA NIH-AARP Cohort	N = 160 209	RR = 1.02 (0.99-1.04)	2000-2009
(N = [~95 965 M + ~64 245 F]; full baseline model: $PM_{2.5}$ by zip code; Table 3) (all natural causes of death)				
Enstrom 2016 unpublished	CA NIH-AARP Cohort	N = 160 368	RR = 1.001 (0.949-1.055)	2000-2009
(N = [~96 059 M + ~64 309 F]; full baseline model: 2000 $PM_{2.5}$ by county)				

[a]Krewski D. "Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality: HEI Special Report. July 2000". 2000. Figure 5 and Figure 21 of Part II: Sensitivity Analyses http://www.scientificintegrityinstitute.org/HEIFigure5093010.pdf.

[b]Krewski D. August 31, 2010 letter from Krewski to Health Effects Institute and CARB with California-specific $PM_{2.5}$ mortality results from Table 34 in Krewski 2009. 2010. http://www.arb.ca.gov/research/health/pm-mort/HEI_Correspondence.pdf

[c]McDonnell WF, Nishino-Ishikawa N, Petersen FF, Chen LH, Abbey DE. Relationships of mortality with the fine and coarse fractions of long-term ambient PM_{10} concentrations in nonsmokers. *J Expo Anal Environ Epidemiol.* 2000;10(5):427-436. http://www.scientificintegrityinstitute.org/JEAEE090100.pdf

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[e]Enstrom JE. Fine particulate air pollution and total mortality among elderly Californians, 1973-2002. *Inhal Toxicol.* 2005;17(14):803-816. http://www.arb.ca.gov/planning/gmerp/dec1plan/gmerp_comments/enstrom.pdf, and http://www.scientificintegrityinstitute.org/IT121505.pdf

[f]Enstrom JE. Response to "A Critique of 'Fine Particulate Air Pollution and Total Mortality Among Elderly Californians, 1973-2002" by Bert Brunekreef, PhD, and Gerard Hoek, PhD'. *Inhal Toxicol.* 2006:18:509-514. http://www.scientificintegrityinstitute.org/IT060106.pdf, and http://www.scientificintegrityinstitute.org/ITBH060106.pdf

[g]Zeger SL, Dominici F, McDermott A, Samet JM. Mortality in the Medicare Population and Chronic Exposure to Fine Particulate Air Pollution in Urban Centers (2000-2005). *Environ Health Perspect.* 2008;116:1614-1619. http://ehp03.niehs.nih.gov/article/info: doi/10.1289/ehp.11449

[h]Jerrett M. February 26, 2010 CARB Symposium Presentation by Principal Investigator, Michael Jerrett, UC Berkeley/CARB Proposal No. 2624-254 "Spatiotemporal Analysis of Air Pollution and Mortality in California Based on the American Cancer Society Cohort". 2010. http://www.scientificintegrityinstitute.org/CARBJerrett022610.pdf

[i]Jerrett M. October 28, 2011 Revised Final Report for Contract No. 06-332 to CARB Research Screening Committee, Principal Investigator Michael Jerrett, "Spatiotemporal Analysis of Air Pollution and Mortality in California Based on the American Cancer Society Cohort" Co-Investigators: Burnett RT, Pope CA III, Krewski D, Thurston G, Christakos G, Hughes E, Ross Z, Shi Y, Thun M. 2011. http://www.arb.ca.gov/research/rsc/10-28-11/item1dfr06-332.pdf, and http://www.scientificintegrityinstitute.org/Jerrett012510.pdf, and http://www.scientificintegrityinstitute.org/JerrettCriticism102811.pdf

[j]Lipsett MJ, Ostro BD, Reynolds P, et al. Long-term Exposure to Air Pollution and Cardiorespiratory Disease in the California Teachers Study Cohort. *Am J Respir Crit Care Med.* 2011;184(7);828-835. http://ajrccm.atsjournals.org/content/184/7/828.full.pdf

[k]Ostro B, Lipsett M, Reynolds P, et al. Long-Term Exposure to Constituents of Fine Particulate Air Pollution and Mortality: Results from the California Teachers Study. *Environ Health Perspect.* 2010;118(3):363-369. http://ehp03.niehs.nih.gov/article/info: doi/10.1289/ehp.0901181

[l]Jerrett M, Burnett RT, Beckerman BS, et al. Spatial analysis of air pollution and mortality in California. *Am J Respir Crit Care Med.* 2013;188(5):593-599. doi:10.1164/rccm.201303-0609OC. PMID:23805824.

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[n]Thurston GD, Ahn J, Cromar KR, et al. Ambient Particulate Matter Air Pollution Exposure and Mortality in the NIH-AARP Diet and Health Cohort. *Environ Health Perspect.* 2016;124(4):484-490. http://ehp.niehs.nih.gov/1509676/

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Appendix C

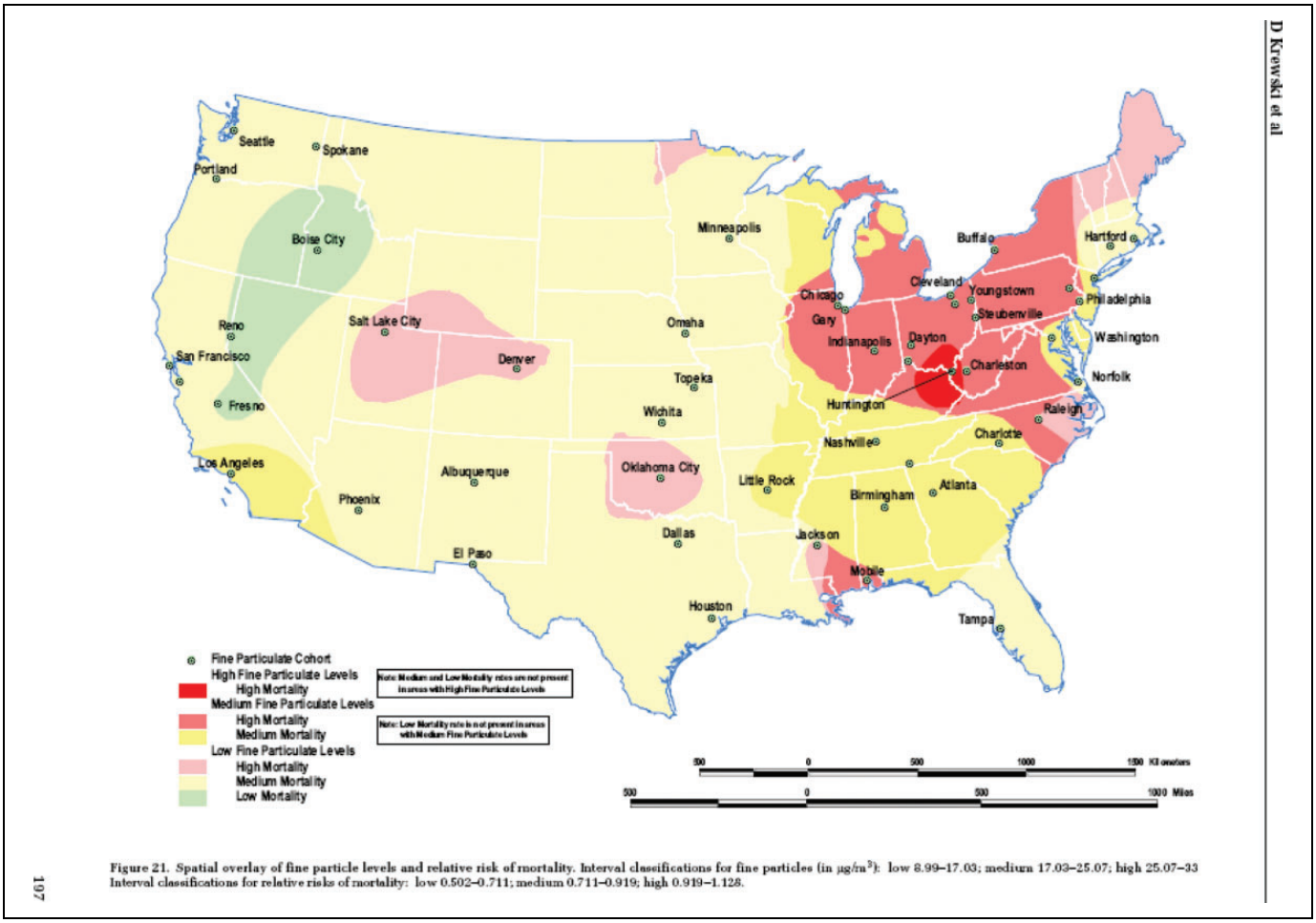

Figure C1. 1982 to 1989 $PM_{2.5}$ mortality risk (MR) in 50 cities (metropolitan areas) shown in Figure 21 on page 197 of HEI 2000[7,9] and listed in Appendix Table B1. Figure 21. Spatial overlay of fine particle levels and relative risk of mortality. Interval classifications for fine particles (in g/m^3): low 8.99 to 17.03: medium 17.03 to 25.07; high 25.07 to 33. Interval classifications for relative risks of mortality: low 0.052 to 0.711; medium 0.711 to 0.919; high 0.919 to 1.128.

Acknowledgments

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Supplemental Material

The online supplemental material is available at http://journals.sagepub.com/doi/suppl/10.1177/1559325817693345.

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$PM_{2.5}$ Does Not *Cause* Premature Deaths

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Twelfth International Conference on Climate Change
Washington, DC

March 23, 2017

Major Points

1. Basics of $PM_{2.5}$ & Premature Death Claims
2. Problems with Epidemiology of $PM_{2.5}$ Deaths
3. ACS CPS II & $PM_{2.5}$ Death Claims Since 1995
4. New Analysis of CPS II Finds No $PM_{2.5}$ Deaths
5. Scientists & Journals Block Null $PM_{2.5}$ Results
6. End 'Secret Science' & Reassess EPA NAAQS

‘$PM_{2.5}$-related Co-Benefits’ Largely Justify EPA’s Clean Power Plan

June 2, 2014 EPA Blog

EPA claims the CPP will: “Avoid up to 6,600 premature deaths . . . providing up to $93 billion in climate and public health benefits.”

(http://blog.epa.gov/blog/2014/06/our-clean-power-plan-will-spur-innovation- and-strengthen-the-economy/)

June 2, 2014 EPA Regulatory Impact Analysis

Section *4.3.2 Economic Valuation for Health Co-benefits* :

“Avoided premature deaths account for 98 percent of monetized PM-related co-benefits.”

(http://www2.epa.gov/sites/production/files/2014-06/documents/20140602ria-clean-power-plan.pdf)

March 15, 2017 *Energize Weekly*

President Trump to Rescind Clean Power Plan by Executive Order

https://www.euci.com/trump-to-rescind-epas-clean-power-plan/

Fine Particulate Matter ($PM_{2.5}$) Defined By Size (≤2.5 μm Diameter), Not Composition

$PM_{2.5}$ is mainly from combustion: forest fires, residential burning, diesel engines, and China $PM_{2.5}$ (up to 30% in CA)

US EPA established the 1997 Annual National Ambient Air Quality Standard (NAAQS) for $PM_{2.5}$ as 15 μg/m^3 , which was lowered to 12 μg/m^3 in 2012, based largely on "secret science" epidemiology

The $PM_{2.5}$ NAAQS has been used to justify numerous EPA regulations that have multi-billion dollar economic impacts in US: State Implementation Plans, Air Quality Management Plans, CARB Truck and Bus Regulation, EPA Clean Power Plan, etc.

Average US Adult Inhales About One Teaspoon of $PM_{2.5}$ in 80 Years

Amount of Air Inhaled by an Adult Breathing at Rest:
~ 10,000 liters/day ~ 292 M m^3/80 years

$PM_{2.5}$ Inhaled at original NAAQS level of 15 $\mu g/m^3$:
~4.38 grams/80 years = 0.88 teaspoons/80 years

$PM_{2.5}$ Inhaled from 100 Cigarettes ~ 4.0 grams

Benefit of EPA $PM_{2.5}$ Regulations Based on Claim of '$PM_{2.5}$ Premature Deaths' and Assumed $10 Million 'Value of Statistical Life' for Each Death

EPA claim that $PM_{2.5}$ ***causes*** 'premature deaths' is based on invalid evidence that the relative risk (RR) between $PM_{2.5}$ and total mortality is greater than 1.0 in US epidemiologic cohort studies

EPA uses unjustified and exaggerated assumptions to claim that the 'value of statistical life (VLS)' is $10 million for each 'premature death'

Problems with '$PM_{2.5}$ Premature Deaths'

1) 'Secret Science' Data:
$PM_{2.5}$ studies (like ACS CPS II) need objective reanalysis

2) No Etiologic Mechanism:
No experimental proof that 5 gm of $PM_{2.5}$ causes death

3) Epidemiology Limits:
Positive relative risks do not prove that $PM_{2.5}$ causes death

4) Geographic & Temporal Variation:
Small and declining $PM_{2.5}$-mortality risk in most of US

5) Ecological Fallacy:
$PM_{2.5}$ monitors exaggerate actual human exposure

6) Confounding Variables:
Co-pollutants, etc. weaken $PM_{2.5}$-mortality relationship

ACS Cancer Prevention Study (CPS II) Has Exaggerated $PM_{2.5}$ Premature Deaths

1995 *AJRCCM* Article by Pope Thun
Used Inferior $PM_{2.5}$ Data and 'Secret' ACS CPS II Data

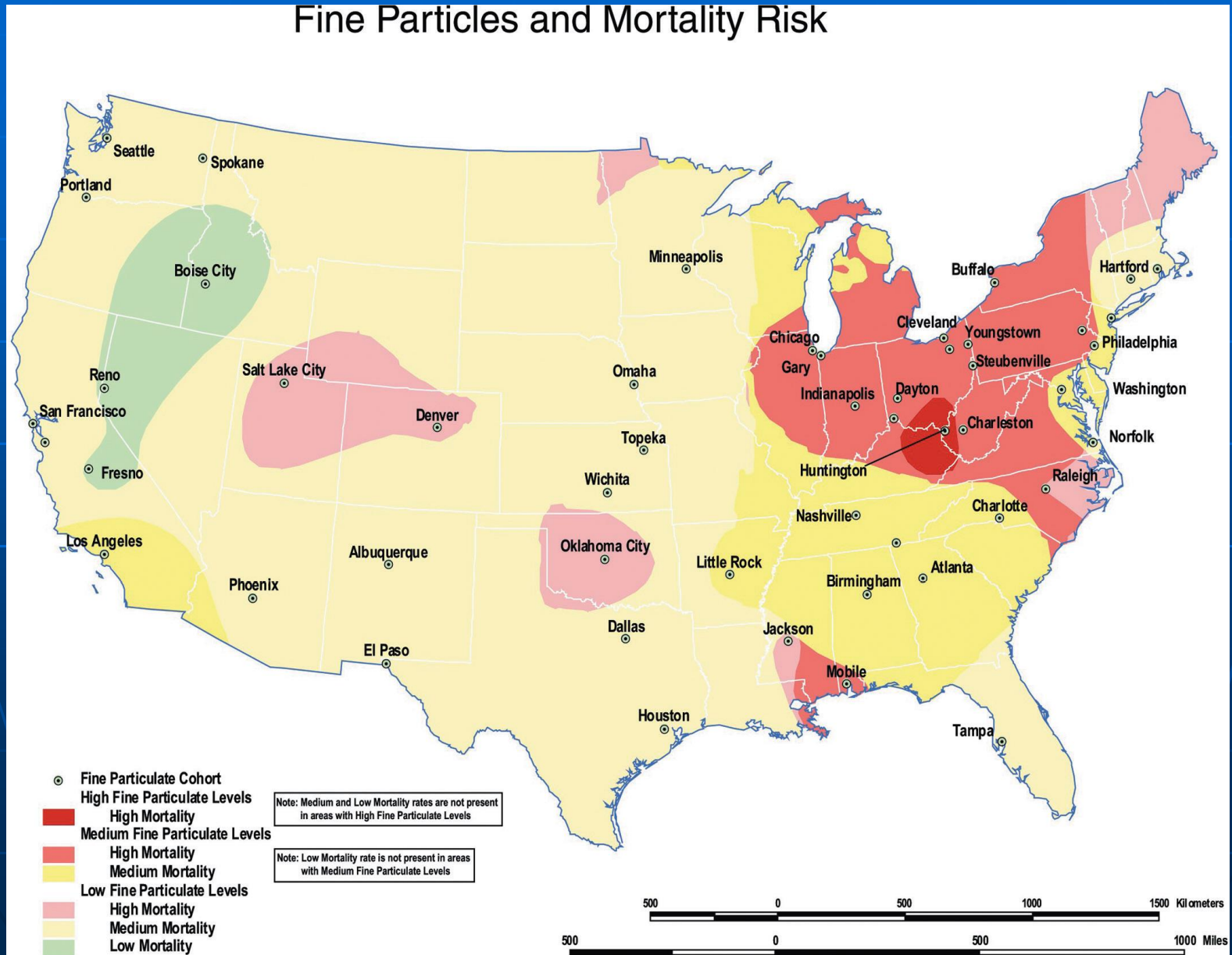
2000 HEI Reanalysis Report by Krewski Jerrett
Never Did Sensitivity Analysis Based on Best $PM_{2.5}$ Data

2009 HEI Research Report 140 by Krewski Jerrett Pope Thun
Clearly Ignored $PM_{2.5}$ Risk Variation and Best $PM_{2.5}$ Data

2017 *Dose Response* Article by Enstrom
Found NO $PM_{2.5}$ Risk in CPS II Based on Best $PM_{2.5}$ Data

"Fine Particulate Matter and Total Mortality in Cancer Prevention Study Cohort Reanalysis"

2000 Krewski HEI Reanalysis Report Figure 21
1982-1989 CPS II $PM_{2.5}$ Mortality Risk Varies in US



Enstrom 2017 Analysis of $PM_{2.5}$ and Total Mortality During 1982-1988 in ACS CPS II Cohort

1979-83 $PM_{2.5}$	Subjects	Relative Risk (95% CI)
Fully Adjusted for 50 Counties in Continental US		
IPN	195,215	1.025 (0.990-1.061)
HEI	195,215	1.082 (1.039-1.128)
Fully Adjusted for Ohio Valley (IN,KY,OH,PA,WV)		
IPN	42,174	1.050 (0.918-1.201)
HEI	42,174	1.111 (0.983-1.256)
Fully Adjusted for States Other Than Ohio Valley		
IPN	153,041	0.975 (0.936-1.051)
HEI	153,041	1.025 (0.975-1.078)

Enstrom 2017 Analysis of $PM_{2.5}$ and Total Mortality During 1982-1988 in California ACS CPS II Cohort Compared with Krewski 2010 HEI Special Analysis

1979-83 $PM_{2.5}$	Subjects	Relative Risk (95% CI)
Enstrom 2017 Fully Adjusted For 1982-1988 Deaths		
IPN (4 Counties)	36,201	0.879 (0.805-0.960)
HEI (4 Counties)	36,201	0.870 (0.788-0.960)
Krewski 2010 Fully Adjusted For 1982-1989 Deaths		
"Same" Standard Cox Model		
HEI (4 Counties)	40,408	0.872 (0.805-0.944)
"Different" Standard Cox Model		
HEI (4 Counties)	38,925	0.893 (0.823-0.969)

$PM_{2.5}$ and Total Mortality in US and California: Enstrom 2017 re 1982-1988 ACS CPS II Cohort Thurston 2016 re 2000-2009 NIH AARP Cohort

Geographic Area	Subjects	Relative Risk (95% CI)
United States		
Enstrom Analysis Fully Adjusted for 1982-1988 Deaths		
85 Counties	269,766	1.023 (0.997-1.049)
Thurston Analysis Fully Adjusted for 2000-2009 Deaths		
6 States & 2 Cities	517,041	~1.025 (1.000-1.049)
California		
Enstrom Analysis Fully Adjusted for 1982-1988 Deaths		
11 Counties	60,521	0.992 (0.954-1.032)
Thurston Analysis Fully Adjusted for 2000-2009 Deaths		
58 Counties	160,209	~1.017 (0.990-1.040)

$PM_{2.5}$ and Total Mortality in California: Six Cohorts

Author & Year	CA Cohort	Relative Risk (95% CI)
McDonnell 2000	AHSMOG	RR ~ 1.03 (0.95-1.12)
Enstrom 2005	CA CPS I	RR = 1.00 (0.98-1.02)
Zeger 2008	MCAPS "West"	RR = 0.99 (0.97-1.01)
Jerrett 2011 9 RRs	CA CPS II	RR = 1.00 (0.99-1.01)
Ostro 2015	CA Teachers	RR = 1.01 (0.98-1.05)
Thurston 2016	CA NIH AARP	RR = 1.02 (0.99-1.04)
Weighted Average (Six Cohorts)		**RR = 1.00 (0.99-1.01)**

(http://scientificintegrityinstitute.org/NoPMDeaths081516.pdf)

C. Arden Pope, III, Ph.D., BYU Economics

("World's Leading Expert on the Effects of Air Pollution on Health")

Cited Enstrom 2005 in 2006 JAWMA Review, but Never Again

Ignored July 11, 2008 CARB Teleconference re Null CA Results

Ignored February 26, 2010 CARB $PM_{2.5}$ Deaths Symposium

Ignored August 1, 2013 House Science Committee Subpoena

Omitted Many Null CA results from Jerrett 2013 AJRCCM paper

Ignored Enstrom Invitation to Attend June 11, 2015 ICCC-10

(http://scientificintegrityinstitute.org/Pope111513.pdf)

Michael L. Jerrett, Ph.D., USC, UCB, UCLA

(PM2.5 'Expert' Who Never Cites His or Others' Null Evidence)

2013 *AJRCCM* Jerrett Krewski Thun Pope: PM2.5 & CA Deaths

Browns Filed 2014 Claim with UCLA re Jerrett 2013 Paper:
Claim Ignored by UCLA Chancellor Block & Provost Waugh

Enstrom Refiled Browns' Claim with UCLA in 2015:
Claim Dismissed by UCLA Research Integrity Officer Goldberg

Enstrom Filed 2016 Detailed Claim with UCLA re Jerrett 2013:
Claim & Null Findings Dismissed by UCLA RIO Karagozian

Enstrom Filed 2016 Detailed Claim with US ORI re Jerrett 2013:
ORI Officer Concluded Jerrett 2013 shows NO PM2.5 Deaths

(http://scientificintegrityinstitute.org/ORI111116.pdf)

American Cancer Society Epidemiologists Michael Thun, M.D. & Susan Gapstur, Ph.D. Refuse to Clarify CPS II Findings re $PM_{2.5}$

ACS Has Misused the "Secret Science" CPS II Data Since 1995 to Claim $PM_{2.5}$ Causes Premature Deaths

ACS Refused to Comply with 2013 House Subpoena and Has Provided NO CPS II Data for Independent Analysis

ACS Has Refused to Cooperate with Qualified Ph.D.-level $PM_{2.5}$ Critics, including Enstrom, Young, and Briggs

ACS Continues to Participate in Falsification of $PM_{2.5}$ Deaths in CPS II Cohort and WILL NOT Respond to Critics

(http://scientificintegrityinstitute.org/GapsturEns092013.pdf)

Health Effects Institute President Daniel W. Greenbaum and Chief Scientist Aaron J. Cohen Have Never Clarifed 2000 HEI Reanalysis Findings re CPS II

HEI 2000 Reanalysis Never Tested Sensitivity of PM2.5 Mortality Risk in Pope 1995 with best $PM_{2.5}$ Data

Since 2002 HEI has not provided $PM_{2.5}$ Mortality Risk for 50 Cities in Pope 1995 and HEI 2000 Figures 5 and 21

Krewski 2010 HEI Analysis: No $PM_{2.5}$ Deaths in CA CPS II

HEI Has Not Conducted Requested Analysis of $PM_{2.5}$ Mortality Risk in CPS II for Ohio Valley and Other States

(http://scientificintegrityinstitute.org/Greenbaum031017.pdf)

Science Rejection of $PM_{2.5}$ Deaths Papers

Editor Marcia McNutt Rejected June 2015 Letter re Falisfication in Jerrett 2013 and Need for Secret Science Reform Act

July 2015 Policy Forum on $PM_{2.5}$ Rejected Without Review

August 2015 Perspective on $PM_{2.5}$ Rejected Without Review

June 2016 $PM_{2.5}$ Deaths CPS II Paper Rejected Without Review

Enstrom 2017 Findings That $PM_{2.5}$ Does Not Cause Deaths and Other Evidence Shows Publication Bias of *Science*

(https://www.nas.org/articles/nas_letter)

March 9, 2017 US House Science Committee

H.R. 1430 "Honest and Open New EPA Science Treatment (HONEST) Act of 2017"

"To prohibit the Environmental Protection Agency from proposing, finalizing, and disseminating regulations or assessments based upon science that is not transparent or reproducible."

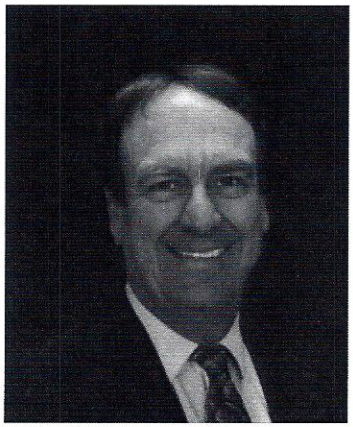
H.R. 1431 "EPA Science Advisory Board Reform Act of 2017"

"the scientific and technical points of view represented on and the functions to be performed by the Board are fairly balanced among the members of the Board"

Conclusions

1) Strong Evidence from Two Major US Cohorts That $PM_{2.5}$ Does Not *Cause* Premature Deaths
2) Strong Evidence That EPA, HEI, and Lead $PM_{2.5}$ Researchers Have Falsified the $PM_{2.5}$ and Total Mortality Relationship Since 1995
3) H.R. 1430 and H.R. 1431 Must Become Law and There Must Be Complete Reassessment of EPA $PM_{2.5}$ NAAQS as per Those Laws
4) California Waivers (Clear Air Act Section 209) Must Not Be Granted: They Are Misused to Implement Unjustified Regulations in CA

Guest Speaker: James E. Enstrom, Ph.D., M.P.H.



Dr. Enstrom is a native Californian who has lived most of his life in Los Angeles County. In 1965 He graduated co-valedictorian of his class at Harvey Mudd College in Claremont, CA, where he obtained a B.S. in physics. In 1970 Dr. Enstrom obtained his Ph.D. in experimental elementary particle physics at Stanford University from Nobel Laureate Melvin Schwartz. During 1971-1973 he worked as a physicist at the Lawrence Berkeley Laboratory in research group of Nobel Laureate Luis Alvarez. He then came to the UCLA School of Public Health as a postdoctoral fellow in cancer epidemiology and received an M.P.H. and postdoctoral certificate in 1976 from renowned public health epidemiologist Dr. Lester Breslow.

He then joined the UCLA School of Public Health faculty as a Research Professor / Researcher and he held that position for 36 years until June 2012. He currently retains a similar affiliation with UCLA, although he is now drawing retirement. He has been a Fellow of the American College of Epidemiology since 1981, he has been listed in Who's Who in America since 1990, and he has been President of the Scientific Integrity Institute in Los Angeles since 2005.

During his long career, he has explored many important epidemiological issues, particularly focusing on California. A major theme of his research has been identifying healthy lifestyles. He has shown that it is possible to reduce mortality risk from cancer and heart disease by 70% in the middle age range and to increase longevity by as much as 10 years. Examples of healthy populations that he has examined include religiously active California Mormons, California Cancer Prevention Study subjects, California PREVENTION Magazine Readers, and California and national samples of adults adhering to good health practices.

He has also examined the influence of environmental factors on mortality. In December 2005 he published a major paper on fine particulate matter and mortality in California and he has numerous other fm. Since then he has conclusively documented that fine particulate matter does not cause premature death in California. Since 2013, following the lead of the US House Science Committee, he has been involved with efforts to obtain the access to the "secret science" data that EPA has used to justify its fine particulate and ozone air pollution regulations in California and the United States. These efforts include the August 1, 2013 House subpoena of EPA, as well as the Secret Science Reform Acts of 2014 and 2015.

He is currently conducting important new air pollution epidemiology research that is relevant to the EPA, CARB, and SCAQMD regulations. More information can be found at his Scientific Integrity Institute website (http://www.scientificintegrityinstitute.org/).

A Section 508–conformant HTML version of this article is available at http://dx.doi.org/10.1289/ehp.1509676.

Ambient Particulate Matter Air Pollution Exposure and Mortality in the NIH-AARP Diet and Health Cohort

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Background: Outdoor fine particulate matter (≤ 2.5 μm; $PM_{2.5}$) 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: We aimed to test the relationship between long-term exposure $PM_{2.5}$ and death risk from all nonaccidental 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 $PM_{2.5}$ exposure estimates across the continental United States for a 2000–2009 follow-up period when matching census tract–level $PM_{2.5}$ exposure data were available. Participants enrolled ranged from 50 to 71 years of age, residing in six U.S. states and two cities. Cox proportional hazard models yielded hazard ratio (HR) estimates per 10 μg/m^3 of $PM_{2.5}$ exposure.

Results: $PM_{2.5}$ 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/m^3 $PM_{2.5}$ exposures in yearly participant residential annual mean, or in metropolitan area-wide mean, were consistent with baseline exposure model results. Associations with $PM_{2.5}$ were similar when adjusted for ozone exposures. Analyses of California residents alone also yielded statistically significant $PM_{2.5}$ mortality HRs for total and CVD mortality.

Conclusions: Long-term exposure to $PM_{2.5}$ air pollution was associated with an increased risk of total and CVD mortality, providing an independent test of the $PM_{2.5}$–mortality relationship in a new large U.S. prospective cohort experiencing lower post-2000 $PM_{2.5}$ exposure levels.

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Introduction

Over the past several decades, numerous published epidemiologic studies have documented a consistent association between long-term exposure to fine particulate matter mass (≤ 2.5 μm; $PM_{2.5}$) air pollution and an increase in the risk of mortality around the globe (e.g., Beelen et al. 2014; Brook et al. 2010; Crouse et al. 2012; Dockery et al.1993; Eftim et al. 2008; Ostro et al. 2010; Ozkaynak and Thurston 1987; Pope et al. 1995, 2002, 2004). Pope and collaborators notably found elevated relative risks of cardiovascular (CVD) mortality in association with long-term $PM_{2.5}$ exposure [hazard ratio (HR) per 10 μg/m^3 = 1.12; 95% confidence interval (CI): 1.08, 1.15] in the largest and most definitive U.S. nationwide cohort considered to date (Pope et al. 2002, 2004), providing a cardiovascular mortality HR of 1.12 per 10 μg/m^3 (95% CI: 1.08,1.15). However, existing U.S. cohort studies of $PM_{2.5}$ health effects are still being questioned (e.g., Reis 2013). In addition, particulate matter air pollution levels have been declining in recent years in the United States, so there is a need to confirm whether studies conducted in the past at higher levels are replicable today. Thus, 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 $PM_{2.5}$ exposure years, as we report here. This research addresses these needs using the newly available U.S. National Institutes of Health–AARP Diet & Health cohort (NIH-AARP Study) (Schatzkin et al. 2001).

Methods

Study population. The NIH-AARP Study was initiated when members of the AARP, 50–71 years of age from six U.S. states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and two metropolitan areas (Atlanta, Georgia, and Detroit, Michigan), responded to a mailed questionnaire in 1995 and 1996. Details of the NIH-AARP Study have been described previously (Schatzkin et al. 2001). Among 566,398 participants enrolled in the NIH-AARP cohort and available for analysis in 2014, we first excluded for this analysis those individuals for whom the forms were filled out by a proxy (n = 15,760, or 2.8%); who moved out of their study region before January 2000 (n = 13,863, or 2.4%); who died before 1 January 2000 (n = 21,415, or 3.8%); and those for whom census-level outdoor $PM_{2.5}$ exposure was not estimable using the methods discussed below (n = 737, or 0.1%). After accounting for overlapping exclusions, the analytic cohort includes 517,041 (91.3%) participants for whom matching $PM_{2.5}$ air pollution data were available. The NIH-AARP cohort questionnaires elicited information on demographic and anthropometric characteristics, dietary intake, and numerous health-related variables (e.g., marital status, body mass index, education, race, smoking status, physical activity, and alcohol consumption) at enrollment only. Contextual environment characteristics (e.g., median income) for the census tract of each of this cohort's participants have also been compiled for this population by the NIH-AARP Study (NIH-AARP 2006), allowing us to also incorporate contextual socioeconomic variables at the census-tract level. All participants provided informed consent before completing the study

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G.D.T. has provided expert witness testimony on the human health effects of air pollution before the U.S. Congress, in the U.S. EPA public hearings, and in legal cases. The other authors declare they have no actual or potential competing financial interests.

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questionnaire. The study was approved by the institutional review boards of the National Cancer Institute and New York University School of Medicine.

Cohort follow-up and mortality ascertainment. Vital status was ascertained through a periodic linkage of the cohort to the Social Security Administration Death Master File and follow-up searches of the National Death Index Plus for participants who matched to the Social Security Administration Death Master File (unpublished data, available on request from https://www.ssa.gov/dataexchange/), cancer registry linkage, questionnaire responses, and responses to other mailings. Participants were followed for address changes using the U.S. Postal Service's National Change of Address database, responses to other study-related mailings such as newsletters, and directly from cohort members' notifications (Michaud et al. 2005). We used the *International Classification of Diseases, 9th Revision* (ICD-9) and the *International Statistical Classification of Diseases, 10th Revision* to define death due to CVD (ICD-10: I00–I99), nonmalignant respiratory disease (ICD-10: J00–J99), and deaths from nonexternal and nonaccidental deaths (ICD-10 A00–R99). During the follow-up period considered here (2000 through 2009), 86,864 (16.8%) participants died, of whom 84,404 (97.2% of deaths) participants died of nonexternal and nonaccidental causes.

Air pollution exposure assessment. Outdoor annual $PM_{2.5}$-related exposures at the census-tract level for residences at NIH-AARP cohort entry were estimated using data from the U.S. Environmental Protection Agency (EPA) nationwide Air Quality System (AQS, formerly AIRS) (http://www.epa.gov/airdata/). The nationwide AQS Network includes nearly 3,000 sites, has operated since the 1970s, and has included measurement of $PM_{2.5}$ mass since mid-1999. The year 2000 was selected as the start of follow-up in this study because that is the first full year that outdoor $PM_{2.5}$ exposure data were available nationwide. The contiguous U.S. map in Figure 1 displays the census tracts in which the members of this cohort resided at the start of the study. Private residence locations were not included in the original NIH-AARP Cohort data set in order to protect participant privacy. As a result, we employed census tract centroid estimates of monthly average $PM_{2.5}$ mass exposures available through the year 2008, as obtained from a published hybrid land-use regression (LUR) geostatistical model (Beckerman et al. 2013), and as matched with individuals by NIH to further protect participant anonymity. Exposure was considered only through 2008 because the time-dependent model matched deaths with exposure in each prior year, and follow-up ended in 2009 for these analyses. These estimates used ambient AQS $PM_{2.5}$ as the dependent variable and traffic and land use information as predictors (Beckerman et al. 2013). Residuals from this model were interpolated with a Bayesian maximum entropy (BME) model, and the estimates from the LUR and BME were combined post hoc to derive monthly estimates of $PM_{2.5}$. To allow investigation of possible confounding by O_3 exposure, annual primary metropolitan statistical area (PMSA) mean ozone (O_3) exposures were also estimated for the year 2000 by averaging annual O_3 means from all ambient monitoring sites with > 75% of possible days of data in each PMSA (including 391 sites among 93 PMSAs) (U.S. EPA 2014). The PMSA mean $PM_{2.5}$ mass concentrations in 2008, at the end of the exposure period, were lower than but highly correlated with their paired PMSA mean concentration in 2000 (R^2 = 0.77), suggesting that the spatial rank ordering of $PM_{2.5}$ concentrations remained consistent over the follow-up period. However, the number of cohort participants living below the U.S. annual $PM_{2.5}$ standard (12 μg/m^3) increased over time, rising steadily from only 33% of cohort participants in 2000 (mean ± SD = 13.6 ± 3.6 μg/m^3) up to 78% of cohort participants living below the 12 μg/m^3 annual $PM_{2.5}$ standard in 2008 (mean ± SD = 10.2 ± 2.3 μg/m^3). Therefore, to incorporate these exposure level changes over the follow-up time, we also developed annual mean exposures at the census tract centroid of each participant's residence at baseline to incorporate into a time-dependent sensitivity analysis of the $PM_{2.5}$–mortality association, with censoring for those known to have moved.

Statistical methods. Person-years of follow-up were included for each participant from 1 January 2000 to the date of death, the end of follow-up (31 December 2009), or the date the participant moved out of the state or city where s/he lived at enrollment, whichever occurred first. This period was selected because that is the time period for which outdoor $PM_{2.5}$ exposure estimates were available nationwide at the census-tract level for matching with the cohort mortality data (Beckerman et al. 2013). For the time-independent exposure model, the exposure metric was each participants's annual mean enrollment census tract–centroid $PM_{2.5}$ exposure in the first year of this mortality analysis, 2000, which was the first complete year of $PM_{2.5}$ data availability across the United States. In addition, we also considered a time-dependent (annual mean) model, for which annual mean census tract–level exposure to $PM_{2.5}$ was treated as time-varying, with a 1-year lag. For example, mortality risk during 2000 was related to each participant's enrollment residence census tract–specific average $PM_{2.5}$ for 1999.

We used the Cox proportional hazards models (Cox and Oakes 1984; Fleming and Harrington 1991) to estimate relative risks (RRs) of mortality and 95% confidence intervals (CIs) in relation to ambient $PM_{2.5}$ (per 10 μg/m^3). In multivariate models including individual-level variables, we treated age (in 3-year groupings), sex and region (six U.S. States and two municipalities of residence at study entry) as strata and adjusted for the following individual covariates and potential risk factors at enrollment: race (non-Hispanic white, non-Hispanic black, other), education (< 8 years, 8–11 years, high school, some college, college graduate), marital status (married, never married, or other, including widowed/divorced/separated and unknown), body mass index (BMI; < 18.5, 18.5 to < 25.0, 25.0 to < 30.0, 30 to < 35, and ≥ 35 kg/m^2), alcohol consumption (none, < 1, 1–2, 2–5, and ≥ 5 drinks per day), and smoking history (never smoker, former smoker who quit at least 1 year ago of ≤ 1 pack/day, former smoker who quit at least 1 years ago of > 1 pack/day, quit less than 1 year ago or current smoker of ≤ 1 pack/day, quit less than 1 year ago or current smoker of > 1 pack/day). We also included two contextual characteristics of the

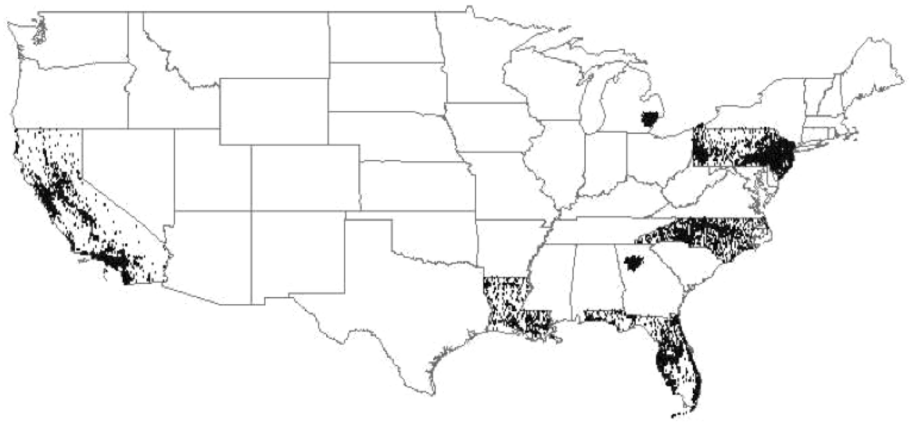

Figure 1. Continental U.S. map of NIH-AARP study participants' census tracts.

participants' residential census tracts found to modify the $PM_{2.5}$–mortality HR estimates and have statistical significance in our analyses (data not shown): *a*) median census tract household income; and *b*) percent of census tract population with less than a high school education, based on the 2000 decennial census for the residence at study entry, as included in the cohort data set (NIH-AARP 2006). Potential effect modification was assessed by including multiplicative interaction terms between $PM_{2.5}$ concentrations and each covariate [e.g., sex, age < 65 or ≥ 65 years, age and sex combined, education (< high school, high school, > high school), and smoking (never, former, current) at baseline] in the proportional hazards models. Likelihood ratio statistic *p*-values (two-sided) comparing model fit with and without interaction terms were used to test the statistical significance of each interaction, with *p*-values of < 0.05 defined as statistically significant. Statistical analyses were carried out in SAS (version 9.3; SAS Institute Inc.) and R (version 3.0.1), using the "survival" package (R Core Team 2013).

Additional sensitivity analyses were conducted, including models without adjusting for contextual variables; limiting the analysis to California residents; without censoring data after people moved; adjusting for O_3, and using $PM_{2.5}$ exposures estimated at the metropolitan area average level (rather than at the census tract level). In addition, other contextual characteristics were also considered: *a*) Gini coefficient, a metric of income inequality; *b*) percent of census tract population who are black; *c*) percent of census tract population who are unemployed; and *d*) percent of census tract population living below the poverty level, but were not included in the final model, as addition of these variables did not significantly affect results. To allow more direct comparisons with past work applying random effects methods (e.g., Krewski et al. 2009), we also evaluated HRs in relation to baseline (2000) $PM_{2.5}$ exposure levels while incorporating random effects for state of residence using the "coxme" package in R.

To show how the shape of the $PM_{2.5}$–mortality relationship response varies with concentration in this cohort, $PM_{2.5}$ natural spline (ns) plots with 4 degrees of freedom (df) were prepared for both total (all cause) and cardiovascular mortality using standard Cox models for the baseline case, stratified by age and sex, and adjusted for all individual-level covariates and contextual variables, as described above.

Results

The cohort was exposed to a wide range of $PM_{2.5}$ concentrations (Table 1), with a concentration range similar to the nation as a whole (U.S. EPA 2009). Except for race (for which Table 1 indicates a rising exposure with increasing percentage of black participants), cohort characteristics were generally similar across $PM_{2.5}$ exposure level, limiting the potential for confounding in our $PM_{2.5}$ mortality relationship analyses.

In our time-independent baseline exposure Cox model analyses of the selected cohort (using the study entry tract of residence $PM_{2.5}$ mean as the exposure reference for each participant), higher levels of ambient $PM_{2.5}$ exposure were significantly associated with increased mortality due to all causes of (nonaccidental) death (HR = 1.03 per 10 μg/m^3 $PM_{2.5}$; 95% CI: 1.00, 1.05) and cardiovascular disease (HR = 1.10; 95% CI: 1.05, 1.15), as presented in Table 2. Stratified analyses by sex, age, and education for this cohort did not indicate significant differences in $PM_{2.5}$ effect estimates across categories (Table 2). However, although $PM_{2.5}$ exposure was not significantly associated overall with increased risk of respiratory mortality (HR = 1.05; 95% CI: 0.98, 1.13), an association was found for never smokers (HR = 1.27; 95% CI: 1.03, 1.56). Figure 2 graphically demonstrates, for the time-independent model, the monotonically rising nature of the concentration–response curve for both all-cause and CVD mortality (vs. a referent HR = 1.0 at the mean level of exposure).

A number of sensitivity analyses for alternative models were also conducted (Table 3). In general, associations were stronger and *p*-values were smaller when we did not adjust for census tract–level contextual environmental variables, including the association with respiratory mortality (HR = 1.09; 95% CI: 1.02, 1.18). Adding random-effects terms to the time-independent model yielded very similar results to those without random-effects terms. Time-dependent yearly exposure models gave comparable results to the year 2000 time-independent baseline exposure model for total mortality (HR = 1.03; 95% CI: 0.99, 1.05), CVD mortality (HR = 1.11; 95% CI: 1.06, 1.16), and respiratory mortality (HR = 1.05; 95% CI: 0.97, 1.15). Limiting the analysis to only California (the state with the largest number of cohort participants) gave similar results to the entire cohort. To assess the extent to which our censoring of those who moved out of the study state/city might have affected the results, we also present overall results for participants without that censoring, retaining those who moved after 2000, finding that it gave similar results to our base model case with censoring (as shown in Table 2). In addition, in a model that simultaneously also included exposure to the gaseous pollutant O_3 along with $PM_{2.5}$, the $PM_{2.5}$ effect estimate was found to be still significant and its CVD mortality effect estimate not statistically different from the model without the addition of O_3, indicating the $PM_{2.5}$–CVD mortality association to be robust to the addition of O_3.

Discussion

In this large prospective cohort study with detailed baseline individual-level risk factor information on study participants (e.g., smoking, BMI, alcohol use), we confirmed a monotonically increasing, and statistically significant, relationship between long-term exposure to $PM_{2.5}$ air pollution and both all-cause and CVD mortality, even at the decreased $PM_{2.5}$ levels experienced in the United States since 2000. Comparisons by sex, age, and education for this cohort did not indicate statistically significant differences in the mortality–$PM_{2.5}$ association across categories.

With significant overall associations with all-cause and cardiovascular mortality, the results presented here are consistent with many, but not all, of the prior published results examining $PM_{2.5}$ and mortality. We estimated a 3% increase (95% CI: 0, 5%) in all-cause mortality for a 10-μg/m^3 annual increase in $PM_{2.5}$ that, though statistically significant in this large cohort, is lower than many other past estimates. For example, a recent literature review reported a pooled effect estimate of 6% per 10 μg/m^3 $PM_{2.5}$ (95% CI: 4, 8%) for all-cause mortality (Hoek et al. 2013). Our overall estimate for CVD mortality (10% effect per 10 μg/m^3; 95% CI: 5, 15%), agrees more closely with the pooled estimate for CVD mortality reported by Hoek et al. (2013) (11% per 10 μg/m^3; 95% CI: 6, 16%).

Comparisons with the American Cancer Society (ACS) cohort, a similarly large nationwide cohort, provides an opportunity to evaluate the issue of association consistency over time in the United States. Although participants in the ACS cohort (Pope et al. 2002) were somewhat younger (mean 56 years at recruitment, vs. mean 65 years in the NIH-AARP cohort in 2000), and were exposed during that study's follow-up to pollution at an earlier period of time (when the mix of air pollution sources was likely different), it has a similar racial (> 90% white) and educational (> 50% post–high school education) composition, is of similar size (> 500,000 participants), and also spans the United States, making it probably the most similar U.S. cohort for comparison here. The ACS cohort reported that a 10-μg/m^3 increase in $PM_{2.5}$ was associated with a 4% increase in all-cause mortality (95% CI: 1, 8%) (Pope et al. 2002), which is consistent with the corresponding estimate from the present analysis (3% per 10 μg/m^3; 95% CI: 0, 5%), as shown in Figure 3. Moreover,

the $PM_{2.5}$–CVD mortality effect estimate reported for the ACS cohort (12% per 10 μg/m^3; 95% CI: 8, 15%) (Pope et al. 2004) is very similar to the corresponding association in the NIH-AARP cohort (10% per 10 μg/m^3; 95% CI: 5, 15%) (Figure 3). This new prospective cohort study's follow-up begins at approximately the time that most of the published ACS cohort's follow-up analyses ended, providing an independent test as to whether the effects continue to the lower $PM_{2.5}$ levels in the 21st century. The ACS cohort study started in 1982 with follow-up through 1998, with an annual $PM_{2.5}$ study period mean ± SD = 17.7 ± 3.7 μg/m^3 (Pope et al. 2002); in contrast, this new NIH-AARP analysis started in 2000 with much lower study follow-up mean $PM_{2.5}$ of 12.2 ± 3.4 μg/m^3 through 2008. Our study therefore documents for the first time that the $PM_{2.5}$–mortality effects still occur at the much lower post-2000 levels of exposures across the United States. In California, the ACS follow-up ended with a mean 1998–2002 $PM_{2.5}$ concentration of 14.1 μg/m^3 (Jerrett et al. 2013), versus a much lower end of follow-up mean 2008 $PM_{2.5}$ concentration of 10.4 μg/m^3 in the present study. Figure 3 provides comparative plots of these two cohort's $PM_{2.5}$ mortality estimates across mortality outcomes, for both the United States and the State of California (Jerrett et al. 2013; Krewski et al. 2009; Pope et al. 2002, 2004), indicating consistency in their effect estimates, despite the notable decline in pollution levels after 2000.

We have also considered and compared effect estimates per 10 μg/m^3 $PM_{2.5}$ as a function of alternative $PM_{2.5}$ exposure metrics. In addition to the year 2000 base $PM_{2.5}$ exposure index, we also considered time-dependent annual mean exposure models for each mortality outcome that directly addressed the declining concentration levels of $PM_{2.5}$ exposures during follow-up.

Table 1. Selected participant characteristics according to quintile of $PM_{2.5}$ exposure in 2000 [mean ± SD or *n* (%)].

	$PM_{2.5}$ concentration (μg/m^3)				
Characteristic	2.9–10.7	10.7–12.6	12.6–14.2	14.2–15.9	15.9–28.0
n[a]	103,576	103,330	103,345	103,410	103,380
Age in 2000 (years)	66.1 ± 5.3	65.8 ± (5.4)	65.6 ± (5.4)	65.6 ± (5.4)	65.6 ± (5.4)
Sex					
Male	60,996 (58.9)	61,716 (59.7)	61,541 (59.5)	61,076 (59.1)	58,053 (56.2)
Female	42,580 (41.1)	41,614 (40.3)	41,804 (40.5)	42,334 (40.9)	45,327 (43.8)
BMI (kg/m^2)					
≤ 18.5	845 (0.8)	817 (0.8)	842 (0.8)	809 (0.8)	860 (0.8)
18.5–25	37,390 (36.1)	34,657 (33.5)	33,316 (32.2)	32,861 (31.8)	35,545 (34.4)
> 25 and ≤ 30	42,709 (41.2)	43,141 (41.8)	43,329 (41.9)	43,327 (41.9)	41,781 (40.4)
> 30 and ≤ 35	14,714 (14.2)	15,959 (15.4)	16,546 (16.0)	16,794 (16.2)	15,823 (15.3)
> 35	5,329 (5.1)	6,041 (5.8)	6,510 (6.3)	6,816 (6.6)	6,531 (6.3)
Unknown	2,589 (2.5)	2,715 (2.6)	2,802 (2.7)	2,803 (2.7)	2,840 (2.7)
Smoking status					
Never smoking	34,685 (33.5)	35,363 (34.2)	37,100 (35.9)	37,413 (36.2)	38,377 (37.1)
Former, ≤ 1 pack/day	28,700 (27.7)	27,572 (26.7)	27,307 (26.4)	27,219 (26.3)	27,442 (26.5)
Former, > 1 pack/day	23,163 (22.4)	22,575 (21.8)	21,285 (20.6)	20,414 (19.7)	19,696 (19.1)
Currently, ≤ 1 pack/day	8,555 (8.3)	8,709 (8.4)	8,855 (8.6)	9,541 (9.2)	9,368 (9.1)
Currently, > 1 pack/day	4,657 (4.5)	5,232 (5.1)	4,895 (4.7)	4,812 (4.7)	4,543 (4.4)
Unknown	3,816 (3.7)	3,879 (3.8)	3,903 (3.8)	4,011 (3.9)	3,954 (3.8)
Race/ethnicity					
White	95,786 (92.5)	95,942 (92.9)	96,283 (93.2)	94,670 (91.5)	88,741 (85.8)
Black	1,807 (1.7)	2,501 (2.4)	3,532 (3.4)	5,421 (5.2)	7,067 (6.8)
Hispanic	2,691 (2.6)	1,974 (1.9)	1,180 (1.1)	920 (0.9)	3,011 (2.9)
Asian	1,957 (1.9)	1,573 (1.5)	1,004 (1.0)	1,043 (1.0)	2,863 (2.8)
Unknown	1,335 (1.3)	1,340 (1.3)	1,346 (1.3)	1,356 (1.3)	1,698 (1.6)
Marital status					
Married	71,327 (68.9)	72,457 (70.1)	72,094 (69.8)	70,980 (68.6)	65,450 (63.3)
Widowed/divorced/separated	26,664 (25.7)	25,923 (25.1)	25,816 (25.0)	26,592 (25.7)	30,330 (29.3)
Never married	4,743 (4.6)	4,135 (4.0)	4,563 (4.4)	5,019 (4.9)	6,646 (6.4)
Unknown	842 (0.8)	815 (0.8)	872 (0.8)	819 (0.8)	954 (0.9)
Education					
Less than 11 years	5,081 (4.9)	6,011 (5.8)	6,829 (6.6)	7,198 (7.0)	5,672 (5.5)
High school completed	17,019 (16.4)	19,880 (19.2)	22,604 (21.9)	24,055 (23.3)	17,750 (17.2)
Post–high school	9,560 (9.2)	10,590 (10.2)	10,652 (10.3)	10,933 (10.6)	8,890 (8.6)
Some college	25,852 (25.0)	24,470 (23.7)	21,809 (21.1)	21,616 (20.9)	25,854 (25.0)
College and post graduate	43,103 (41.6)	39,343 (38.1)	38,347 (37.1)	36,498 (35.3)	42,001 (40.6)
Unknown	2,961 (2.9)	3,036 (2.9)	3,104 (3.0)	3,110 (3.0)	3,213 (3.1)
State of residence					
California	49,086 (47.4)	26,087 (25.2)	12,303 (11.9)	13,238 (12.8)	59,495 (57.5)
Florida	47,001 (45.4)	42,769 (41.4)	14,647 (14.2)	5,851 (5.7)	82 (0.1)
Georgia	0 (0.0)	0 (0.0)	0 (0.0)	156 (0.2)	14,331 (13.9)
Louisiana	265 (0.3)	3,717 (3.6)	12,150 (11.8)	3,295 (3.2)	145 (0.1)
Michigan	78 (0.1)	1,157 (1.1)	3,051 (3.0)	15,546 (15.0)	6,307 (6.1)
North Carolina	156 (0.2)	8,022 (7.8)	11,596 (11.2)	18,402 (17.8)	4,583 (4.4)
New Jersey	4,585 (4.4)	14,568 (14.1)	29,238 (28.3)	14,657 (14.2)	2,149 (2.1)
Pennsylvania	2,405 (2.3)	7,010 (6.8)	20,360 (19.7)	32,265 (31.2)	16,288 (15.8)
Contextual variables					
Median income ($)	57,399 ± 27,037	52,980 ± 23,695	53,453 ± 22,793	51,280 ± 20,502	53,746 ± 22,979
Percent high school or less	13.6 ± 9.6	15.5 ± 10.0	15.6 ± 9.7	16.2 ± 9.8	18.0 ± 13.7

[a]Number of participants in $PM_{2.5}$ quintile, after accounting for missing covariate data.

The fixed exposure model has the advantage that it provides results using methods directly comparable to those used in many past such analyses (e.g., the ACS CP-II cohort). We found that the annual mean model yielded results consistent with the baseline (year 2000) exposure time-independent model. Lepeule et al. (2012) also found that varying the exposure metric choice had little effect on $PM_{2.5}$ effect estimates in their analysis of the Harvard Six Cities Study cohort. Not censoring those participants who moved out

Table 2. NIH-AARP cohort time independent Cox model $PM_{2.5}$ mortality hazard ratios (and 95% CIs) per 10 μg/m^3, by cause and cohort subgroup.

	All-cause mortality			Cardiovascular mortality			Respiratory mortality		
Cohort subset	HR (95% CI)	*n* deaths	*p*-int	HR (95% CI)	*n* deaths	*p*-int	HR (95% CI)	*n* deaths	*p*-int
All	1.03 (1.00, 1.05)	84,404		1.10 (1.05, 1.15)	26,009		1.05 (0.98, 1.13)	8,397	
Age (years)									
< 65	1.00 (0.95, 1.05)	20,422		1.09 (0.99, 1.19)	5,614		1.00 (0.85, 1.19)	1,592	
≥ 65	1.03 (1.00, 1.06)	63,982	0.67	1.10 (1.05, 1.15)	20,395	0.97	1.06 (0.98, 1.15)	6,805	0.24
Sex									
Male	1.03 (1.00, 1.06)	55,685		1.09 (1.04, 1.15)	18,200		1.02 (0.93, 1.12)	5,193	
Female	1.02 (0.98, 1.06)	28,719	0.77	1.10 (1.02, 1.19)	7,809	0.33	1.10 (0.98, 1.23)	3,204	0.73
Sex and age (years)									
Male: < 65	0.99 (0.94, 1.06)	13,117		1.08 (0.97, 1.21)	3,975		0.99 (0.80, 1.23)	923	
Male: ≥ 65	1.04 (1.01, 1.08)	42,568		1.10 (1.03, 1.16)	14,225		1.03 (0.92, 1.14)	4,270	
Female: < 65	1.01 (0.94, 1.10)	7,305		1.11 (0.94, 1.30)	1,639		1.01 (0.78, 1.31)	669	
Female: ≥ 65	1.02 (0.97, 1.06)	21,414	0.88	1.10 (1.01, 1.19)	6,170	0.82	1.12 (0.99, 1.28)	2,535	0.56
Education									
< High school education	1.02 (0.97, 1.07)	25,886		1.05 (0.97, 1.15)	8,176		1.04 (0.91, 1.19)	2,900	
High school education	1.06 (0.98, 1.15)	8,668		1.21 (1.05, 1.40)	2,708		1.00 (0.79, 1.26)	883	
> High school education	1.02 (0.99, 1.05)	46,577	0.65	1.10 (1.04, 1.16)	14,057	0.86	1.07 (0.97, 1.18)	4,275	0.38
Smoking									
Never smoked	1.04 (0.99, 1.08)	19,785		1.11 (1.02, 1.20)	6,384		1.27 (1.03, 1.56)	1,004	
Former smoker	1.02 (0.99, 1.06)	44,590		1.07 (1.01, 1.14)	13,934		1.04 (0.94, 1.14)	4,677	
Current smoker	1.01 (0.95, 1.06)	16,354	0.58	1.14 (1.02, 1.25)	4,451	0.46	1.01 (0.88, 1.16)	2,372	0.70

p-int, *p*-value for interaction.

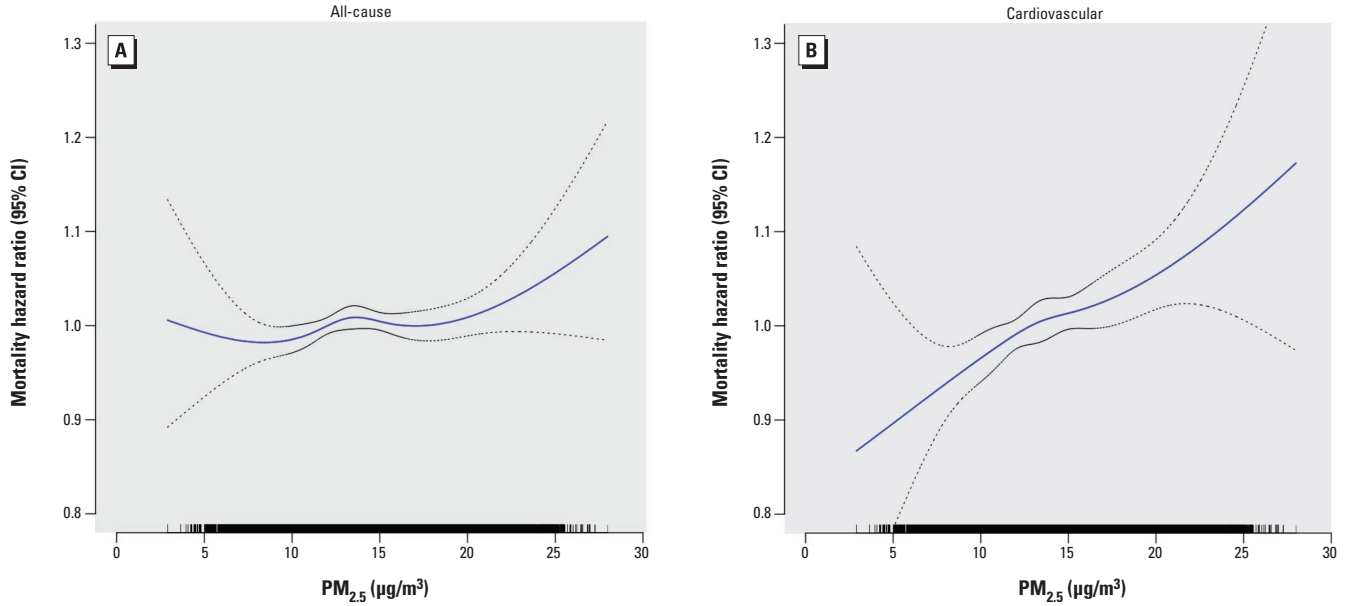

Figure 2. Concentration–response curves (solid lines) and 95% CIs (dashed lines) based on natural spline models with 4 df, standard Cox models stratified by age and sex, adjusted for all individual-level covariates (race, education, marital status, BMI, alcohol consumption, and smoking history) and contextual covariates [median income ($), and percent high school or less] for (*A*) all nonaccidental causes and (*B*) cardiovascular disease. The tick marks on the *x*-axis identify the distribution of observations according to $PM_{2.5}$ concentrations.

Table 3. NIH-AARP cohort $PM_{2.5}$ mortality hazard ratios and 95% CIs per 10 μg/m^3 $PM_{2.5}$ for alternative model specifications.

Model	*n*	All	Cardiovascular	Respiratory
Full baseline model, time-independent 2000 census tract mean $PM_{2.5}$ exposures	517,041	1.03 (1.00, 1.05)	1.10 (1.05, 1.15)	1.05 (0.98, 1.13)
Full model, time-dependent annual census tract mean $PM_{2.5}$ exposures	517,041	1.03 (0.99, 1.05)	1.11 (1.06, 1.16)	1.05 (0.97, 1.15)
Full baseline model, 2000 PMSA mean $PM_{2.5}$ exposures	474,565	1.01 (0.98, 1.04)	1.10 (1.04, 1.16)	1.06 (0.97, 1.16)
Full baseline model without contextual variations	517,041	1.06 (1.03, 1.08)	1.15 (1.10, 1.20)	1.09 (1.02, 1.18)
Full baseline model with random effects	517,041	1.03 (1.00, 1.05)	1.10 (1.05, 1.14)	1.06 (0.99, 1.14)
Full baseline model with O_3	466,121	1.02 (0.99, 1.05)	1.07 (1.02, 1.12)	1.02 (0.94, 1.11)
Full baseline model retaining all who moved from study area after 2000	517,041	1.02 (1.00, 1.05)	1.10 (1.06, 1.15)	1.04 (0.97, 1.12)
Full baseline model for California only	160,209	1.02 (0.99, 1.04)	1.10 (1.05, 1.16)	1.01 (0.93, 1.10)

of the study areas between 2000 and 2006 (n = 28,923) had little effect on these results. We also compared the results using both PMSA and census tract–level mean exposure metrics, finding similar and confirmatory results with either approach. This may suggest that the fact that people are mobile, and often do not stay at their home residence all day, may limit the exposure assessment accuracy gain derived from knowing home residence locale versus an area-wide average. Overall, we found that the $PM_{2.5}$–mortality associations in this work are robust to various $PM_{2.5}$ exposure modeling choices.

Numerous past long-term $PM_{2.5}$–mortality analyses have found higher relative risks among those with less education. For example, Krewski et al. (2000), in their reanalysis of the Six Cities and ACS cohorts, found that the relative risk of mortality associated with fine particles was greater among individuals with high school education or less, compared to those with more than high school education in the Six Cities Study, and that the fine particle air pollution mortality risk decreased significantly ($p < 0.05$) with increasing educational attainment in the ACS cohort. They concluded that "it is possible that educational attainment is a marker for socioeconomic status, which in turn may be correlated with exposure to fine particle air pollution." Similarly, Brunekreef et al. (2009) found in their NLCS (Netherlands Cohort Study on Diet and Cancer)–AIR cohort examination of long-term exposure to traffic air pollution that associations with mortality tended to be stronger in case–cohort participants with lower levels of education, but that differences between strata were not statistically significant. Ostro et al. (2008) also estimated stronger associations with components of $PM_{2.5}$ among individuals with lower educational attainment, attributing this trend to the effects of lower socioeconomic status. However, no such trend was found in this NIH-AARP cohort, perhaps because the reported annual incomes of this cohort did not vary with $PM_{2.5}$ concentration (Table 1). Indeed, although the association of education with median income in this cohort was strong (r = 0.49), the correlation between $PM_{2.5}$ and median income was much lower (p = 0.03). Thus, it may be that the lack of a strong socioeconomic–$PM_{2.5}$ covariation in this cohort is the reason we did not see the mortality effect modification by education status found in past studies.

This study has both strengths and limitations relative to past such studies. One strength is that we have employed estimates of $PM_{2.5}$ exposure at the participant residence census tract level, rather than applying the overall county or metropolitan area average exposure that has been used in some major prior studies (e.g., the Medicare and ACS cohorts, respectively) (Eftim et al. 2008; Krewski et al. 2009). In addition, most previous studies have assigned only a single fixed exposure level for each study participant (e.g., at the start of the follow-up), whereas we also considered a sensitivity model applying time-varying exposure estimates to address the declining $PM_{2.5}$ exposure levels over time. Another strength of this study is that covariate risk factors were collected at the individual level, but a limitation is that this was ascertained only at enrollment, and we could not account for temporal changes in risk factors (e.g., smoking and BMI) during follow up. Another limitation is that, other than knowing if and when participants leave the NIH-AARP cohort study areas, we presently lack information on residence location after those participants moved out of the study region. Despite these limitations, as discussed above, our derived effect estimates were found to be largely consistent with other $PM_{2.5}$ mortality results, notably the ACS cohort study (Pope et al. 2002, 2004), the only prior prospective U.S. cohort study of such size with detailed individual-level risk factor information.

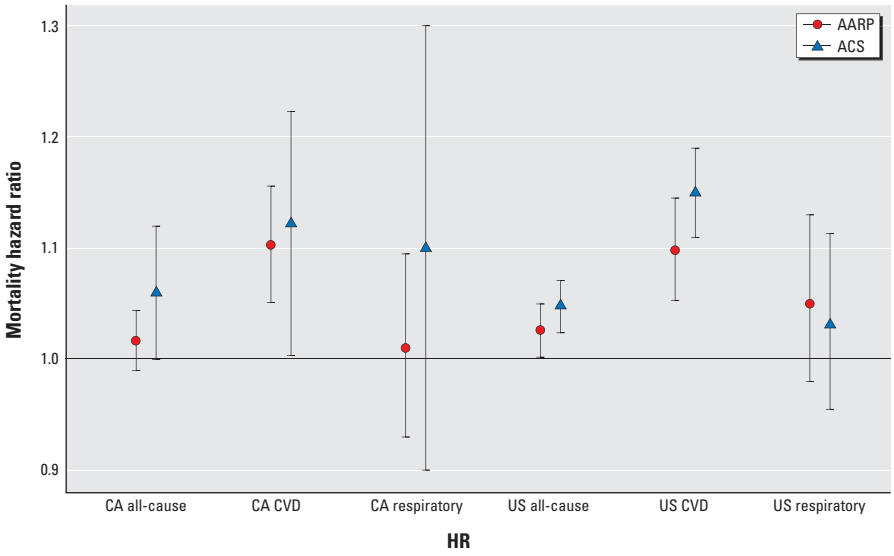

Figure 3. Comparison of NIH-AARP cohort vs. published ACS cohort all-cause and by-cause mortality hazard ratios per 10 μg/m^3 $PM_{2.5}$, with 95% CIs, for the state of California (CA) and nationwide (US) (Jerrett et al. 2013; Krewski et al. 2009).

Conclusions

Long-term exposure to $PM_{2.5}$ air pollution was associated with a significant increase in CVD and total nonaccidental mortality in the cohort as a whole, as well as with a significant increase in respiratory mortality among never smokers, in a new, large, U.S. cohort having detailed individual level participant data and census tract–level $PM_{2.5}$ exposure information. This independent evaluation of the $PM_{2.5}$–mortality association, in this new large cohort, was robust to various model specification and $PM_{2.5}$ exposure assessment sensitivity analyses, and has found effect estimates (per 10 μg/m^3 of $PM_{2.5}$ exposure) that are consistent with past estimates, even at the much lower $PM_{2.5}$ air pollution levels experienced in the United States since 2000.

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From: jfahrenkamp@science-int.co.uk
Sent: Monday, August 24, 2015 3:42 AM
To: jenstrom@ucla.edu
Cc: jfahrenkamp@science-int.co.uk
Subject: Decision on your Science Manuscript aad2566

24-Aug-2015
Retired Research Faculty
University of California Los Angeles Jonathan and Karin Fielding School of Public Health Los Angeles CA 90024-2905

Dear Dr. Enstrom,

Manuscript number: aad2566

Thank you for submitting your manuscript "Particulate Matter Does Not Cause Premature Deaths" to Science. Because your manuscript was not given a high priority rating during the initial screening process, we have decided not to proceed to in-depth review. The article is a resubmission of manuscript aad0615 ("Transparent Science is Necessary for EPA Regulations"), which we returned to you on 3 August; the two submissions are very similar in substance, and we have reexamined and confirmed the basis for our earlier decision. It is simply a fact that every day we reject many research and commentary submissions because of stringent space requirements and the need to keep the journal to a manageable size. Furthermore, most articles in our Perspectives section are invited, leaving limited room for uninvited contributions. In the context of other articles under consideration we did not find your submission to be competitive. I am sorry to disappoint you again.

We wish you every success when you submit the paper elsewhere.

Sincerely,

Julia Fahrenkamp-Uppenbrink, Ph.D.
Senior Editor
Science

August 17, 2015

Julia Fahrenkamp-Uppenbrink, Ph.D.
Senior Editor & Perspectives Editor
Education: Ph.D., University of Cambridge
Areas: Perspectives in physical sciences and ecology, chemistry, climate, science policy, history of science
jfahrenkamp@science-int.co.uk

Dear Dr. Fahrenkamp-Uppenbrink,

I am submitting the attached manuscript "Particulate Matter Does Not Cause Premature Deaths" for consideration as a *Science* Perspective. The Abstract for this manuscript is:

"A 2014 *Science* Policy Forum stated: "With the estimated benefits of PM reductions playing such a central role in regulatory policy, it is critical to ensure that the estimated health benefits are based on the best available evidence." We challenge the "$1.7 trillion" claim that EPA's fine particulate matter ($PM_{2.5}$) regulations are beneficial because they prevent thousands of "premature deaths" annually. We present strong evidence that $PM_{2.5}$ does not *cause* premature deaths in the U.S.: the major increase in U.S. life expectancy since 1970 is not due to reductions in $PM_{2.5}$; there is no established etiologic mechanism by which $PM_{2.5}$ causes premature death; misrepresentation (falsification) of $PM_{2.5}$–death findings has undermined their credibility; prominently cited American Cancer Society "secret science" data cannot be independently analyzed. Transparent science, as required by the Secret Science Reform Act, is as essential for determining the value of EPA regulations as it is for the research published by *Science.*"

For a full understanding of this submission, it is important that you read the manuscript and this cover letter. In addition, we have provided Supplementary Material, which contains one publication by each of the nine co-authors, in co-author order (71 total pages). These nine publications are all relevant to the contents and background of the manuscript. The names, email addresses, and websites for the co-authors are shown below.

As I explained in my August 10, 2015 email message to Editor-in-Chief McNutt (see below), *Science* has extensively covered the importance of $PM_{2.5}$-related deaths (references 3, 4, 14, 15, and more dating back to 1997), but it has never published a critique of the $PM_{2.5}$ -death relationship. We make a very strong case that there is no *causal* relationship and that scientific misconduct (falsification and unethical use of data) has occurred. The misconduct dates back at least to 2000 and involves the willful collaboration of several EPA-favored scientists. The extensive irrefutable evidence we have presented (particularly in references 10, 12, and 13) is certainly worthy of peer review by *Science*.

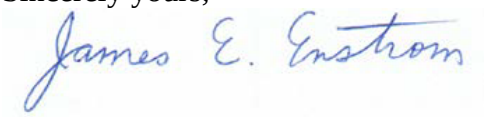
The first two co-authors (Enstrom and Young) are primarily responsible for the writing of the manuscript and we are both long-term AAAS members. I am a 40-year AAAS member, who was once nominated to be an AAAS Fellow, and Dr. Young is an AAAS Fellow. The other co-authors, some of whom have a history as AAAS members, provided input from seven different perspectives and we all support the contents of the manuscript. We are a diverse group of experienced, accomplished, and independent scientists and physicians. We have expertise in the

following relevant disciplines: epidemiology, statistics, toxicology, medicine, environmental economics, environmental law, environmental physics, particle physics, and anthropology. The first five authors have recently spoken and/or written on the subject of this Perspective (see Reference 10 and elsewhere).

We are sure that most AAAS members support transparent science in the way we do and we hope that our viewpoint on PM2.5-related deaths and the need for transparent science can be published in *Science*. We are willing to clarify any aspect of this manuscript that you do not understand and we are willing to make modifications that improve it.

Thank you very much for your consideration.

Sincerely yours,



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From: Marcia McNutt <mmcnutt@aaas.org>
Sent: Monday, August 10, 2015 12:29 PM
To: James E. Enstrom <jenstrom@ucla.edu>
Subject: Re: Reconsider Decision on Science Manuscript aad0615

Dear Dr. Enstrom:

I looked into the history of this submission and discussed it with the Editor. As you can perhaps appreciate, we need to be consistent in how we handle various types of content that we receive. In the case of your submission, on one hand the essay was presented as an alternative view to the Rosenberg et al. PF. We have already published quite a few letters to the editor that express alternate viewpoints and support for the Secret Science Act. If you have additional points that have not already been made in any of the letters we have already published, our Letters editor would be pleased to consider publishing an additional letter from you.

On the other hand, there were some elements of your policy forum submission that were only marginally connected to the Rosenberg piece, and were instead discussing the public health impacts of PM2.5. That issue needs to be submitted as a research article and reviewed as such, rather than as a policy forum. That would be a rather different sort of submission.

I hope this explanation helps you decide in what direction to take your manuscript.

Marcia McNutt

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From: "James E. Enstrom" <jenstrom@ucla.edu>
Date: Monday, August 10, 2015 at 5:59 AM
To: Marcia McNutt <mmcnutt@aaas.org>
Subject: Reconsider Decision on Science Manuscript aad0615

August 10, 2015

Marcia K. McNutt, Ph.D.
Editor-in-Chief, *Science*
mmcnutt@aaas.org

Dear Editor-in-Chief McNutt,

I request that you reconsider the August 3, 2015 rejection by Editor Brad Wible of the July 20, 2015 *Science* Policy Forum Manuscript aad0615 "Transparent Science is Necessary for EPA Regulations". Because of the strength of the evidence that it contains, I request that the manuscript undergo full in-depth review. If you have not done so, I request that you briefly examine the manuscript itself (http://www.scientificintegrityinstitute.org/PFPaper072015.pdf), the detailed cover letter (http://www.scientificintegrityinstitute.org/PFLetter072015.pdf), the 71-page supplement (http://www.scientificintegrityinstitute.org/PFSupp072015.pdf), my June 4, 2015 email message to you (http://www.scientificintegrityinstitute.org/McNuttWSJ060415.pdf), and the outstanding credentials of the nine co-authors (as stated on their personal websites).

Reference 10 of the manuscript contains overwhelming and indisputable evidence of scientific misconduct (falsification) by major investigators who have published key epidemiologic research on the relationship between PM2.5 and mortality. Reference 12 contains clear evidence that the research of these same investigators has violated a 1982 ACS confidentiality statement to CPS II research subjects. This evidence warrants in-depth peer review by *Science*.

For the record, *Science* has never published a major article which challenges the claim the air pollution (particularly PM2.5) currently *causes* "premature death" in the United States, particularly in California. However, *Science* has published several major articles which promote the dangers of air pollution, including the August 21, 1970 article on "Air Pollution and Human Health" (http://www.sciencemag.org/content/169/3947/723.full.pdf), the February 14, 1992 article on "Valuing the Health Benefits of Clean Air" (http://www.sciencemag.org/content/255/5046/812.full.pdf), the April 18, 2014 Policy Forum on "Particulate Matter Matters" (http://www.sciencemag.org/content/344/6181/257.full.pdf), and the May 29, 2015 Policy Forum on "Congress's Attacks on Science-based Rules" (http://www.sciencemag.org/content/348/6238/964.full.pdf).

In the interest of objectivity and integrity regarding an environmental science issue of national significance, *Science* should peer review this manuscript. Please let me know your decision.

Thank you very much.

Sincerely yours,

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Particulate Matter Does Not Cause Premature Deaths

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Peter W. Wood, Ph.D., AAAS Member
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August 17, 2015

An extensive 2011 U.S. Environmental Protection Agency (EPA) cost-benefit report estimates the annual costs required to meet 1990 Clean Air Act (CAA) Amendment regulations to be about $65 billion in 2020. The annual economic benefits of these regulations are estimated to be about $2 trillion in 2020, based primarily on EPA-projected reductions in air pollution-related premature deaths and illness (1). This report has been challenged because the benefits are unproven and depend upon several questionable and unverified assumptions. Among these are assumptions that a linear, no-threshold, *causal* relation exists between fine particulate air pollution ($PM_{2.5}$) and total mortality and that additional life expectancy gained at a median age of about 80 years should be valued at about $80,000 per month. These assumptions are essential because $1.7 trillion (85%) of the $2.0 trillion total benefit estimate is attributable to reductions in premature deaths due to reductions in $PM_{2.5}$. Using discrete uncertainty analysis with plausible alternative assumptions, Cox found that the costs of CAA amendments actually exceed their benefits (2).

Dominici et al. have stated: "With the estimated benefits of PM reductions playing such a central role in regulatory policy, it is critical to ensure that the estimated health benefits are based on the best available evidence. If the estimates are biased upward (downward), then the regulations may be too stringent (lenient)." (3). Because of the urgent need to verify the health benefits of EPA regulations, Congress is enacting the Secret Science Reform Act (SSRA) (4). The SSRA would "prohibit the Environmental Protection Agency from proposing, finalizing, or disseminating regulations or assessments based upon science that is not transparent or reproducible."

Based on the data and research findings that are currently available without the SSRA, we challenge the validity of the annual $1.7 trillion health benefit attributed to reductions in $PM_{2.5}$. Specifically, we present four types of evidence that $PM_{2.5}$ does not *cause* premature deaths.

1) The major increase in U.S. life expectancy since 1970 is not due to reduction in $PM_{2.5}$. In 2009 Pope claimed that from 1980 to 2000 a decrease of 10 $\mu g/m^3$ of $PM_{2.5}$ was associated nationally with a 0.61 year increase in life expectancy based on a correlation involving 51 U.S. metropolitan areas (USMAs) (5). This association was vigorously contested by four independent analyses because the underlying data was available, as would be required by the SSRA. Enstrom found no association whatsoever in 11 California counties (5). Krstic found that the national association claimed by Pope lost statistical significance with the removal of one USMA (Topeka, KS) and that the correlation between changes in $PM_{2.5}$ and life expectancy had so much scatter that it explained almost none of the association (6). Young showed that there was no association in the Western U.S., thereby supporting Enstrom, and showed that the national association was much stronger with income than with $PM_{2.5}$ (7). Cox found no significant association between reductions in $PM_{2.5}$ and total mortality rate between 2000 and 2010 in 483 counties in the 15 most populated states, including California (8). The inconsistencies and weaknesses found in the association means that Pope did not prove the hypothesis that a reduction in $PM_{2.5}$ *causes* an increase in life expectancy. However, since 1970, the year that EPA was established, health-related factors other than air pollution have had a major impact on increasing the longevity of Americans. The total annual age-adjusted death rate in the U.S. has declined by 40% from 12.226 deaths/1000 in 1970 to 7.319 deaths/1000 in 2013. The death rate in California has declined by 45% from 11.370 deaths/1000 in 1970 to 6.301 deaths/1000 in 2013. Life expectancy from birth has increased from 70.8 years in 1970 to 78.8 years in 2013 in the U.S. and from 71.7 years in 1970 to 80.8 years in 2013 in California (9).

2) No plausible etiologic mechanism by which $PM_{2.5}$ *causes* premature death is established. It is implausible that a never-smoker's death could be *caused* by inhalation over an 80 year lifespan of about one teaspoon (~5 grams) of invisible fine particles as a result of daily exposure to 15 $\mu g/m^3$. This level of exposure is equivalent to smoking about 100 cigarettes over a lifetime or 0.004 cigarettes per day, which is the level often used to define a never-smoker. The notion that $PM_{2.5}$ *causes* premature death becomes even more implausible when one realizes that a person who smokes 0.2 cigarettes/day has a daily exposure of about 750 $\mu g/m^3$. If a 10 $\mu g/m^3$ increase in $PM_{2.5}$ actually *caused* a 0.61 year reduction in life expectancy, equivalent to the claim of Pope, then a 0.2 cigarettes/day smoker would experience about a 45-year reduction in life expectancy, assuming a linear relationship between changes in $PM_{2.5}$ and life expectancy. In actuality, never-smokers and smokers of 0.2 cigarettes/day do not experience any increase in

total death rate or decrease in life expectancy, in spite of a 50-fold greater exposure to $PM_{2.5}$ (10). Furthermore, hundreds of toxicology experiments on both animals and humans have not proven that $PM_{2.5}$ at levels up to 750 µg/m³ *causes* death. Finally, the small relative risks of death and other biases and weaknesses of the $PM_{2.5}$ epidemiologic studies do not meet the standards of causality set by the 2011 Federal Judicial Center Reference Manual on Scientific Evidence (11). The legal standard for causality in epidemiologic studies is a large relative risk ($RR \geq 2.0$), not the small relative risk ($RR \sim 1.1$) typically found in $PM_{2.5}$-mortality studies.

3) Misrepresentation of $PM_{2.5}$–death findings has harmed the credibility of epidemiology. The $PM_{2.5}$-mortality relationship has been contested since 1993 because this small risk could be due to well-known biases, such as, confounding variables and the ecological fallacy. In spite of these biases, several major $PM_{2.5}$ investigators continue to assert that selected positive findings prove that $PM_{2.5}$ *causes* death and they continue to ignore or dismiss null $PM_{2.5}$ results. Enstrom prepared a detailed November 15, 2013 document (5000 words of text with 77 URLs) which describes many misrepresentations and exaggerations (12). In particular, Pope and others have ignored null $PM_{2.5}$ findings in California. Serious concerns about the $PM_{2.5}$-mortality relationship in California were expressed at a February 26, 2010 Symposium on "Estimating Premature Deaths from Long-term Exposure to PM2.5" by the California Air Resources Board (CARB). Vastly different viewpoints were expressed by scientists like Enstrom and Pope. Although this Symposium could have led to better understanding and cooperation among $PM_{2.5}$ investigators, it did not. For instance, three Symposium attendees (Pope, Jerrett, and Krewski), published extensive findings in their October 28, 2011 CARB report showing that there was an overall null relationship between $PM_{2.5}$ and mortality in California, if one averaged the results from all nine of their models. This null finding agrees exactly with the null findings of Enstrom and others. However, in their subsequent September 1, 2013 *AJRCCM* paper, "Air Pollution and Mortality in California," they selectively published the positive findings found in one model, but omitted the null findings of the eight other models in their 2011 report.

4) The American Cancer Society actively supports "secret science" $PM_{2.5}$ epidemiology. Since 1995 ACS has repeatedly allowed its 1982 Cancer Prevention Study (CPS II) data to be selectively used for $PM_{2.5}$ epidemiology research. However, ACS has refused to release the CPS II data or allow analysis that addresses the legitimate concerns raised by qualified critics of this "secret science" research. ACS is well aware of the scientific controversy generated by the original 1995 Pope *AJRCCM* paper and subsequent papers that have been used by EPA as a primary justification for its $PM_{2.5}$ regulations. The demand for CPS II data access has increased as $PM_{2.5}$–related regulations have gotten stricter, more expensive, and more implausible. While ACS refuses any independent access to its CPS II data, because of alleged concerns about subject confidentiality, it has repeatedly allowed Pope and his collaborators to violate a confidentiality pledge made to CPS II subjects. When personal questionnaire data was collected from CPS II subjects upon enrollment in late 1982, ACS informed them with this exact sentence: "We will **never** release information about any particular person and will not release addresses to any agency for any purpose, whatsoever" (13). Both the September 1, 2013 *AJRCCM* paper and the new January 2, 2015 *Circulation Research* paper by Pope include findings based on linking the home address of each study subject to a geographically estimated $PM_{2.5}$ concentration, in violation of the 1982 agreement.

Our evidence that $PM_{2.5}$ does not *cause* premature deaths invalidates the $1.7 trillion annual benefit that EPA attributes to reductions in $PM_{2.5}$ and supports Cox's findings that the economic costs of EPA CAA Amendment regulations exceed the resulting health benefits. Because the scientific and economic stakes are high for America, there is an urgent need for transparency and reproducibility in the science and data underlying EPA regulations, as required by the SSRA. The data access requirement in the SSRA is very similar to the one *Science* has for its research papers and to the one recently recommended by the editors of 30 major journals, including *Science* (14). Even an environmental organization that objects to the SSRA, the Union of Concerned Scientists, realizes that "public trust in science increases when we all have access to the same base of evidence" (15).

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From: Hohmann, Ann (HHS/OASH) <Ann.Hohmann@hhs.gov>
Sent: Wednesday, December 21, 2016 10:46 AM
To: jenstrom@ucla.edu
Cc: Garfinkel, Susan J (HHS/OASH) <Susan.Garfinkel@hhs.gov>; Trenkle, William (OS/OASH) <William.Trenkle@hhs.gov>
Subject: DIO 6351

Dear Dr. Enstrom,

As the ORI expert in biostatistics and public health, Dr. Garfinkel gave me the materials that ORI has regarding your November 7 conversation with Dr. Trenkle about the Jerrett et al. 2013 paper and your emailed materials to AskORI on November 11, 2016. I have read and reviewed all of the materials. I understand your concern about the way the data were presented in the paper and used elsewhere. Though I have no clinical training, it appears that the relative risks reported do not seem to rise to the level of clinical significance and do not provide evidence that air pollution is directly responsible for mortality. Presenting this data as such, may be a question only of bad science.

However, "bad" or sloppy science is not the same as research misconduct. ORI's regulation (42 CFR 93.103) defines research misconduct, as you know, as "fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results." While it is true that Dr. Jerrell and colleagues did not cite all the research showing that the relative risk is very, very close to 1 and only emphasized specific numbers, they did not, as far as I can tell, change their data to get a statistically and clinically significant result. The weak results are there for all to see. Thus, there does not appear to be falsification.

To overinterpret one's data is certainly inappropriate, but would be a matter to raise with the reviewers and the journal editors, who apparently did not insist that the authors tone down their conclusions. ORI is aware that the research on the effects of air pollution is certainly not the only area of science where there is open controversy. Just this morning, *The Scientist* ran an article on the controversy regarding the effects of sugar intake (http://www.the-scientist.com/?articles.view/articleNo/47819/title/Industry-Funded-Sugar-Study--Don-t-Trust-Other-Sugar-Studies/&utm_campaign=NEWSLETTER_TS_The-Scientist-Daily_2016&utm_source=hs_email&utm_medium=email&utm_content=39616948&_hsenc=p2ANqtz-8Q5JhLgCWe4CJboPROHvuwP0x1fr3XLwxkrNXixW4tqdO_29UCNh4fj6q1IwpolH0ferca7iYMwC0oyjX7kTTvwmW8mA&_hsmi=39616948). Unfortunately, we all are aware that science loses when research is influenced by special interest groups.

The Public Health Service (PHS) regulation, under which ORI acts, is not meant to be a way to put the brakes on controversial science. The mission of our Office is to protect PHS research funds from researchers who knowingly and intentionally make up data or change them to serve their purposes. In the documents you provided, there does not appear to be evidence that Dr. Jerrell and his colleagues have done that. Without clear evidence of fabrication and/or falsification of data (and not just failing to cite contrary data), ORI is unable to further pursue your allegations. What you do and have been doing for decades – promoting your own research results – in scientific and other venues may be the best way to combat opposing viewpoints. Good luck in the future.

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Allegation of Research Misconduct by Dr. Michael Jerrett and Co-Authors

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November 11, 2016

I allege research misconduct (falsification) by UCLA Professor Michael Jerrett, Ph.D., and his primary co-authors C. Arden Pope, Ph.D., Daniel Krewski, Ph.D., George Thurston, Sc.D., Richard T. Burnett, Ph.D., Michael J. Thun, M.D., and Susan P. Gapstur, Ph.D., regarding their attached September 1, 2013 *AJRCCM* paper "Spatial Analysis of Air Pollution and Mortality in California" (http://www.atsjournals.org/doi/abs/10.1164/rccm.201303-0609OC). The authors received a portion of their funding for this research from NIEHS and CDC within DHHS. While claiming that fine particulate matter ($PM_{2.5}$) was associated with mortality from all causes (total mortality) in their study, the authors omitted their own null findings and the null findings of others. These omitted findings clearly show NO association. Thus, they have engaged in falsification as defined by DHHS and the Public Health Service: "omitting data or results such that the research is not accurately represented in the research record" (Section 93.103(b) of 42 CFR 93) (http://ori.hhs.gov/sites/default/files/42_cfr_parts_50_and_93_2005.pdf).

The *AJRCCM* paper claims there is a positive relationship between $PM_{2.5}$ and mortality from all causes in California because their "conurbation" land use regression (LUR) model yielded a slightly positive relative risk of RR=1.060 (1.003-1.120), as shown in Table 6. However, complete study results are in the October 28, 2011 Jerrett CARB Final Report "Spatiotemporal Analysis of Air Pollution and Mortality in California Based on the American Cancer Society Cohort: Final Report" (http://www.arb.ca.gov/research/apr/past/06-332.pdf). The eight entirely null models, shown in the attached Report Table 22, were omitted from the paper. The results for all nine models are shown in my Summary Table on the next page. The weighted average relative risk for all nine models is RR=1.002 (0.992-1.012), which means NO relationship.

Furthermore, the *AJRCCM* paper does not cite any of the null California $PM_{2.5}$-mortality results from other papers and reports dating back to 2000, including earlier findings by Dr. Jerrett. These results are shown on the next page, as well as on the attached August 15, 2016 Summary Table that I presented to SCAQMD (http://www.aqmd.gov/home/library/clean-air-plans/air-quality-mgt-plan/Draft2016AQMP/2016-aqmp-appendix-i-comment-letter (letter #7). The weighted average relative risk for the most recent result from each of the six different California cohorts is RR=0.999 (0.988-1.010), which means NO relationship.

I contend that the falsification in the paper was deliberate because it was done after extensive criticism of the June 9, 2011 Draft Report and the October 28, 2011 Final Report. This criticism was presented to the authors via CARB by myself, William M. Briggs, Ph.D., John D. Dunn, M.D., S. Stanley Young, Ph.D., Gordon Fulks, Ph.D., and Frederick W. Lipfert, Ph.D. A compilation of all criticism of the 2011 Report is attached (http://www.scientificintegrityinstitute.org/JerrettCriticism102811.pdf). Detailed criticism of the *AJRCCM* paper, including its misrepresentation of the results contained in the CARB Report, was given by Dr. Briggs in his statistical blogs of August 6, 2013 (http://wmbriggs.com/blog/?p=8720), September 11, 2013 (http://wmbriggs.com/blog/?p=8990), and September 25, 2013 (http://wmbriggs.com/blog/?p=9241).

In conclusion, Dr. Jerrett and his co-authors falsified the relationship between $PM_{2.5}$ and total mortality in California in their *AJRCCM* paper by deliberately omitting their own null evidence and the null evidence of others. This is quite disturbing because $PM_{2.5}$-mortality claims in the paper are being used as public health justification for the very costly SCAQMD 2016 Air Quality Management Plan (http://www.aqmd.gov/).

Summary Table. Epidemiologic cohort studies of $PM_{2.5}$ and total mortality in California, 2000-2016
Relative risk of death from all causes (RR and 95% CI) associated with increase of 10 µg/m³ (IQR=10) in $PM_{2.5}$

Study (Year)	Cohort	RR	95% CI	F-U Years
Jerrett 2013 (*AJRCCM* Table 6 Model)	CA CPS II	1.060	(1.003–1.120)	1982-2000
Jerrett 2011 (CARB Report Figure 22)	CA CPS II			
KRG IND Model (Table 30, IQR=8.52902→10.0)		0.992	(0.965-1.020)	1982-2000
KRG ZIP Model (Table 28, IQR=8.4735→10.0)		0.993	(0.964-1.023)	1982-2000
KRG IND+O3 Model (Figure 22 extrapolated, IQR=10.0)		1.020	(0.980-1.060)	1982-2000
IDW IND Model (Table 29, IQR=8.74→10.0)		1.003	(0.978-1.028)	1982-2000
IDW ZIP Model (Table 27, IQR=9.37→10.0)		0.995	(0.967-1.025)	1982-2000
BME IND Model (Figure 22 extrapolated, IQR=10.0)		1.000	(0.975-1.025)	1982-2000
LUR IND Model (Table 31, IQR=5.35→10.0)		1.009	(0.980-1.039)	1982-2000
LUR IND+5 Metro Model (Abstract Table 1, IQR=10.0) [Jerrett 2013 Model]		1.080	(1.000-1.150)	1982-2000
RS IND Model (Table 32, IQR= 5.39→10.0)		0.998	(0.968-1.029)	1982-2000
Weighted Average of All Nine Models		1.002	(0.992-1.012)	1982-2000
Other Results by Jerrett and Other Investigators				
Krewski Jerrett 2000 (RR for CA 2010)	CA CPS II	0.872	(0.805-0.944)	1982-1989
McDonnell 2000 *	CA AHSMOG	~ 1.00	(0.95 – 1.05)	1977-1992
Jerrett 2005	CPS II (LA Basin Only)	1.11	(0.99 - 1.25)	1982-2000
Enstrom 2005 *	CA CPS I	0.997	(0.978-1.016)	1983-2002
Zeger 2008 *	MCAPS "West=CA+OR+WA"	0.989	(0.970-1.008)	2000-2005
Jerrett 2010	CA CPS II	~ 0.994	(0.965-1.025)	1982-2000
Krewski Jerrett 2009 (RR for CA 2010)*	CA CPS II	0.968	(0.916-1.022)	1982-2000
Lipsett Jerrett 2011	CA Teachers	1.01	(0.95 – 1.09)	2000-2005
Ostro 2011	CA Teachers	1.06	(0.96 – 1.16)	2002-2007
Ostro 2015 *	CA Teachers	1.01	(0.98 - 1.05)	2001-2007
Thurston 2016 *	CA NIH-AARP	1.02	(0.99 - 1.04)	2000-2009
Weighted Average of Latest Results (*) from Six California Cohorts		0.999	(0.988-1.010)	

Spatial Analysis of Air Pollution and Mortality in California

Michael Jerrett[1], Richard T. Burnett[2], Bernardo S. Beckerman[1], Michelle C. Turner[3], Daniel Krewski[3,4], George Thurston[5], Randall V. Martin[6], Aaron van Donkelaar[6], Edward Hughes[7], Yuanli Shi[3], Susan M. Gapstur[8], Michael J. Thun[8], and C. Arden Pope III[9]

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***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 [O_3], and nitrogen dioxide [NO_2]) with the risk of mortality in a large cohort of California adults using individualized exposure assessments.**

***Methods*: For fine particulate matter and NO_2, we used land use regression models to derive predicted individualized exposure at the home address. For O_3, 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, O_3, and NO_2 was positively associated with ischemic heart disease mortality. NO_2 (a marker for traffic pollution) and fine particulate matter were also associated with mortality from all causes combined. Only NO_2 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, O_3, and NO_2 with mortality. The positive associations of NO_2 suggest that traffic pollution relates to premature death.**

Keywords: air pollution; mortality; survival analyses; GIS; spatial analyses

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Several cohort studies have examined whether long-term exposure to air pollution is associated with premature death. The results of these studies have been mixed, possibly due to errors introduced in the exposure assessment process.

What This Study Adds to the Field

To address this potential problem, this study assigned members of the American Cancer Society Cancer Prevention Study II Cohort residing in California more precise exposure assignments at their home address using advanced exposure models. The study provides the first evidence that ozone is significantly associated with cardiovascular mortality, particularly from ischemic heart disease; shows a strong association between nitrogen dioxide (NO_2) and lung cancer; and demonstrates that that fine particulate matter with aerodynamic diameter of 2.5 μm or less ($PM_{2.5}$) and NO_2 associate independently with premature death from all causes and cardiovascular disease. The findings from this study confirm earlier evidence on $PM_{2.5}$ associations with mortality and expand the evidence base markedly on associations between ozone or NO_2 and premature death.

A substantial body of evidence suggests that long-term exposure to combustion-related air pollution contributes to the development of chronic disease and can lead to premature death (1–6). Exposure to air pollution affects huge populations globally. As a result, the public health impact can be large (7, 8).

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Author Contributions: M.J. conceived the study, led all analyses, contributed to the development of the exposure models, drafted much of the text, and responded to comments from co-author reviewers. B.S.B. ran many of the statistical models that led to the exposure assessments, conducted geographic analyses, contributed text, and assisted with interpreting the results. R.T.B. supplied expert statistical advice on the analyses, drafted sections of the paper, and assisted with the interpretation of the results. E.H. developed the statistical programs used to interpret the random effects models, helped to interpret the results, and supplied key statistical advice on the interpretation. D.K. contributed to the original grant proposal, assisted with interpretation of the results, and wrote sections of the paper. C.A.P. contributed to the statistical analyses, wrote sections of the text, and assisted with interpreting the results. S.M.G. is the Principal Investigator of the ACS CPS-II cohort and commented on the final draft of the paper. She also oversaw the geocoding process for exposure assignment. M.J.T. assisted with interpretation of the statistical models and supplied expert medical epidemiological advice on the results. G.T. assisted with the conception of the study, supplied key information on interpreting the pollution models, and commented on several drafts of the paper, which changed the interpretation of the results. M.C.T. contributed text and tables, helped to assemble supporting data, assisted with the statistical modeling, interpreted the results, and served as a liaison with the American Cancer Society for code review and data access. R.V.M. and A.v.D. contributed the remote sensing models used to derive estimates of $PM_{2.5}$, supplied text, edited versions of the paper, and gave advice on atmospheric chemistry issues. Y.S. ran the statistical models, managed the data, prepared code for review by the American Cancer Society, prepared all of the tables and associated text, and assisted with the interpretation of the results.

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Using data from the American Cancer Society's (ACS) Cancer Prevention Study II (CPS-II), a nationwide cohort study of nearly 1.2 million adults who have been followed for mortality since 1982, several studies have been published examining associations of metropolitan-level air pollution and mortality (3, 9–11). In those studies, exposure data were derived at the metropolitan scale, relying on between-city exposure contrasts using central monitor data.

In addition, two studies using CPS-II data evaluated within-city (i.e., Los Angeles and New York) exposure contrasts in fine particulate matter with aerodynamic diameter of 2.5 μm or less ($PM_{2.5}$) (2, 3). Both studies assigned exposure to the ZIP code postal area of residence, but in the study from Los Angeles (2), the $PM_{2.5}$–mortality dose–response relationship was stronger than that for the full nationwide cohort, and in the study from New York City, the relationship was weaker (3). Although the ZIP code areas were more specific than the metropolitan area, they may have introduced error in the exposure assignment that led to the inconsistent results. Another recent study based on individualized exposures found little association between $PM_{2.5}$ exposure and mortality in a cohort of male health professionals (12); however, in that study if home address records were missing, then workplace addresses were used for exposure assignment, possibly leading to measurement error. Conversely, an earlier study based on a large cohort of nurses reported strong and significant associations of $PM_{2.5}$ with mortality, using essentially the same exposure model but with complete home address information for exposure assignment (13). Viewed together, these findings suggest that uncertainties in the characterization of the dose–response relationship may be due partly to the errors in exposure estimates arising from the lack of specificity of the coordinates used to link addresses to the exposure estimates. A need therefore exists to investigate how individualized estimates of exposure at the home address influence the observed dose–response function.

In the present analysis, individualized exposure estimates were developed and assigned to the home address for more than 73,000 California residents enrolled in CPS-II. These estimates were used to assess the association of three types of air pollutants ($PM_{2.5}$, ozone [O_3], and nitrogen dioxide [NO_2]) with risk of mortality. We also sought to understand the joint effects of the pollutants in co- and multipollutant models. Although CPS-II is a nationwide cohort, we limited this analysis to California because the state has a wide range of pollution exposures and a good monitoring network.

TABLE 1. PARTICIPANT CHARACTERISTICS IN THE NATIONWIDE STUDY COMPARED WITH THE CALIFORNIA COHORT

Variable	Nationwide	California
Participants, n	485,426	73,711
Participants died from, %		
All causes	26.4	26.8
CPD	13.1	13.6
CVD	10.9	10.9
IHD	6.1	6.2
Respiratory	2.2	2.7
Lung cancer	2.0	2.0
All other causes	11.3	11.2
Demographics		
Mean (SD) age, yr	56.6 (10.5)	57.4 (10.6)
Female, %	56.6	56.2
White, %	94.2	91.6
Education, %		
<High school	12.1	8.7
High school	31.3	22.9
>High school	56.6	68.4
Alcohol consumption, %		
Beer	22.9	24.1
No beer	9.5	10.9
Missing beer	67.6	65.0
Liquor	27.6	35.1
No liquor	8.7	8.9
Missing liquor	63.7	56.0
Wine	23.1	37.3
No Wine	8.9	7.7
Missing wine	68.0	55.0
Smoking status		
Current smoker, %	21.6	19.4
Cigarettes per day	22.1 (12.4)	21.5 (12.6)
Years of smoking	33.5 (11.0)	34.1 (11.4)
Former smoker, %	25.9	28.9
Cigarettes per day	21.4 (14.7)	20.8 (14.7)
Years of smoking	22.2 (12.6)	22.1 (12.7)
Age when started smoking, %		
<18 yr (current smoker)	8.9	7.7
<18 yr (former smoker)	10.0	10.3
Hours per day exposed to smoking	3.2 (4.4)	2.7 (4.1)

Definition of abbreviations: CPD = cardiopulmonary disease; CVD = cardiovascular disease; IHD = ischemic heart disease.

METHODS

The ACS CPS-II cohort was enrolled in 1982 (details are presented in References 3 and 14). For the purposes of this paper, vital status was ascertained through to 2000. Subjects with valid postal addresses had their residential locations geocoded. After limiting to residence in the State of California and making exclusions for missing data on key covariates, there were 73,711 subjects available for analysis.

We assigned exposure for $PM_{2.5}$, NO_2, and O_3. Monthly average monitoring data for $PM_{2.5}$ were available at 112 sites between 1998 and 2002. NO_2 and O_3 data were available over the period 1988 to 2002 at 138 and 262 sites, respectively. $PM_{2.5}$ and NO_2 exposures were assessed using land use regression (LUR) models that were selected from more than 70 possible land use covariates (15). The $PM_{2.5}$ model included an advanced remote sensing model coupled with atmospheric modeling (16). LUR models were selected with the deletion/substitution/addition algorithm (17). The deletion/substitution/addition algorithm, which aggressively tests nearly all polynomial covariate combinations, uses v-fold cross-validation to evaluate potential models. In this instance of v-fold cross-validation, data are first partitioned into 10 roughly equal parts (i.e., folds). The model is then trained on nine folds and cross-validated on the left out fold. This is repeated 10 times so every fold is used as a cross-validation data set. The model selection method avoids the potential problems of over-fitting on all the data or on a large training set and then using a cross-validation subset (details presented References 15 and 18). For O_3, we extracted monthly averaged values from 1988 to 2002 and calculated the inverse distance weighting (IDW) models with the decay parameter set to the inverse of the square of the distance from all sites within a 50-km radius of operational monitors during any particular month. Estimates for all pollutants were then assigned to geocoded baseline residential addresses of the CPS-II subjects, and the monthly values were averaged for the entire time period available.

We used a comprehensive set of individual risk factor variables operationalized through 42 covariates similar to those used in previous studies of the CPS-II cohort (3, 18). Individual-level variables controlled for lifestyle, dietary, demographic, occupational, and educational factors, and ecological variables extracted from the 1990 US Census in the ZIP code of residence were used to control for potential "contextual" neighborhood confounding (including unemployment, poverty, income inequality, and racial composition).

We assessed the association between air pollution and mortality using standard and multilevel Cox proportional hazards regression models. Control for place of residence was also applied in the five largest conurbations—defined by the four consolidated metropolitan statistical areas of California and the metropolitan statistical area of San Diego—that potentially have lower mortality rates than nonmetropolitan areas. This pattern is consistent with what has been termed the "nonmetropolitan mortality penalty," where nonmetropolitan areas tend to have higher death rates compared with metropolitan areas (19). Because metropolitan areas generally have higher pollution, failure to control for residence in large urban areas has the potential to confound associations between mortality and air pollution.

TABLE 2. DISTRIBUTION OF AIR POLLUTANTS AT THE INDIVIDUAL LEVEL*

Air Pollution	Subjects (n)	Mean	Variance	Percentiles								
				0	5	10	25	50	75	90	95	100
$PM_{2.5}$ LUR, $\mu g/m^3$	73,711	14.09	12.42	4.25	8.29	9.45	11.60	14.03	16.90	18.42	19.36	25.09
NO_2 LUR, ppb	73,711	12.27	8.54	3.04	7.93	8.81	10.21	12.12	14.33	16.22	17.09	21.94
Ozone IDW, ppb	73,711	50.35	212.18	17.11	28.81	31.13	36.83	50.80	61.00	68.56	74.18	89.33

Definition of abbreviations: IDW = inverse distance weighting model; LUR = land use regression.
*Years represented by air pollution exposure estimates: $PM_{2.5}$ LUR, 1998–2002; NO_2 LUR and ozone IDW, 1988–2002.

We evaluated the association between air pollution and several causes of death, including cardiovascular disease (CVD), ischemic heart disease (IHD), stroke, respiratory disease, and lung cancer. We also evaluated "all other" causes of death, excluding the preceding causes, to serve as a negative control. Finally, we evaluated mortality from all causes combined.

RESULTS

Table 1 compares characteristics of the nationwide CPS-II cohort used in previous analyses to the subset selected for this analysis (a detailed description of exclusions and sample selection is provided in Reference 18). Minor differences in alcohol consumption and education are apparent, but overall the California cohort appears to have characteristics similar to the nationwide cohort. Subjects included in this analysis were widely distributed across California, giving comprehensive coverage for much of the State's population (54/58 California counties were represented).

Table 2 shows the mean, variance, and percentiles of each pollutant as estimated by the different models used in this study. All models display considerable variation in the exposures assigned to the home address. Most pollutants show moderate to high positive correlations (Table 3). The exception is between interpolated ozone and NO_2 estimates, which displays a weak negative correlation.

Estimates of adjusted relative risk (RR) and 95% confidence intervals (CIs) are reported in Table 4. All RR estimates are given over the interquartile range of each pollutant. We assessed residual spatial autocorrelation in the health effect estimates with a multilevel Cox model (3). Because the multilevel clustering and autocorrelation analysis had minimal impact on the risk estimates, only results for the standard Cox models are reported.

For $PM_{2.5}$ we observed significantly elevated RR for mortality from all causes (RR, 1.032; 95% CI, 1.002–1.068), CVD (RR, 1.064; 95% CI, 1.016–1.114), and IHD (RR, 1.111; 95% CI, 1.045–1.181). Deaths from stroke, respiratory causes, and lung cancer had positive RRs with less precision and CIs that included unity. No association is present with other causes.

NO_2 is significantly and positively associated with all-cause (RR, 1.031; 95% CI, 1.008–1.056), CVD (RR, 1.048; 95% CI, 1.010–1.087), IHD (RR, 1.066; 95% CI, 1.015–1.119), stroke (RR, 1.078; 95% CI, 1.016–1.145), and lung cancer (RR, 1.111; 95% CI, 1.020–1.210) mortality. Respiratory deaths and those from all other causes were not associated with NO_2.

Although there was no association between O_3 and all-cause mortality, there was a positive association with CVD mortality (RR, 1.045; 95% CI, 0.986–1.108) and a significantly elevated risk for IHD death (RR, 1.104; 95% CI, 1.021–1.194). O_3 had a positive association with stroke and respiratory deaths that lacked precision and a marginally significant negative association with deaths from lung cancer. There was no association with other causes.

We compared the risk estimates obtained from single-pollutant models with risk estimates from two-pollutant and multipollutant models (Table 5). In models that included $PM_{2.5}$ and NO_2, the $PM_{2.5}$ associations with mortality from all causes were reduced to about half the size of those in the single pollutant models, and the estimates became insignificant. When O_3 and $PM_{2.5}$ were included in the same all-cause mortality model, the effects from $PM_{2.5}$ remained significantly elevated and became slightly larger. A similar pattern was observed with CVD and IHD, where the effects of $PM_{2.5}$ were attenuated with NO_2 but remained unchanged in the presence of the O_3 estimates (Figure 1).

The NO_2 associations with CVD and IHD were attenuated when $PM_{2.5}$ was included in the model, but they became slightly larger when O_3 was included. O_3 continued to show elevated risks for CVD and IHD in the two-pollutant models with either NO_2 or $PM_{2.5}$ included. For respiratory deaths, $PM_{2.5}$ continued to have elevated but insignificant risk estimates, whereas neither of the other pollutants was associated with respiratory mortality. For lung cancer, NO_2 consistently displayed significantly elevated risks in two-pollutant models. When combined with O_3, $PM_{2.5}$ associations with lung cancer increased but remained insignificant.

In multipollutant models containing all three pollutants, NO_2 had the strongest associations with all-cause mortality and CVD and with lung cancer, whereas $PM_{2.5}$ tended to have stronger effects on deaths from IHD. Intercorrelations among the various pollutants, however, likely contribute to bias in individual pollutant risk estimates in such simultaneous pollutant models, so these results must be interpreted with caution. In multipollutant models, $PM_{2.5}$ continued to produce elevated risks for all-cause, CVD, IHD, and respiratory mortality, but none of these estimates were statistically significant. O_3 had elevated risks on CVD and remained a significant predictor of IHD deaths even with the other pollutants in the model.

There was little evidence of associations with the other causes of death in the two-pollutant or multipollutant models.

Figure 1 presents results from cumulative risk index (CRI) models for CVD and IHD mortality that show the extent to which one pollutant confounds the others (details of the CRI methods are provided in the online supplement). Comparisons of CRI based on combinations of pollutants estimated jointly and independently can also provide a means of understanding the joint impacts of the atmospheric mixture on survival. For example, with CVD mortality, the combined hazard ratio (HR) of NO_2 and O_3 assuming independence is $1.048 \times 1.045 = 1.095$. However, the combined HR based on the two-pollutant survival model is 1.121, suggesting a synergy of effect among the pollutants. A similar pattern of synergy is also observed for IHD mortality.

Such a comparative assessment is illustrated in Figure 1 for three pollutants (NO_2, O_3, and $PM_{2.5}$) and two causes of death (CVD and IHD). The HRs evaluated at their respective interquartile

TABLE 3. PEARSON CORRELATIONS (×100) BETWEEN AIR POLLUTANTS (CALIFORNIA OVERALL)

	$PM_{2.5}$ LUR	NO_2 LUR
$PM_{2.5}$ LUR	—	—
NO_2 LUR	55.10	—
Ozone IDW	55.81	−0.71

Definition of abbreviations: IDW = inverse distance weighting model; LUR = land use regression; $PM_{2.5}$ = particulate matter with aerodynamic diameter of 2.5 μm or less.

TABLE 4. AMERICAN CANCER SOCIETY COHORT WITH FOLLOW-UP FROM 1982 TO 2000, ADJUSTING FOR 42 INDIVIDUAL-LEVEL COVARIATES, FIVE CONSOLIDATED METROPOLITAN STATISTICAL AREA CITY INDICATORS, SEVEN 1990 ECOLOGIC COVARIATES STRATIFYING THE BASELINE HAZARD FUNCTION BY AGE (1-YR GROUPINGS), GENDER, AND RACE USING THE STANDARD COX SURVIVAL MODEL

	Cause of Death						
Air Pollutant	All Causes (*n* = 19,733)	Cardiovascular (*n* = 8,046)	Ischemic Heart (*n* = 4,540)	Stroke (*n* = 3,068)	Respiratory (*n* = 1,973)	Lung Cancer (*n* = 1,481)	All Others (*n* = 8,233)
$PM_{2.5}$ LUR	1.032 (1.002–1.062)*	1.064 (1.016–1.114)	1.111 (1.045–1.181)	1.065 (0.988–1.148)	1.046 (0.953–1.148)	1.062 (0.954–1.183)	0.994 (0.950–1.040)
NO_2 LUR	1.031 (1.008–1.056)	1.048 (1.010–1.087)	1.066 (1.015–1.119)	1.078 (1.016–1.145)	0.999 (0.927–1.077)	1.111 (1.020–1.210)	1.009 (0.973–1.046)
Ozone IDW	0.998 (0.960–1.036)	1.045 (0.986–1.109)	1.104 (1.021–1.194)	1.011 (0.919–1.112)	1.017 (0.902–1.147)	0.861 (0.747–0.992)	0.967 (0.911–1.027)

Definition of abbreviations: IDW = inverse distance weighting model; LUR = land use regression; $PM_{2.5}$ = particulate matter with aerodynamic diameter of 2.5 μm or less.

* Relative risks are shown for the interquartile range of exposure in each pollutant (i.e., 5.3037 $\mu g/m^3$ for $PM_{2.5}$, 4.1167 ppb NO_2, and 24.1782 ppb for O_3). Values in parentheses are 95% confidence intervals.

ranges for the three pollutants are presented singly, based on the three possible two-pollutant models, and based on the single three-pollutant model. There is some modest increase in the CRI for models containing $PM_{2.5}$ and either NO_2 or O_3 compared with each of the single-pollutant models. The model with NO_2 and O_3, however, is larger than either of the other two-pollutant models and has a similar CRI to the three-pollutant model, suggesting that a combination of NO_2 and O_3 is sufficient to characterize the toxicity of the pollutant mixture in this study, at least with respect to the three pollutants considered.

The CRI implies that there is little marginal contribution to CVD and IHD mortality from the addition of $PM_{2.5}$ in the presence of the mixture represented by NO_2 and O_3. We also caution that in this interpretation the CIs clearly overlap each of the CRIs we have calculated. This limits our ability to infer the set of minimally sufficient pollutants required to fully capture the toxicity of the atmosphere in California.

DISCUSSION

We sought to estimate the effects of three criteria air pollutants on premature death in California. This study was motivated by earlier research from Los Angeles that showed $PM_{2.5}$ exerted a large significant effect on all-cause mortality and mortality from CVD. Other studies, including those based on data from the ACS CPS-II, showed heterogeneous health effect estimates that potentially resulted from a lack of precision in the exposure assessment. To address this problem, we developed detailed exposure assessment models that included auxiliary information and assigned resulting estimates of exposure to the baseline residential address of more than 73,000 subjects with valid data from the ACS CPS-II cohort.

Several important results deserve mention. First, findings of associations of $PM_{2.5}$ with all-cause and cardiovascular mortality are consistent with those reported from our previous analyses of the full, nationwide CPS-II cohort (3). Table 6 shows that results for all-cause, CVD, and IHD mortality from the current study are similar, although they are slightly weaker than from the study of the nationwide cohort. The difference in exposure metrics had little impact on the risk estimates for $PM_{2.5}$. We also fit models specifically for Los Angeles to compare with earlier results (2). Although the sample size is different here due to limitations in the geocoding, the results show that the effects in Los Angeles continue to be higher than those in the national study or in the rest of the state. We also examined the dose–response function for nonlinearity because levels in Los Angeles are generally higher than in many other parts of the state, but we found no evidence of nonlinearity in the dose–response function based on visual inspection of spline plots and formal measures of model fit (Akaike information criteria and Bayesian information criteria results not shown). This suggests that the population of Los Angeles is more susceptible to air pollution, that the air pollution there is more toxic, or both.

The strongest associations with mortality appear to be for exposures that are markers for traffic-related air pollution. The largest predictors of NO_2 in the LUR model were measures of roadway length near the monitors, although we cannot rule out other contributions to the modeled concentrations, such as heating and industrial sources, particularly given the generally higher

TABLE 5. TWO-POLLUTANT AND MULTIPOLLUTANT MODEL RESULTS FROM THE AMERICAN CANCER SOCIETY COHORT WITH FOLLOW-UP FROM 1982 TO 2000, ADJUSTING FOR 42 INDIVIDUAL-LEVEL COVARIATES, FIVE CONSOLIDATED METROPOLITAN STATISTICAL AREA CITY INDICATORS, SEVEN 1990 ECOLOGIC COVARIATES STRATIFYING THE BASELINE HAZARD FUNCTION BY AGE (1-YR GROUPINGS), GENDER, AND RACE USING THE STANDARD COX SURVIVAL MODEL

	Cause of Death						
Air Pollutant	All Causes (*n* = 19,733)	Cardiovascular (*n* = 8,046)	Ischemic Heart (*n* = 4,540)	Stroke (*n* = 3,068)	Respiratory (*n* = 1,973)	Lung Cancer (*n* = 1,481)	All Others (*n* = 8,233)
$PM_{2.5}$ LUR	1.015 (0.980–1.050)†	1.043 (0.989–1.101)	1.090 (1.015–1.170)	1.019 (0.934–1.112)	1.064 (0.954–1.185)	0.985 (0.867–1.119)	0.984 (0.933–1.038)
NO_2 LUR	1.025 (0.997–1.054)	1.030 (0.987–1.075)	1.029 (0.972–1.090)	1.070 (0.998–1.147)	0.973 (0.891–1.063)	1.118 (1.010–1.236)	1.016 (0.973–1.060)
$PM_{2.5}$ LUR	1.035 (1.004–1.067)	1.057 (1.008–1.109)	1.093 (1.027–1.165)	1.067 (0.987–1.153)	1.045 (0.949–1.151)	1.103 (0.985–1.234)	1.002 (0.955–1.050)
Ozone IDW	0.985 (0.947–1.025)	1.025 (0.964–1.089)	1.070 (0.987–1.161)	0.988 (0.894–1.091)	1.001 (0.883–1.134)	0.832 (0.719–0.964)	0.966 (0.908–1.029)
NO_2 LUR	1.032 (1.008–1.057)	1.055 (1.016–1.095)	1.082 (1.029–1.137)	1.082 (1.019–1.150)	1.001 (0.928–1.080)	1.097 (1.006–1.196)	1.006 (0.970–1.043)
Ozone IDW	1.006 (0.968–1.046)	1.062 (1.000–1.127)	1.132 (1.045–1.227)	1.034 (0.938–1.140)	1.017 (0.901–1.149)	0.882 (0.764–1.019)	0.968 (0.912–1.029)
$PM_{2.5}$ LUR	1.015 (0.977–1.055)	1.024 (0.965–1.086)	1.048 (0.969–1.133)	1.008 (0.915–1.110)	1.070 (0.949–1.207)	1.040 (0.902–1.198)	0.995 (0.938–1.056)
NO_2 LUR	1.025 (0.995–1.056)	1.044 (0.996–1.093)	1.059 (0.995–1.126)	1.079 (1.000–1.163)	0.969 (0.881–1.066)	1.078 (0.967–1.201)	1.008 (0.963–1.056)
Ozone IDW	0.999 (0.957–1.042)	1.050 (0.982–1.122)	1.106 (1.012–1.209)	1.031 (0.925–1.149)	0.984 (0.860–1.126)	0.866 (0.739–1.015)	0.971 (0.908–1.038)

Definition of abbreviations: IDW = inverse distance weighting model; LUR = land use regression model; $PM_{2.5}$ = particulate matter with aerodynamic diameter of 2.5 μm or less.

† Relative risks are shown for the interquartile range of exposure in each pollutant (i.e., 5.3037 $\mu g/m^3$ for $PM_{2.5}$; 4.1167 ppb NO_2; and 24.1782 ppb for O_3). Values in parentheses are 95% confidence intervals.

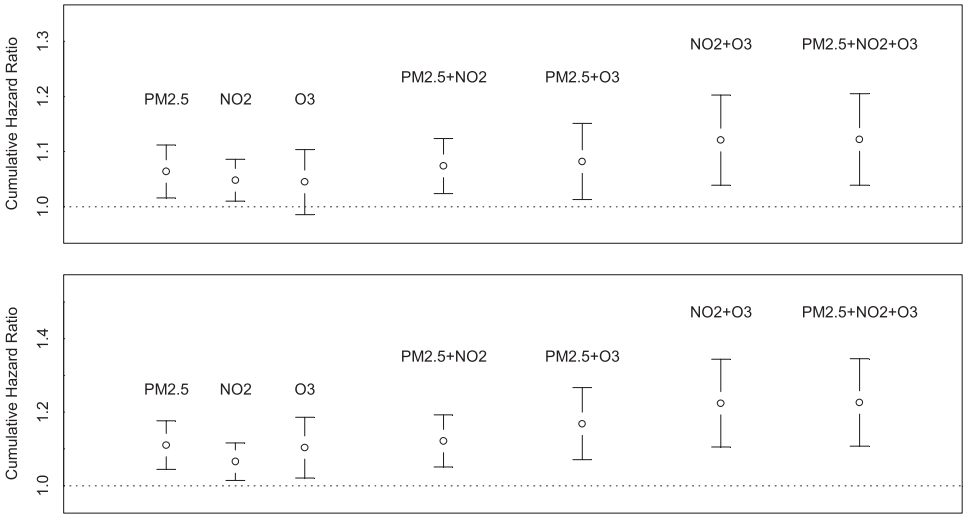

Figure 1. Summary plot of individual and multipollutant cumulative hazard ratios. *Top*: Cardiovascular mortality. *Bottom*: Ischemic heart disease mortality.

concentrations of NO_2 during the winter when home heating contributes to emissions of NO_2 precursors (20). This exposure measure demonstrated significant associations with all-cause, CVD, IHD, and lung cancer mortality. In multipollutant models, these associations remained elevated but became insignificant in some models, possibly due to multicollinearity among the pollutants. We also examined direct measures of proximity to roadways in earlier studies (18) and found these markers of traffic had positive coefficients, but the findings were null, suggesting that the improved exposure estimates with the LUR model may have reduced exposure measurement error.

Our results are broadly consistent with several studies from Europe in which NO_2 exposure was positively associated with mortality (21, 22). In an American study of male truck drivers, NO_2 was found to be independently associated with all-cause and cause-specific mortality even after controlling for occupational exposures (23). In a comprehensive review by the Health Effects Institute, effects of traffic-related pollution on mortality were identified as suggestive but insufficient to establish a causal association (24). When viewed in the context of the emerging literature, our results strengthen the evidence base on the effects of traffic-related air pollution on mortality.

Although acute exposure to O_3 has been related to mortality (25), here we observed a significant positive association between long-term O_3 exposure and CVD mortality, notably for IHD. The strength of association for O_3 was similar to that of $PM_{2.5}$ and NO_2. The association of O_3 with IHD was mildly confounded by $PM_{2.5}$; however, the two exposures had moderately high correlation, and, given the extensive auxiliary information in the $PM_{2.5}$ model, the $PM_{2.5}$ estimates may have dominated by virtue of lower exposure measurement error (26). Nevertheless, O_3 continued to exhibit a significant association with IHD, even with $PM_{2.5}$ in the model.

Positive RR estimates for O_3 became larger when NO_2 was included in the model (*see* Figure 1). We hypothesize that this results from the negative correlation between the two pollutants due to the atmospheric chemistry, such that in areas where O_3 is high, NO_2 tends to be low, and *vice versa* (27, 28). If both pollutants represent harmful constituents of the complex mixture of ambient air pollutions, each would contaminate the comparison for calculating "clean" atmospheres when assessing the risk of the other pollutant. In such instances, the comparison groups with lower pollution levels may also have higher mortality, resulting in part from higher levels of the other pollutant that occupies the opposite spatial pattern. We found a negative, significant association between O_3 and lung cancer, which became insignificant when NO_2 was included in the model. These findings together suggest the importance of having both O_3 and NO_2 in models that attempt to predict health effects from either pollutant. We did observe a weak negative correlation between the two pollutants; however, subsequent analyses showed that in four of the five major urban regions of California, NO_2 had moderately high negative correlations with O_3 (details are provided in the online supplement), which supports the possibility of the positive confounding we have observed here and of the hypothesis that both pollutants need to be in the model for correct inference on either.

Unlike previous analyses (14), we did not see a significant association between respiratory disease and O_3. In the present analysis, however, the number of respiratory deaths was much smaller than in the earlier national study. The point estimate here was elevated and of similar size to that reported in an earlier analysis of the nationwide cohort (3); consequently, the lack of significant association may have resulted from the lower event numbers. In contrast to earlier results, $PM_{2.5}$ did have a positive association with respiratory mortality, which tended to get stronger with the inclusion of copollutants, particularly O_3. In the correlational analyses done by major urban regions (*see* APPENDIX), we observed significant negative correlations between O_3 and $PM_{2.5}$ suggesting again the potential for positive confounding.

TABLE 6. COMPARISON OF RELATIVE RISK ESTIMATES FROM THE CALIFORNIA AND NATIONAL AMERICAN CANCER SOCIETY COHORTS FOR $PM_{2.5}$ USING A 10 $\mu g/m^3$ EXPOSURE INCREMENT*

	California†	National Level‡	Los Angeles Only†
All-cause	1.060 (1.003–1.120)§	1.065 (1.035–1.096)	1.104 (0.968–1.260)
CVD	1.122 (1.030–1.223)	1.141 (1.086–1.198)	1.124 (0.918–1.375)
IHD	1.217 (1.085–1.365)	1.248 (1.160–1.342)	1.385 (1.058–1.814)

Definition of abbreviations: CVD = cardiovascular disease; IHD = ischemic heart disease; $PM_{2.5}$ = particulate matter with aerodynamic diameter of 2.5 μm or less.

* Models for both risk estimates control for an identical set of individual risk factors (e.g., smoking) and contextual risk factors (e.g., unemployment in area of residence) and are stratified by age, race, and sex. Results for the California cohort are additionally adjusted for place of residence in five major urban conurbations. The follow-up period for all studies was from 1982 to 2000.

† California and Los Angeles use residential address with a land use regression estimate of exposure results using standard Cox model.

‡ The national-level study uses metropolitan area of residence with the average of all fine particulate matter ($PM_{2.5}$) monitors within the metropolitan area as the exposure estimate; results were determined using two-level random effects assuming no spatial autocorrelation.

§ Values are relative risk with 95% confidence interval in parentheses.

Several strengths and limitations merit mention. For NO_2 and $PM_{2.5}$, we used advanced exposure assessment models informed by auxiliary information that had good predictive capacity. These models, however, were based on government monitoring data, and the placement of the government monitoring sites might be less representative of all exposure domains because they are chosen to represent background conditions. For the most part, near-road environments are not well represented in this network, limiting the ability to predict small-area variations near roadways. Our estimates of O_3 exposure likely do not capture the small area variation that can occur in open space areas and other areas away from roadways (27). Nonetheless, by assigning exposures that vary among individuals within cities, this study extends the applicability of the risk estimates to support studies that have an interest in assessing the health impacts of air pollutants within cities, which is being increasingly done to justify the health benefits of urban planning and climate mitigation interventions (29, 30).

Regarding limitations, there were no follow-up surveys conducted in the full CPS-II, and key lifestyle characteristics may have changed during the follow-up (e.g., smoking rates declined precipitously across California between 1982 and 2000) (31). If the declines in smoking rates were spatially associated with the air pollution levels, these would have the potential to confound our air pollution risk estimates. We also lacked information on mobility during the follow-up and on key microenvironments such as in-transit exposures, which contribute substantially to interindividual variability in air pollution exposures (32).

In conclusion, our results suggest that several components of the combustion-related air pollution mixture are significantly associated with increased all-cause and cause-specific mortality. Associations with CVD deaths in general and with IHD in particular stand out as most consistent in our analyses. The strong associations of NO_2 with all-cause, CVD, and lung cancer mortality are suggestive of traffic-related pollution as a cause of premature death. The potential for positive confounding between O_3 and NO_2 requires increased attention in future research. Given the indications that O_3 may relate significantly to CVD mortality, future research may lead to refined O_3 exposure assessment with lower measurement error. In sum, the associations observed here reduce key uncertainties regarding the relationship between air pollution and mortality and confirm that air pollution is a significant risk factor for mortality.

Author disclosures are available with the text of this article at www.atsjournals.org.

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Spatiotemporal Analysis of Air Pollution and Mortality in California Based on the American Cancer Society Cohort: Final Report

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ABSTRACT

Problem: Studies using the American Cancer Society (ACS) Cancer Prevention II (CPS II) cohort to assess the relation between particulate air pollution and mortality rank among the most influential and widely cited. The original study, a reanalysis that introduced new random effects methods and spatial analytic techniques, and recent studies with longer follow-up and improved exposure assignment, have all demonstrated statistically significant and substantively large air pollution effects on all-cause and cause-specific mortality. Due to this robust association and a lack of other large cohort studies on the long-term effects, the ACS studies have proven important to government regulatory interventions and health burden assessments.

At present there are no ACS CPS II statewide studies in California that investigate whether the risks are similar to or different from those reported in the above-mentioned analyses. Existing estimates come from either national-level ACS studies, in which the California subjects comprise less than 15% of the total national sample, or from select metropolitan or county areas of California, where questions remain about their generalizability to the rest of the state. A need therefore exists to investigate whether the results hold across California. In addition, none of the existing ACS studies have used high-resolution exposure assignment or investigated the temporal dimensions of the dose-response relationship. In this study we used advanced exposure modeling to reduce problems of measurement error, and we investigated time windows of exposure.

Previous Work: Our previous work includes the original ACS study of particulate air pollution and mortality, the reanalysis of the ACS study, as well as studies involving analytic extensions to both these studies using new spatial models, and a study providing the first assessment of particulate air pollution at the within-city or "intraurban" scale using Los Angeles as the test site. Our Los Angeles results suggest the chronic health effects associated with intraurban gradients in exposure to fine particulate matter ($PM_{2.5}$) are even larger than those previously reported for the metropolitan areas used in both the original study by Pope et al. [1]and the reanalysis by Krewski et al. [2]. For the within-city models, we observed effects nearly three times greater than those using models relying on between-community exposure contrasts. These findings were confirmed using more refined exposure models in a subsequent Health Effects Institute report [3]. In that report, we also found risks for the national study that were greater than those in earlier studies for deaths due to cardiovascular causes.

Objectives: In this context, we pursued the following research objectives: (1) to derive detailed assessments of the health effects from particulate and gaseous air pollution on all-cause and cause-specific mortality in California based on the ACS CPS II cohort, (2) to investigate whether specific particle characteristics associate with larger health effects through examination of intraurban gradients in exposure to different particle constituents and sources, and (3) to determine whether critical exposure time windows exist in the relationship between air pollution and mortality in California.

Description: We identified more than 76,000 California subjects in the ACS cohort to serve as the study population (20,432 deaths with an 18 year follow-up ending in 2000). These subjects were widely distributed across California, giving comprehensive coverage for much of the

population of the state (i.e., 54 of 58 California counties have ACS subjects). For the first time in using the ACS CPS-II data, we have geocoded subjects to their home address to refine our exposure assignment.

As a basis for exposure assessment, we utilized interpolation estimates derived by Air Resources Board staff for the California Teachers Cohort Study led by Dr. Michael Lipsett, with Dr. Jerrett as co-investigator. We also implemented geostatisical kriging, advanced remote sensing coupled with atmospheric modeling, land use regression, and Bayesian models capable of assessing space-time patterns in exposure to improve exposure assignment.

We employed a comprehensive set of 20 individual risk factor variables similar to those used in previous ACS studies. These variables control for lifestyle, dietary, demographic, occupational, and educational influences that may confound the air pollution-mortality association. We used ecological variables in the neighborhoods of residence to control for "contextual" neighborhood confounding (e.g., unemployment). Although we used similar variables as in previous analyses to promote comparison to earlier results, we also tested other model specifications.

We assessed the association between air pollution and several causes of death, including cardiovascular (CVD), ischemic heart disease (IHD), respiratory, lung cancer, and other causes. We also evaluated all-cause mortality. There is some debate about the efficacy of evaluating associations between all-cause mortality and air pollution because several causes of deaths in this broad categorization likely have little association with air pollution. We have included the all-cause metric for several reasons. First, the all-cause metric has been used in most of the other published studies to date, and therefore we used this outcome for comparability with previous results. Second, the all-cause measure avoids the potential cross-classification bias between respiratory and CVD deaths. Third, the all-cause metric can be useful in burden of mortality assessments, and it has been used extensively for this purpose. Finally, we use the all-cause metric to compare with the cause-specific effects that we hypothesized should be more strongly related to pollution exposures (i.e., CVD deaths). A related point is the use of the combined "all other" causes of death to serve as a negative "control". The overall results are more compelling if one observes associations only for those causes of deaths for which there exists biological plausibility or where previous results have provided an a priori hypothesis (CVD, IHD, lung cancer), and where the risks for all other effects are null.

We assessed the association between air pollution and death using standard and multilevel Cox proportional hazards models. Control was also applied for residence in the five largest urban conurbations, which potentially have different mortality rates than non-metropolitan areas. We also assessed spatial autocorrelation in the health effect estimates.

Key Results: Below we summarize the key results from our investigation.

1. Cardiovascular disease (CVD) deaths, especially those from ischemic heart disease (IHD), are consistently and robustly associated with measures of fine particulate and traffic-related air pollution. The effects on CVD and IHD in California are virtually identical to those of the national ACS study (**see Abstract Table 1**).

Abstract Table 1: Comparison of Relative Risk Estimates from the California and National American Cancer Society Cohorts for $PM_{2.5}$ using a 10 µg/m^3 Exposure Increment

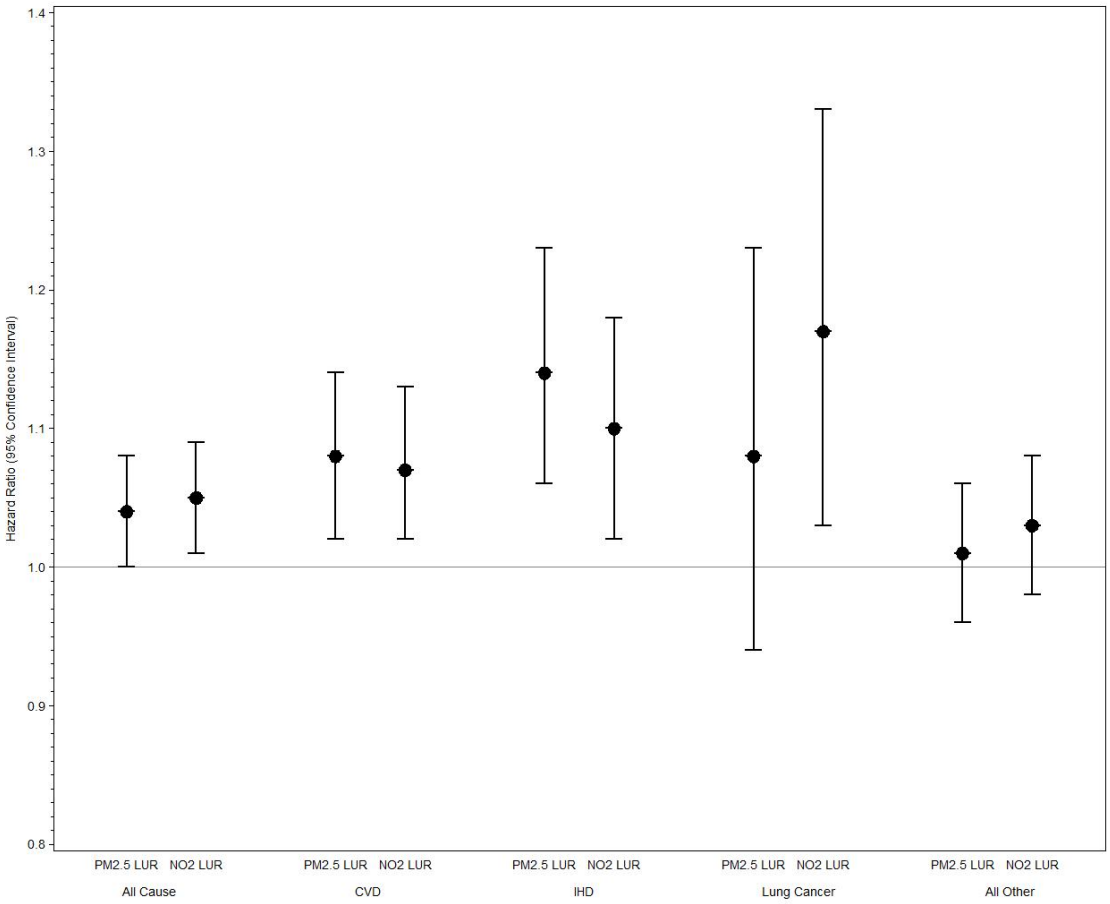
	California*		National Level**	
	Hazard Ratio	**95% CI**	**Hazard Ratio**	**95% CI**
All-cause	1.08	(1.00, 1.15)	1.08	(1.04, 1.11)
CVD	1.15	(1.04, 1.28)	1.17	(1.11, 1.24)
IHD	1.28	(1.12, 1.47)	1.29	(1.18, 1.40)

* California study uses residential address with a Land Use Regression estimate of exposure with statistical control for individual and ecologic covariates and residence in the five largest conurbations in California.
**National level study uses metropolitan area of residence with the average of all $PM_{2.5}$ monitors within the metropolitan area as the exposure estimate; source for the National estimate for all-cause and IHD from Krewski et al. 2009 [3] Table 9; CVD estimate produced for this report for comparison with the California using the same model and sample as in the Krewski report (i.e., two level random effects, with no spatial autocorrelation – referred to as MSA and DIFF in Table 9). Note numbers slightly differ from the Krewski report due to rounding.

Models for both risk estimates control for individual risk factors (e.g., smoking), contextual risk factors (e.g., unemployment in area of residence) and are stratified by age, race and sex. Results for the California cohort are also additionally adjusted for place of residence in five major urban conurbations. Follow up period for both studies was from 1982-2000.

2. All-cause mortality is significantly associated with $PM_{2.5}$ exposure, but the results are sensitive to statistical model specification and to the exposure model used to generate the estimates. When we applied control for residence in the largest urban conurbations, and we employed the land use regression (LUR) model, we found significantly elevated effects on all-cause mortality. For reasons explained in the main report this model specification with land use regression exposures and control for residence in the large conurbations is most likely to produce scientifically valid results. Many of the other results presented were included to satisfy contractual requirements to investigate methodological issues of interest to the Air Resources Board. When we use the fully specified models, the effect sizes are the same as those in the national study (see **Abstract Table 1** for a comparison). We observed effects that were of similar size, but of borderline significance when using other exposure models.

3. The strongest and most consistent effects are observed when there is finer-scale spatial resolution in the exposure predictions. In models using the LUR estimate that serve as markers of relatively local variation in pollution we see all-cause effects from NO_2 and $PM_{2.5}$ (see **Abstract Figure 1** for a comparison of the risks from statewide LUR models of $PM_{2.5}$ and NO_2 for various causes of death).



Abstract Figure 1: Summary of key results for $PM_{2.5}$ and NO_2 with all-cause and cause specific death. Estimates derived from single pollutant models and calibrated to the inter-quartile range of exposure for each pollutant where statistical models control for individual and ecologic covariates and residence in the five largest conurbations in California.

4. The strongest evidence of mortality effects is with exposure models that are markers of traffic-related air pollution. The NO_2 LUR estimate has significant associations with all-cause, CVD, IHD, and lung cancer deaths. Exposure estimates based on roadway proximity had elevated, but insignificant risks, suggesting weaker effects than with the NO_2 model, probably due to increased exposure measurement error.

5. With regard to other causes of death, there was no evidence of an air pollution effect. In fact for some regional $PM_{2.5}$ exposure there was some evidence of negative association, but when residence in the five largest urban conurbations was accounted for in the model, the effects became positive, but insignificant.

6. Other pollutants − namely PM_{10}, sulfate derived from PM_{10} filters, NO_2, and ozone estimates from interpolation models − all showed consistent associations with CVD that are similar in size to those observed for $PM_{2.5}$. In general, the interpolation estimates of these pollutants were highly correlated with each other and with $PM_{2.5}$. Therefore caution

must be exercised in interpreting effects from any single pollutant when the exposure estimate relies solely on interpolation.

CONCLUSION

Taken together, the results from this investigation indicate consistent and robust effects of $PM_{2.5}$ − and other pollutants commonly found in the combustion-source mixture with $PM_{2.5}$ − on deaths from CVD and IHD. We also found significant associations between $PM_{2.5}$ and all causes of death, although these findings were sensitive to model specification. In Los Angeles, where the monitoring network is capable of detecting intraurban variations in $PM_{2.5}$, we observed large effects on death from all causes, CVD, IHD, and respiratory disease. These results were consistent with past ACS analyses and with findings from other national or international studies reviewed in this report. Our strongest results were from a land use regression estimate of NO_2, which is generally thought to represent traffic sources, where significantly elevated effects were found on deaths from all causes, CVD, IHD, and lung cancer. **We therefore conclude that combustion-source air pollution is significantly associated with premature death in this large cohort of Californians.**

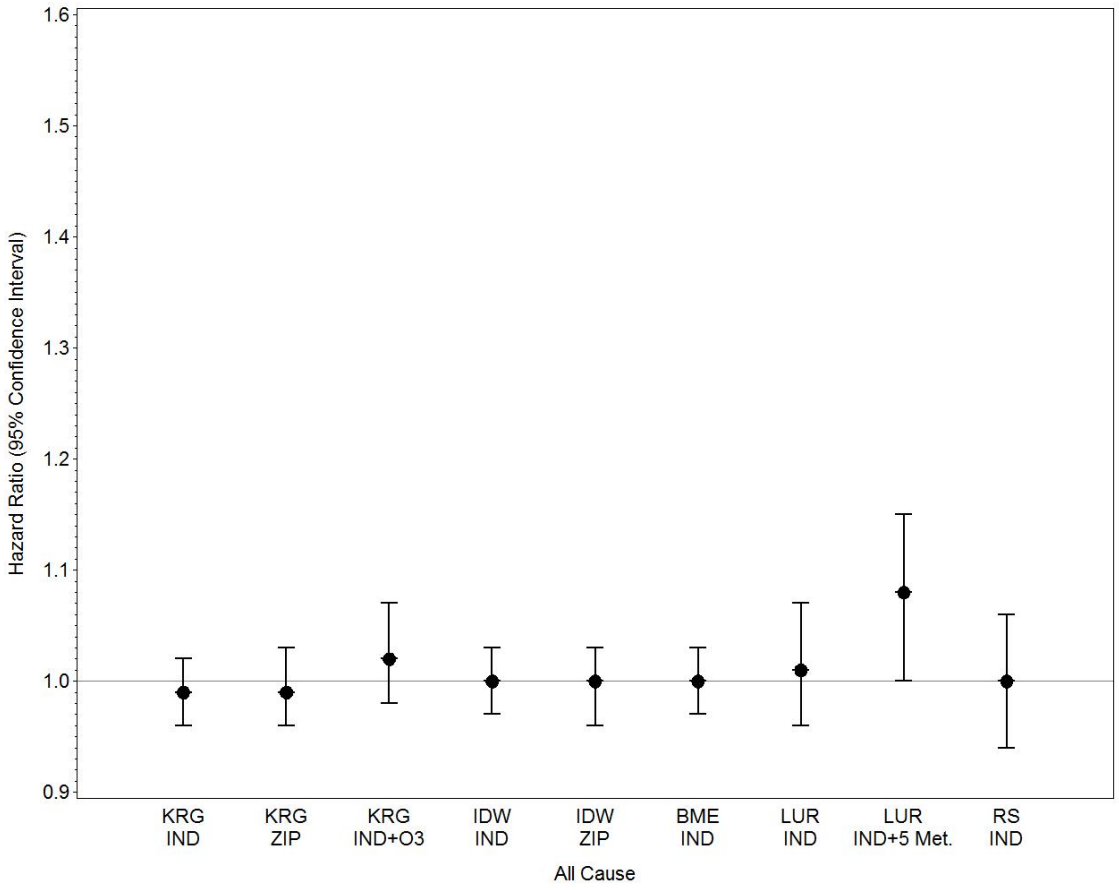


Figure 22: Hazard ratios and 95% confidence intervals for the association between different $PM_{2.5}$ indicators (each 10 ug/m3) at both the individual and ZIP code-level and all cause mortality, follow-up from 1982 to 2000, adjusting for individual level covariates and ecologic level covariates (1990), stratifying the baseline hazard function by age (1-year groupings), gender and race using the Random Effects model, 1 cluster level (ZIP)

DISCUSSION

In these analyses we sought to estimate the effects of $PM_{2.5}$ and other air pollutants on premature death in California. This study was motivated by earlier research from Los Angeles that showed $PM_{2.5}$ exerted a large, significant effect on all cause mortality and mortality from CVD and by a lack of statewide dose-response functions for benefits estimates. In the earlier analyses, effects for all causes, CVD, and IHD outcomes were larger than those observed in our national level studies using the ACS CPS II [5]. But in a more recent follow up [3], the effects tended to increase for CVD and IHD in the national study and were of similar size to those observed in LA. The effects on all cause mortality were still about twice the size in LA compared to the recent national study, although they were more uncertain due to the smaller sample size. Consequently, uncertainty exists as to the effects that would be observed in a statewide model for California.

Below we summarize the key findings from the present investigation. We then offer narrative interpretation.

Key Findings

1. Cardiovascular disease (CVD) deaths, especially those from ischemic heart disease (IHD), are consistently and robustly associated with measures of fine particulate and traffic-related air pollution. The effects on CVD and IHD in California are virtually identical to those of the national ACS study (**see Abstract Table 1**).

Abstract Table 1: Comparison of Relative Risk Estimates from the California and National American Cancer Society Cohorts for $PM_{2.5}$ using a 10 µg/m^3 Exposure Increment

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**National level study uses metropolitan area of residence with the average of all $PM_{2.5}$ monitors within the metropolitan area as the exposure estimate; source for the National estimate for all-cause and IHD from Krewski et al. 2009 [3] Table 9; CVD estimate produced for this report for comparison with the California using the same model and sample as in the Krewski report (i.e., two level random effects, with no spatial autocorrelation – referred to as MSA and DIFF in Table 9). Note numbers slightly differ from the Krewski report due to rounding.

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2. All-cause mortality is significantly associated with $PM_{2.5}$ exposure, but the results are sensitive to statistical model specification and to the exposure model used to generate the estimates. When we applied control for residence in the largest urban conurbations, and

Summary Table. Epidemiologic cohort studies of $PM_{2.5}$ and total mortality in California, 2000-2016
Relative risk of death from all causes (RR and 95% CI) associated with increase of 10 µg/m³ in PM2.5
(http://scientificintegrityinstitute.org/NoPMDeaths112215.pdf)

Krewski 2000 & 2010 CA CPS II Cohort N=40,408 RR = 0.872 (0.805-0.944) 1982-1989
(N=[18,000 M + 22,408 F]; 4 MSAs; 1979-1983 PM2.5; 44 covariates)

McDonnell 2000 CA AHSMOG Cohort N~3,800 RR ~ 1.00 (0.95 – 1.05) 1977-1992
(N~[1,347 M + 2,422 F]; SC&SD&SF AB; M RR=1.09(0.98-1.21) & F RR~0.98(0.92-1.03))

Jerrett 2005 CPS II Cohort in LA Basin N=22,905 RR = 1.11 (0.99 - 1.25) 1982-2000
(N=22,905 M & F; 267 zip code areas; 1999-2000 PM2.5; 44 cov + max confounders)

Enstrom 2005 CA CPS I Cohort N=35,783 RR = 1.039 (1.010-1.069) 1973-1982
(N=[15,573 M + 20,210 F]; 11 counties; 1979-1983 PM2.5) RR = 0.997 (0.978-1.016) 1983-2002

Enstrom 2006 CA CPS I Cohort N=35,783 RR = 1.061 (1.017-1.106) 1973-1982
(11 counties; 1979-1983 & 1999-2001 PM2.5) RR = 0.995 (0.968-1.024) 1983-2002

Zeger 2008 MCAPS Cohort "West" N=3,100,000 RR = 0.989 (0.970-1.008) 2000-2005
(N=[1.5 M M + 1.6 M F]; Medicare enrollees in CA+OR+WA (CA=73%); 2000-2005 PM2.5)

Jerrett 2010 CA CPS II Cohort N=77,767 RR ~ 0.994 (0.965-1.025) 1982-2000
(N=[34,367 M + 43,400 F]; 54 counties; 2000 PM2.5; KRG ZIP; 20 ind cov+7 eco var; Slide 12)

Krewski 2010 (2009) CA CPS II Cohort
(4 MSAs; 1979-1983 PM2.5; 44 cov) N=40,408 RR = 0.960 (0.920-1.002) 1982-2000
(7 MSAs; 1999-2000 PM2.5; 44 cov) N=50,930 RR = 0.968 (0.916-1.022) 1982-2000

Jerrett 2011 CA CPS II Cohort N=73,609 RR = 0.994 (0.965-1.024) 1982-2000
(N=[32,509 M + 41,100 F]; 54 counties; 2000 PM2.5; KRG ZIP Model; 20 ind cov+7 eco var; Table 28)

Jerrett 2011 CA CPS II Cohort N=73,609 RR = 1.002 (0.992-1.012) 1982-2000
(N=[32,509 M + 41,100 F]; 54 counties; 2000 PM2.5; Nine Model Ave; 20 ic+7 ev; Fig 22 & Tab 27-32)

Lipsett 2011 CA Teachers Cohort N=73,489 RR = 1.01 (0.95 – 1.09) 2000-2005
(N=[73,489 F]; 2000-2005 PM2.5)

Ostro 2011 CA Teachers Cohort N=43,220 RR = 1.06 (0.96 – 1.16) 2002-2007
(N=[43,220 F]; 2002-2007 PM2.5)

Jerrett 2013 CA CPS II Cohort N=73,711 RR = 1.060 (1.003–1.120) 1982-2000
(N=[~32,550 M + ~41,161 F]; 54 counties; 2000 PM2.5; LUR Conurb Model; 42 ind cov+7 eco var+5 metro; Table 6)

Jerrett 2013 CA CPS II Cohort N=73,711 RR = 1.028 (0.957-1.104) 1982-2000
(same parameters and model as above, except including co-pollutants NO2 and Ozone; Table 5)

Ostro 2015 CA Teachers Cohort N=101,884 RR = 1.01 (0.98 -1.05) 2001-2007
(N=[101,881 F]; 2002-2007 PM2.5) (all natural causes of death)

Thurston 2016 CA NIH-AARP Cohort N=160,209 RR = 1.02 (0.99 -1.04) 2000-2009
(N=[~95,965 M + ~64,245 F]; full baseline model: PM2.5 by zip code; Table 3) (all natural causes of death)

Enstrom 2016 unpub CA NIH-AARP Cohort N=160,368 RR = 1.001 (0.949-1.055) 2000-2009
(N=[~96,059 M + ~64,309 F]; full baseline model: 2000 PM2.5 by county)

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"Spatiotemporal Analysis of Air Pollution and Mortality in California
Based on the American Cancer Society Cohort: Final Report"

Michael Jerrett, Richard T. Burnett, Arden Pope III, Daniel Krewski, George Thurston,
George Christakos, Edward Hughes, Zev Ross, Yuanli Shi, Michael Thun and
Bernardo Beckerman, Michelle Catherine Turner, Jason Su, Seung-Joe Lee

Compiled by
James E. Enstrom, Ph.D., M.P.H.
December 12, 2011

June 9, 2011 and October 28, 2011 CARB Research Screening Committee Meeting Information
(http://www.arb.ca.gov/research/rsc/rsc.htm)

June 9, 2011 Draft Final Report "Spatiotemporal Analysis of Air Pollution and Mortality in California Based on the American Cancer Society Cohort: Final Report" (145 pages)
(http://www.arb.ca.gov/research/rsc/06-09-11/agenda4_contract06-332_draft_report_cynthia_0520_v2.pdf)

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(http://www.arb.ca.gov/research/rsc/10-28-11/item1dfr06-332.pdf)

June 9, 2011 written comments by James E. Enstrom, Ph.D., M.P.H., UCLA, Los Angeles, CA
(Summary read by Enstrom on June 9, 2011)
(http://www.scientificintegrityinstitute.org/Enstrom060911.pdf)

June 9, 2011 written comments by Norman R. "Skip" Brown of Delta Construction Company, Sacramento, CA (Summary read by Brown on June 9, 2011)
(http://www.scientificintegrityinstitute.org/Delta060911.pdf)

June 9, 2011 written comments by John D. Dunn, M.D., J.D., Lake Brownwood, TX
(Summary read by Hank de Carbonel on June 9, 2011)
(http://www.scientificintegrityinstitute.org/Dunn060911.pdf)

June 27, 2011 written comments by Frederick W. Lipfert, Ph.D., Northport, NY
(http://www.scientificintegrityinstitute.org/Lipfert062711.pdf)

August 17, 2011 Bakersfield Californian article by Lois Henry
"New study doesn't hit the mark for air pollution deaths"
(http://www.bakersfield.com/news/columnist/henry/x560461816/New-study-doesnt-hit-the-mark-for-air-pollution-deaths) or (http://www.scientificintegrityinstitute.org/Henry081711.pdf)

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(http://wmbriggs.com/blog/?p=4353) or
(http://www.scientificintegrityinstitute.org/Briggs091311.pdf)

October 20, 2011 Second Delta (Brown) Critique
(Summary read by Allen Faris on October 28, 2011)
(http://www.scientificintegrityinstitute.org/Delta102011.pdf)

October 24, 2011 Briggs Critique
(Summary not read on October 28, 2011)
(http://www.scientificintegrityinstitute.org/Briggs102411.pdf)

October 26, 2011 Second Enstrom Critique
(Statement read by Betty Plowman on October 28, 2011)
(http://www.scientificintegrityinstitute.org/Enstrom102611.pdf)

October 26, 2011 Second Malkan Critique
(Statement read by Richard Fields on October 28, 2011)
(http://www.scientificintegrityinstitute.org/Malkan102611.pdf)

October 26, 2011 Second Dunn Critique
(Summary read by Hank de Carbonel on October 28, 2011
(http://www.scientificintegrityinstitute.org/Dunn102611.pdf)

October 26, 2011 Lipfert Critique
(Summary read by Eric Eisenhammer on October 28, 2011)
(http://www.scientificintegrityinstitute.org/Lipfert102611.pdf)

October 26, 2011 Fulks Critique
(Summary read by Daniel Robertson on October 28, 2011)
(http://www.scientificintegrityinstitute.org/Fulks102611.pdf)

October 30, 2011 Briggs Blog re Jerrett Report
"A Case Of Failed Peer Review: Dust And Death"
(http://wmbriggs.com/blog/?p=4587)
(http://www.scientificintegrityinstitute.org/Briggs103011.pdf)

November 30, 2011 Bakersfield Californian article by Lois Henry
"Air Board Study in Error? They Don't Seem to Care"
(http://www.bakersfield.com/news/columnist/henry/x1347873497/LOIS-HENRY-Air-Board-study-in-error-They-dont-seem-to-care)
(http://www.scientificintegrityinstitute.org/Henry113011.pdf)

December 12, 2011 Briggs Blog re Jerrett Report
"CARB Misinterprets Statistics, Calls For Elimination of Dust"
(http://wmbriggs.com/blog/?p=4857)
(http://www.scientificintegrityinstitute.org/Briggs121211.pdf)

June 9, 2011 verbal comments by Dr. Enstrom, Dr. Matthew A. Malkan of UCLA, Mr. Brown, and Dr. Dunn as read by Hank de Carbonel
(http://www.scientificintegrityinstitute.org/CARBRSC060911.mp3)

October 28, 2011 verbal comments read for Drs. Enstrom, Malkan, Dunn, Lipfert, and Fulks, and Mr. Brown (http://www.scientificintegrityinstitute.org/CARBRSC102811.mp3) or
(http://www.cdtoa.org/CARBdocs/2011-10-28-SRatCARBreJerret.MP3)

December 1, 2014

From:
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To:

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Office of Management and Budget
Office of Information and Regulatory Affairs
Attn: Desk Officer for the EPA
25 17th St. NW.
Washington, DC 20503

Ms. Amy Vasu, Sector Policies and Programs
Division (D205–01), U.S. EPA, Research

Re:
Docket ID No. EPA-HQ-OAR-2013-0602
Public Comments on the Proposed Emission Guidelines for Greenhouse Gas Emissions from Existing Stationary Sources: Electric Utility Generating Units (CPP) including the Regulatory Impact Analysis (RIA) for the Proposed Carbon Pollution Guidelines for Existing Power Plants and Emission Standards for Modified and Reconstructed Power Plants, EPA 542/R-14-002

I am an epidemiologist with substantial expertise in air pollution health effects, particularly the relationship between air pollution and mortality in California and the United States. I challenge the public health basis for the June 2, 2014 EPA Clean Power Plan (Cutting Carbon Pollution from Power Plants) (http://www2.epa.gov/carbon-pollution-standards/clean-power-plan-proposed-rule). In particular, I have substantial evidence challenging the validity of the EPA Fact Sheet claim that "Americans will see billions of dollars in public health and climate benefits, now and for future generations. The Clean Power Plan will lead to climate and health benefits worth an estimated $55 billion to $93 billion in 2030, including avoiding 2,700 to 6,600 premature deaths and 140,000 to 150,000 asthma attacks in children." (http://www2.epa.gov/carbon-pollution-standards/fact-sheet-clean-power-plan-overview).

The June 2, 2014 EPA "Regulatory Impact Analysis for the Proposed Carbon Pollution Guidelines for Existing Power Plants and Emission Standards for Modified and Reconstructed Power Plants" (EPA-452/R-14-002) (http://www2.epa.gov/sites/production/files/2014-06/documents/20140602ria-clean-power-plan.pdf) states in section *4.3.1.1 Mortality Concentration-Response Functions for PM2.5* : "Considering a substantial body of published scientific literature and reflecting thousands of epidemiology, toxicology, and clinical studies, the PM ISA documents the association between elevated PM2.5 concentrations and adverse health effects, including increased premature mortality (U.S. EPA, 2009b). The PM ISA, which was twice reviewed by the Clean Air Scientific Advisory Committee of EPA's Science Advisory Board (SAB-CASAC) (U.S. EPA-SAB, 2009b, 2009c), concluded that there is a causal relationship between mortality and both long-term and short-term exposure to PM2.5 based on the entire body of scientific evidence. . . . For adult PM-related mortality, we use the effect coefficients from the most recent epidemiology studies examining two large population cohorts: the American Cancer Society cohort (Krewski et al., 2009) and the Harvard Six Cities cohort (Lepeule et al., 2012). The PM ISA (U.S. EPA, 2009b) concluded that the ACS and Six Cities cohorts provide the strongest evidence of the association between long-term PM2.5 exposure and premature mortality with support from a number of additional cohort studies."

In addition, this same document states in section *4.3.2 Economic Valuation for Health Co-benefits* : "After quantifying the change in adverse health impacts, we estimate the economic value of these avoided impacts. Reductions in ambient concentrations of air pollution generally lower the risk of future adverse health effects by a small amount for a large population. . . . The unit values applied in this analysis are provided in Table 5-9 of the PM NAAQS RIA for each health endpoint (U.S. EPA, 2012a). . . . Avoided premature deaths account for 98 percent of monetized PM-related co-benefits and over 90 percent of monetized ozone-related co-benefits." Thus, the monetized public health benefits of the Clean Power Plan (CPP) depend heavily upon the co-benefit of reducing PM2.5-related premature deaths. Without PM2.5-related premature deaths the monetized public health benefits of the CPP are far less than the costs of implementing the CPP.

I have assembled overwhelming evidence that challenges the validity of the relationship between PM2.5 and total mortality ("premature deaths") as described in publications based on the American Cancer Society (ACS) Cancer Prevention Study II (CPS II) cohort, such as, Krewski et al., 2009. This evidence is detailed in my attached November 15, 2013 critique "Scientific Misconduct in Fine Particulate Matter Epidemiology by Dr. C. Arden Pope, III, in Collaboration with Drs. Daniel Krewski, Michael Jerrett, and Richard Burnett, with the Complete Cooperation of the American Cancer Society." This 10-page, 5,000-word, 77-URL critique of the publications based upon the ACS CPS II cohort is on my Scientific Integrity Institute website (http://www.scientificintegrityinstitute.org/Pope111513.pdf). In addition, on March 19, 2014 this critique was submitted to the California Air Resources Board (CARB) (http://www.arb.ca.gov/lispub/comm/bccomdisp.php?listname=truckbus14&comment_num=35&virt_num=33), where it has been completely ignored by CARB staff and board members. My critique is supported by my attached November 7, 2013 email request to Dr. Alpa V. Patel of ACS Epidemiology describing my serious concerns about the use of CPS II data for examining PM2.5 and mortality (http://www.scientificintegrityinstitute.org/Patel110713.pdf). My critique is further supported by the 50 attached pages of January 6, 2010 to May 17, 2011 correspondence between an Ad Hoc Group of California businessmen and the UC President Mark G. Yudof regarding UC Berkeley Professor Michael Jerrett and his unethical use of ACS CPS II data in the analysis and characterization of the relationship between PM2.5 and mortality in California during 1982-2000 (http://calcontrk.org/Jerrett051711.pdf).

In conclusion, I challenge the use in the CPP of publications based upon the ACS CPS II cohort, such as, Krewski et al., 2009. EPA must investigate my evidence regarding the following issues regarding the CPS II cohort: unethical use of CPS II subjects' home addresses for PM2.5 epidemiology, failure to fully disclose geographic variation in PM2.5 mortality risk, deliberate misrepresentation of the PM2.5 mortality risk in California, failure to present national PM2.5 mortality findings based on CPS II deaths since 2000, failure of ACS to allow independent and alternative analyses of the CPS II cohort, and other related scientific and ethical issues described in the attached pages.

Until my extensive evidence challenging the public health basis for the CPP is properly investigated the CPP should not be implemented.

Thank you very much for your consideration of my comments.

Sincerely yours,

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Scientific Misconduct in Fine Particulate Matter Epidemiology by Dr. C. Arden Pope, III, in Collaboration with Drs. Daniel Krewski, Michael Jerrett, and Richard Burnett, with the Complete Cooperation of the American Cancer Society

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November 15, 2013

This document presents detailed documented evidence of scientific misconduct in fine particulate matter epidemiology by Clive Arden Pope, III, Ph.D., Mary Lou Fulton Professor of Economics at Brigham Young University (https://economics.byu.edu/Pages/Faculty/C-Arden-Pope.aspx). This scientific misconduct has been conducted with the close collaboration of Daniel Krewski, Ph.D., Professor at the University of Ottawa Faculty of Medicine (http://www.med.uottawa.ca/epid/eng/krewskibio.html), Michael Jerrett, Ph.D., Professor and Chair of Environmental Health Sciences at the UC Berkeley School of Public Health (http://ehs.sph.berkeley.edu/people/jerrett.htm), Richard T. Burnett, Ph.D., Senior Research Scientist at Health Canada, Ottawa (http://www.zoominfo.com/p/Rick-Burnett/52191135). This collaboration has been made possible with the complete cooperation of the American Cancer Society during the past twenty years, involving Vice President of Epidemiology Emeritus Michael J. Thun, M.D. (http://www.cancer.org/research/researchprogramsfunding/epidemiology-cancerpreventionstudies/ourstaff/michael-j-thun) and Vice President of Epidemiology Susan M. Gapstur, Ph.D. (http://www.cancer.org/research/researchprogramsfunding/epidemiology-cancerpreventionstudies/ourstaff/susan-m-gapstur).

The focus here is on Dr. Pope because he is "The World's Leading Expert on the Effects of Air Pollution on Health," as stated at the beginning of his 64 minute February 15, 2007 lecture "Air Pollution and Health" to Sevier Citizens for Clean Air and Water in Richfield, Utah (http://wn.com/arden_pope). This lecture used a PPT presentation that was similar to the one used in his June 19, 2007 lecture to Utah Moms for Clean Air in Salt Lake City, Utah (http://www.utahmomsforcleanair.org/docs/Utah-Moms_Arden-Pope-presentation.pdf). At the beginning of his February 15, 2007 lecture Dr. Pope twice stated he was speaking "the truth the best I know it" (http://www.scientificintegrityinstitute.org/Pope021507.pdf). As will be shown with the evidence below, Pope did not speak the truth as he knew it then and he has gotten progressively more dishonest since 2007. The primary form of scientific misconduct committed by Dr. Pope has been falsification (not properly describing results in the research record and willful perversion of facts).

The evidence here focuses on Dr. Pope's scientific misconduct since I published my December 15, 2005 *Inhalation Toxicology* (*IT*) paper "Fine Particulate Air Pollution and Total Mortality Among Elderly Californians, 1973-2002" and submitted it to the California Air Resources Board

(CARB) (http://www.arb.ca.gov/planning/gmerp/dec1plan/gmerp_comments/enstrom.pdf). In particular, the evidence relates to fine particulate matter (PM2.5) epidemiology and diesel vehicle regulations in California (http://www.forbes.com/2010/06/08/california-diesel-regulation-pollution-opinions-columnists-henry-i-miller-james-e-enstrom.html) and to the August 1, 2013 US House Science Committee subpoena of US Environmental Protection Agency (EPA) "secret science" data from the American Cancer Society Cancer Prevention Study II (CPS II) (http://science.house.gov/press-release/smith-subpoenas-epa-s-secret-science). The focus of this document is on 1) Dr. Pope's clear and consistent pattern of dishonesty and deception regarding his research, publications, and statements on PM2.5 mortality risk in California since 2006, while he participated in research on PM2.5 mortality risk in California funded by CARB and 2) Dr. Pope's direct involvement with CARB during 2006-2009 as a "scientific advisor" on the key report that provided the public health justification for the passage in December 2008 of draconian diesel PM2.5 regulations that have harmed countless California businessmen.

Intense controversy regarding PM2.5 epidemiology dates back to Dr. Pope's March 1, 1995 *AJRCCM* paper "Particulate Air Pollution as a Predictor of Mortality in a Prospective Study of U.S. Adults" based on ACS CPS II data with Dr. Thun of ACS Epidemiology as second author (http://www.atsjournals.org/doi/abs/10.1164/ajrccm/151.3_Pt_1.669). The initial controversy was described in the July 25, 1997 Science article "Showdown Over Clean Air Science" (http://www.sciencemag.org/content/277/5325/466.full) and the August/September 1997 Reason article "Polluted Science" (http://reason.com/archives/1997/08/01/polluted-science).

The current controversy begins with my December 15, 2005 *IT* paper and the January 1, 2006 *IT* editorial about my paper by Dr. Suresh Moolgavkar "Fine Particles and Mortality" (http://www.scientificintegrityinstitute.org/IT010106.pdf). These papers were cited in Dr. Pope's June 1, 2006 *JAWMA* "Critical Review—Health effects of fine particulate air pollution: Lines that connect" (http://www.scientificintegrityinstitute.org/PopeDockery2006.pdf). Then, in conjunction with CARB, Dr. Pope prepared a 47-slide PPT presentation of his PM2.5 review which included my 2005 *IT* paper and the 2006 *IT* editorial, as well as my picture (http://www.scientificintegrityinstitute.org/PopePPT2006.pdf). My 2005 *IT* paper is the first statewide examination of PM2.5 and total mortality in California and it is still the most detailed examination of this relationship published in a peer-reviewed journal. Since his 2006 *JAWMA* paper, Dr. Pope has not properly cited the evidence on PM2.5 mortality risk in California.

On August 21, 2006 CARB scientists conducted a "Public Workshop on Updating the Methodology for Estimating Premature Death Associated with PM2.5 Exposures." The PPT presentation for this Workshop (http://www.arb.ca.gov/research/health/pm-mort/ws-slides.pdf) shows Dr. Pope as a CARB advisor and "Key Steps in ARB's Update of Methodology" and "Tentative Timeline." However, the 2005 Enstrom paper was not shown as one of the "New studies emerged since 2002." Joel M. Schwartz of the American Enterprise Institute testified at the Workshop and then on August 29, 2006 submitted to CARB ten pages of formal comments and three of his AEI papers, including his May 2006 paper "Air Pollution and Health: Do Popular Portrayals Reflect the Scientific Evidence?" (http://joelschwartz.com/pdfs/AirPoll_Health_EPO_0506.pdf). His formal comments stated "The discussions and handouts at the August 21 workshop indicate that CARB's approach to evaluating the association of PM2.5 and mortality tends to omit contrary evidence and to

uncritically accept supportive evidence. This would cause CARB to overstate the magnitude and certainty of the association of air pollution and premature mortality." (http://www.scientificintegrityinstitute.org/Schwartz082906.pdf).

During the latter part of 2006, Dr. Jerrett, serving as Principle Investigator, worked with Drs. Pope, Krewski, and Burnett and six other co-Investigators on preparing the CARB Interagency Proposal No. 2624-254 "Spatiotemporal Analysis of Air Pollution and Mortality in California Based on the American Cancer Society Cohort" (http://www.scientificintegrityinstitute.org/Jerrett012510.pdf). Dr. Pope was included as a consultant to be paid $14,997, with the justification "Dr. Pope will supply expert guidance on the interpretation and analysis of statistical modeling and air pollution epidemiology."

This proposal contains the following claims that Dr. Pope knew in 2006 were dishonest: "California currently has no statewide studies assessing mortality resulting from air pollution in the general population." (page 3); "California has no state-wide estimates of mortality to support policymaking and regulatory activities. Extension of the ACS study to address scientific uncertainties and to derive estimates specific to California will assist the Air Resources Board and others to assess the benefits of policy interventions." (page 4); "*This study will derive the first California wide estimates of mortality associated with PM2.5 exposure and other criteria co-pollutants, thus supplying policymakers with a valuable resource for deriving benefit estimates*." (page 5). Drs. Jerrett, Krewski, and Burnett also knew in 2006 that the above claims were dishonest because they became aware of my 2005 *IT* paper in January 2006 when Dr. Krewski granted me permission to reproduce Figure 21 of the 2000 Krewski Health Effects Institute (HEI) Reanalysis Report (http://pubs.healtheffects.org/view.php?id=6) and use it in my June 1, 2006 *IT* response paper (http://www.scientificintegrityinstitute.org/IT060106.pdf).

The Jerrett Proposal was reviewed by CARB Research Screening Committee on December 14, 2006 (http://www.arb.ca.gov/research/rsc/12-14-06/dec06adv.pdf) and was approved by CARB on January 25, 2007 and it became "ARB/UCB Agreement No. 06-332," with a three-year total budget of $749,706 (http://www.arb.ca.gov/board/books/2007/012507/07-1-4pres.pdf). At both of these meetings false claims were made about no prior statewide studies of PM2.5 and mortality in California. If my paper had been cited in the Jerrett Proposal, the proposal would have had to acknowledge that a very large and detailed statewide study of PM2.5 and mortality in California had already been conducted and published. My study and its null findings would have influenced the specific aims and approval of the Jerrett Proposal by the CARB Research Screening Committee and CARB members. This scientific misconduct by Dr. Jerrett, Dr. Pope, and the other co-investigators was reported in a March 24, 2010 letter to UC President Mark G. Yudof by an Ad Hoc Group of California businessmen impacted by CARB diesel regulations (http://www.calcontrk.org/CARBdocs/letters/AdHocGroupLettertoYudofReJerrettMisconduct032410.pdf). Dr. Pope was involved with this project until 2013, as will be explained later.

On January 25, 2007, the exact same day that the Jerrett Proposal was approved, Drs. Scott L. Zeger, Francesca Dominici, Aidan McDermott, and Jonathan M. Samet posted their Johns Hopkins University Department of Biostatistics Working Paper 133 "Mortality in the Medicare Population and Chronic Exposure to Fine Particulate Air Pollution" (http://biostats.bepress.com/jhubiostat/paper133). These four JHU professors were major air pollution investigators at this time, all much more respected and better known than me, and they

cited my 2005 *IT* paper as being consistent with their finding "No positive association was found between county-level PM2.5 concentration and mortality rates for the 32 urban counties in the western U.S. [California, Oregon, and Washington] in the MCAPS [Medicare Cohort for Air Pollution Studies] cohort. The lack of association for the West is largely because the Los Angeles area counties have higher PM2.5 levels than other western counties, but not higher adjusted mortality rates. . . . In our initial analyses of the MCAPS data, we confirmed the association between PM2.5 and mortality found in other studies but find substantial and unexplained geographic heterogeneity in the effect of PM2.5 across the United States." The null findings in my 2005 *IT* paper and the "substantial and unexplained geographic heterogeneity" findings in Zeger 2007 were completely ignored by Dr. Pope in his February 15, 2007 and June 19, 2007 public lectures. A revised and expanded version of Zeger 2007 was published online August 12, 2008 (http://www.ncbi.nlm.nih.gov/pmc/?term=10.1289/ehp.11449).

The content of his 2007 lectures and the 2007 Jerrett Project are highly relevant to the honesty of Dr. Pope because during 2006-2009 he served as a "scientific advisor" to CARB on PM2.5 health effects. In particular, he provided scientific advice on a 2007 CARB draft report entitled "Methodology for Estimating the Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California." The report was distributed to six peer reviewers with an August 27, 2007 CARB cover letter and the peer review comments were returned during September-October 2007. This draft based the dose-response relationship between PM2.5 and premature deaths (total mortality) in California on the national September 21, 2006 "Expanded Expert Judgment Assessment of the Concentration-Response Relationship Between PM2.5 Exposure and Mortality" (http://www.epa.gov/ttn/ecas/regdata/Uncertainty/pm_ee_report.pdf). Drs. Pope and Krewski were two of the twelve experts used in this major PM2.5 risk assessment, constituting another conflict of interest for Dr. Pope in his role as a CARB scientific advisor.

The 2007 CARB draft report, including the comments of the six peer reviewers, was revised and released as the May 22, 2008 CARB Draft Report (http://scientificintegrityinstitute.org/CARBPMDraft052208.pdf). It was summarized at the May 22, 2008 CARB meeting in a PPT presentation "Revised Estimates of Premature Death Associated with PM2.5 Exposures in California," which cited Dr. Pope as a Scientific Advisor (http://www.arb.ca.gov/board/books/2008/052208/08-5-5pres.pdf). Neither the report nor the PPT addressed my April 24, 2008 comments to CARB about the need to focus on California-specific evidence as the basis for estimating PM2.5-related premature deaths in California (http://www.arb.ca.gov/lists/erplan08/2-carb_enstrom_comments_on_gmerp_042208.pdf).

A July 11, 2008 CARB teleconference was held because of my June 4, 2008 concerns stated to the CARB Chair Mary D. Nichols at her California Senate Rules Committee confirmation hearing in Sacramento (http://scientificintegrityinstitute.org/Nichols060408.pdf). I was very concerned that the May 22, 2008 CARB Draft Report had not properly focused on PM2.5 mortality risk in California (http://scientificintegrityinstitute.org/AgendaSum071108.pdf). During that teleconference I spoke directly with Drs. Pope, Jerrett, and Burnett about failure of the CARB report to properly present and use California-specific PM2.5 mortality risk evidence (http://scientificintegrityinstitute.org/Enstrom071108.pdf). Dr. Pope and the others evaded my repeated requests to them to clarify the Jerrett Project California PM2.5 mortality risk findings, as well as prior PM2.5 findings dating back to Figure 21 in the 2000 Krewski HEI Reanalysis Report. I stated "I'm very concerned that a number of these [CARB diesel vehicle] regulations

are going to move forward based on, well for instance, the Pope 2002 study when more studies are forth coming and I think that if there's an effort made by the ARB to slow down the regulatory process that would relieve a lot of my concerns." In response, Dr. Pope stated "That's something I wouldn't get involved with one way or the other. I'm interested in the science and I hope that the regulation is wise and uses the science in a reasonable way." (http://scientificintegrityinstitute.org/CARB071108.pdf). This was a disingenuous and dishonest statement by Dr. Pope because he has been clearly aware since at least 2006, when he began advising CARB, that his research and reviews on PM2.5 mortality risk were being used by CARB as public health justification for draconian diesel vehicle regulations in California.

When Pope failed to contact me, as per his comments during the teleconference, I sent him an August 20, 2008 email request asking for the same California-specific calculations that I had asked for during the teleconference (http://www.scientificintegrityinstitute.org/Pope082008.pdf). Pope never responded to my email request. During this period, a total of 148 pages of highly critical public comments were received by CARB regarding the May 22, 2008 Draft Staff Report (http://www.arb.ca.gov/research/health/pm-mort/pm-mort_supp.pdf). On October 24, 2008 CARB issued a Final Staff Report "Methodology for Estimating Premature Deaths Associated with Long-term Exposure to Fine Airborne Particulate Matter in California" (http://www.scientificintegrityinstitute.org/CARBPMFinal102408.pdf). In spite of the extensive detailed criticism that Dr. Pope must have seen, the Final Staff Report was essentially unchanged from Draft Staff Report. Both of these reports listed Dr. Pope as a Scientific Advisor and they reflect his failure to address serious criticism and null California-specific PM2.5 risk evidence.

I challenged the scientific integrity of the Final Staff Report with detailed December 10, 2008 CARB public comments regarding the proposed CARB Statewide Truck and Bus Regulation. I described six different sources showing geographic variation in PM2.5 mortality risk nationally and little or no PM2.5 mortality risk in California (http://www.arb.ca.gov/lists/truckbus08/897-carb_enstrom_comments_on_statewide_truck_regulations_121008.pdf). In spite of the massive criticism of scientific, legal, and economic aspects of the CARB Truck and Bus Regulation received from hundreds of commenters, this multi-billion dollar diesel vehicle regulation was approved by CARB on December 12, 2008 (http://www.arb.ca.gov/newsrel/nr121208.htm).

Although we had engaged in direct discussion and correspondence about this issue in 2008, Dr. Pope did not address the issue of geographic variation in PM2.5 mortality risk in his January 22, 2009 NEJM paper "Fine Particulate Air Pollution and Life Expectancy in the United States" (http://www.nejm.org/doi/full/10.1056/NEJMsa0805646). This paper made no mention of the above evidence of geographic variation in PM2.5 mortality risk dating back to 2000. I submitted a February 11, 2009 NEJM letter with specific results showing no relationship in California based on data from me and the paper. Although my letter was rejected by the NEJM on March 16, 2009, it was forwarded to Dr. Pope for comment (http://www.arb.ca.gov/lists/gmove09/1-carb_enstrom_comments_re_pm2.5_and_life_expectancy_052709.pdf).

Dr. Pope has never acknowledged or addressed my null California results and my concerns about his conclusions regarding the relationship between PM2.5 and life expectancy. For instance, he failed to address any such criticism in his May 3, 2009 HEI PPT presentation on this relationship (http://www.healtheffects.org/Slides/AnnConf2009/Pope.pdf). Additional criticism of Pope

2009 is contained in the September 2012 paper of Goran Krstić, Ph.D., whose 2009 letter was also rejected by the NEJM. Reanalyzing Dr. Pope's publicly available data, Dr. Krstić found "The observed loss of statistical significance in the correlation between the reduction of ambient air PM2.5 concentrations and life expectancy in metropolitan areas of the United States, after removing one of the metropolitan areas [Topeka, KS] from the regression analysis, may raise concern for the policymakers in decisions regarding further reductions in permitted levels of air pollution emissions." (http://www.ncbi.nlm.nih.gov/pubmed/23019812). This same Pope 2009 data was reanalyzed in the August 2013 paper of Dr. S. Stanley Young, who concluded "Given the lack of effect in the West and the greater importance of other predictors, we agree with Krstić that this data set does not support the claim that decreasing PM2.5 will increase longevity." (http://onlinelibrary.wiley.com/doi/10.1002/sam.11202/abstract).

During 2002-2009 Dr. Pope worked with Dr. Krewski on an HEI project that resulted in the June 3, 2009 HEI Research Report 140 "Extended Follow-Up and Spatial Analysis of the American Cancer Society Study Linking Particulate Air Pollution and Mortality," which lists Dr. Pope as eighth author (http://pubs.healtheffects.org/view.php?id=315). HEI Heath Review Committee Commentary states "Dr. Krewski's 4-year study, 'Extended Follow-Up and Spatial Analysis of the American Cancer Society Study Linking Particulate Air Pollution and Mortality,' began in May 2002. Total expenditures were $425,000. The draft Investigators' Report from Krewski and colleagues was received for review in January 2007. A revised report, received in January 2008, was accepted for publication in June 2008." The final report results were summarized in a May 21, 2008 Krewski PPT (http://www.scientificintegrityinstitute.org/Krewski052108.pdf). This "spatial analysis" did not analyze or discuss the geographic variation in PM2.5 mortality risk that was found in Figures 5 and 21 of the 2000 Krewski HEI Reanalysis Report and it did not cite papers showing geographic variation like Enstrom 2005, Enstrom 2006, Zeger 2007, and Zeger 2008. As explained previously, the primary authors, including Drs. Pope, Krewski, Jerrett, and Burnett, were all well aware of evidence of national geographic variation dating back to the 2000 HEI Reanalysis Report. Yet they failed to address this issue in the 2009 HEI Research Report.

On November 16, 2009 CARB Member John B. Telles, M.D., raised serious concerns about the integrity of the October 24, 2008 CARB Final Staff Report because of the dishonesty of its lead author, Hien T. Tran (http://www.scientificintegrityinstitute.org/Telles111609.pdf). The dishonesty of Tran is described on a website that describes scientific and ethical misconduct by CARB (http://killcarb.org/tranpage.html). As a result of Dr. Telles' concerns, a February 26, 2010 CARB Symposium "Estimating Premature Deaths from Long-term Exposure to PM2.5" and organized and conducted in Sacramento. Dr. Pope and I participated, along with Drs. Krewski, Jerrett, Moolgavkar, and numerous other PM2.5 mortality risk experts (http://www.arb.ca.gov/research/health/pm-mort/pm-mort-ws_02-26-10.htm). Several dozen California businessmen adversely impacted by the CARB diesel vehicle regulations approved on December 12, 2008 were in the audience of this Symposium. Along with Dr. Telles, they were very concerned about the integrity of the October 24, 2008 CARB Final Staff Report.

At the Symposium Dr. Pope made a 52-slide PPT presentation "Overview of PM2.5-Related Mortality Studies" (http://www.arb.ca.gov/research/health/pm-mort/pope.pdf). On slide 50 he posed the question "Then which health studies are relevant to California?" and followed this with an accurate statement "Some of the highest quality research on the health effects of air pollution

has been conducted in California" and a false statement "The results are similar to studies from elsewhere." His slides 48 and 49 did not accurately reflect all of the existing null California-specific results. Particularly disturbing is the fact that Dr. Pope did not present any California-specific results that should have been in the June 3, 2009 Krewski HEI Research Report. Even more disturbing is the fact that he did not present any results from the ongoing Jerrett Project described earlier. When the Jerrett Project was approved on January 25, 2007, the agreement with CARB called for the California-wide results to be available in eighteen months (July 2008).

Although not shown by Dr. Pope, Dr. Jerrett did show in slide 12 of his Symposium presentation that the Jerrett Project found no relationship between PM2.5 and total mortality in California (RR = 1.00) (http://www.scientificintegrityinstitute.org/JerrettTrans022610.pdf). This null result is in exact agreement with the Enstrom 2005 result (RR =1.00). An Ad Hoc Group of California businessmen who attended February 26, 2010 CARB Symposium were interested in seeing all the California evidence, particularly the California-specific results from the 2009 HEI Research Report. They submitted a request to HEI for these results and their request yielded an August 31, 2010 HEI letter containing California-specific results calculated by Dr. Krewski as a subset of the national results in the 2009 HEI Research Report. Dr. Krewski found no PM2.5 mortality risk in California: RR = 0.87 (0.81-0.94) during 1982-1989 and RR = 0.96 (0.92-1.00) during 1982-2000 (http://www.arb.ca.gov/research/health/pm-mort/HEI_Correspondence.pdf).

The low PM2.5 mortality risk in California during 1982-1989 found by Dr. Krewski is consistent with my September 30, 2010 analysis of Figures 5 and 21 in the 2000 HEI Report (http://www.scientificintegrityinstitute.org/HEIFigure5093010.pdf). Based on my own analysis, Figure 5 showed PM2.5 mortality risk for 49 US cities (metropolitan areas) and Fresno, California ranked second lowest and Los Angeles, California ranked fifth lowest. Figures 5 and 21 were not mentioned in Dr. Pope's Symposium PPT or in the 2009 HEI Report. It certainly should have been included in 2009 HEI Report if Dr. Pope had been honest in addressing Figures 5 and 21, my 2006 and 2008 submissions to CARB, and my 2008 requests to him. The null California results from the Jerrett Project could have been released in early 2008 and then incorporated into the CARB Draft Report and the CARB Final Report. Modified CARB reports that found few or no premature deaths in California due to PM2.5 would probably have changed the December 12, 2008 CARB vote on the Truck and Bus Regulation.

Because of my extensive concerns about the scientific integrity of PM2.5 epidemiology, as described above, I organized a symposium, "Ethical Aspects of Small Epidemiologic Risks," for the Third North American Congress of Epidemiology (CoE) in Montreal, Canada during June 21-24, 2011 (http://www.epiresearch.org/archive/fall10news.pdf). This symposium was sponsored by the American College of Epidemiology and at that time I was Chair of the ACE Ethics Committee (http://acepidemiology.org/content/ethics). I invited 18 experts in PM2.5 epidemiology who held views different than my own to debate me at this ethics symposium. All 18 of the experts declined my invitation, including six co-Investigators of the Jerrett Project: Drs. Jerrett, Pope, Krewski, Burnett, Thun, and Thurston (http://www.scientificintegrityinstitute.org/COEEthics022311.pdf). Because diverse points of view on PM2.5 epidemiology could not be presented at the Symposium, it was cancelled. This disappointing experience illustrates the difficulty of resolving ethical issues in PM2.5 epidemiology, like lack of access to underlying data and deliberate misrepresentation of results.

The June 9, 2011 Draft Jerrett Report, with Dr. Pope as the third author, presented null results from eight of the nine statistical models that they tested, adding to the single null finding presented by Dr. Jerrett on February 26, 2010. However, the Summary and Abstract of this report were heavily criticized by me and several others for stating conclusions that did not reflect the null findings in the report itself. This report was not approved and was deferred by the CARB Research Screening Committee. In spite of the criticism, the October 28, 2011 Final Jerrett Report was essentially unchanged from the June 9, 2011 Draft Jerrett Report. This lead to further criticism that the final report continued to misrepresent and/or ignore its overwhelmingly null findings (http://www.scientificintegrityinstitute.org/JerrettCriticism102811.pdf).

Continuing misrepresentation of PM2.5 mortality risk in California is clearly evident in Dr. Pope's July 28, 2011 EPA Webinar PPT "Health Effects of Particulate Matter Air Pollution" (http://www.epa.gov/burnwise/pdfs/PMHealthEffects-Pope.pdf). He makes no mention of PM2.5 mortality risk in California found in Figure 5 and 21 from Krewski 2000, the February 26, 2010 CARB Symposium, the June 9, 2011 Jerrett Report, or the June 1, 2011 Erratum to Ostro 2009 paper, or the June 23, 2011 Lipsett 2011 paper, all of which were available before his EPA webinar (http://www.scientificintegrityinstitute.org/Enstrom081512.pdf).

The most recent summary of all California evidence is given in my August 1, 2012 American Statistical Association Joint Statistical Meeting 2012 PPT presentation "Are Fine Particulates Killing Californians?" (http://www.scientificintegrityinstitute.org/ASA080112.pdf) and in my subsequent ASA JSM 2012 Proceedings paper "Particulate Matter is Not Killing Californians" (http://www.scientificintegrityinstitute.org/ASAS092812.pdf). There is now overwhelming epidemiologic evidence from ten different analyses of five separate cohorts showing no relationship between PM2.5 and premature death (total mortality) in California. In spite of my many attempts since 2008, this overwhelming evidence has not yet been recognized by Dr. Pope.

The serious misuse of PM2.5 epidemiologic findings by EPA and CARB is reflected in the US House Science Committee criticism of EPA science and regulations dating back to a November 15, 2011 letter to the White House from Congressmen Andy Harris, M.D., and Paul Broun, M.D. (http://science.house.gov/press-release/harris-and-broun-question-administration%E2%80%99s-environmental-cost-benefit-analyses). This letter and numerous additional letters up to a July 22, 2013 letter have requested the Harvard Six Cities Study (H6CS) and ACS CPS II data used by EPA (http://science.house.gov/press-release/committee-threatens-subpoena-epa-secret-science). The basic issues are summarized in a July 30, 2013 Wall Street Journal commentary "The EPA's Game of Secret Science" by US House Science Committee Chairman Lamar Smith (http://online.wsj.com/news/articles/SB10001424127887323829104578624562008231682).

Because EPA did not comply with their prior requests, the US House Science Committee issued an August 1, 2013 subpoena on EPA to produce the "secret science" data from H6CS and ACS CPS II (http://science.house.gov/press-release/smith-subpoenas-epa-s-secret-science). Dr. Pope is co-author on four of the seven papers specifically cited in the subpoena. He is first author on "Pope et al. 2002. Lung Cancer, Cardiopulmonary Mortality, and Long-term Exposure to Fine Particulate Air Pollution." Journal of the American Medical Association 287: 1132-1141" and

"Pope et al. 2009. "Fine Particulate Air Pollution and Life Expectancy in the United States." New England Journal of Medicine 360: 376-386." He is third author on "Jerrett et al. 2009 "Long-term ozone exposure and mortality", New England Journal of Medicine 360; 1085-1095" and eighth author on "Krewski et al. 2009. "Extended Follow-up and Spatial Analysis of the American Cancer Society Study Linking Particulate Air Pollution and Mortality, HEI Research Report 140, Health Effects Institute. Boston, MA." A fifth study is "Krewski et al. 2000. 'Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortaltiy.' Special Report to Health Effects Institute. Cambridge MA. July." This 2000 HEI Reanalysis Report was conducted in order to check the accuracy of the highly controversial Pope 1995 paper, as described in the 1997 Science and Reason articles.

Instead of encouraging the other H6SC and ACS CPS II investigators to comply with the subpoena, Dr. Pope has made several patently false statements to the press that try to justify the investigators' refusal to comply. However, of the 23 primary authors of the seven subpoenaed papers, only Dr. Pope has publicly challenged the appropriateness of the subpoena. The following are three of his most blatantly false public statements:

1) The August 2, 2013 Science *Insider* statement: "Economist C. Arden Pope of Brigham Young University in Provo, Utah, one of the authors on the Six Cities Study, says that turning over what Smith requests would undoubtedly violate the confidentiality agreement made with participants. 'It's extremely hard to give a data set that will allow you to replicate the results in these studies that doesn't include information that then allows you—with an Internet search of obituaries—to quickly figure out who the people were,' he says." (http://news.sciencemag.org/environment/2013/08/house-panel-subpoenas-epa-air-pollution-data)

2) The August 9, 2013 Science statement: "Thursday, Smith asserted the data would be shared with 'various reputable entities and organizations' and would be 'deidentified' so that no names would be made public. But because the six cities were small, it would be easy to quickly figure out who the participants were, according to Pope." (http://www.sciencemag.org/content/341/6146/604.full.pdf)

3) The September 7, 2013 Boston Globe statement: "C. Arden Pope III, an economics professor at Brigham Young University who also was lead author on the American Cancer Society study, said there was no attempt to hide information from Congress or the public. 'Characterizing the ACS and Harvard Six-Cities studies as "secret science" is a misrepresentation of the truth,' Pope said in remarks he e-mailed to the Globe. 'We have continued to be actively involved in open, collaborative, extended analysis efforts,' he added, 'using the data and information in such a way that contributes to scientific understanding and that does not violate commitments to the privacy and confidentiality of research participants.'" (http://www.bostonglobe.com/news/nation/2013/09/06/landmark-harvard-study-health-effects-air-pollution-target-house-gop-subpoena/2K0jhfbJsZcfXqcQHc4jzL/story.html).

The illustrate the dishonesty of Dr. Pope's claim "it would be easy to quickly figure out who the participants were," the first deceased H6CS subject is shown as Record 1259 of the H6CS Excel data file given to EPA in response the subpoena "Lepeule2012_data_0713 final.xlsx":

"STU 409 0.74538 20.9 20.9 1 1 0 0 1"

Dr. Pope cannot possibly identify this H6CS subject using the information provided above. Furthermore, Dr. Pope has not engaged in meaningful collaboration with scientists other than several of the authors of the subpoenaed papers. Their refusal to comply with the subpoena is direct evidence that Dr. Pope and his colleagues have not engaged in "open, collaborative, extended analysis efforts." The characterization of Dr. Pope's research as "secret science" is not "a misrepresentation of the truth."

The final and most glaring example of Dr. Pope's dishonesty is the September 1, 2013 *AJRCCM* paper "Spatial Analysis of Air Pollution and Mortality in California" that he co-authored with Drs. Jerrett, Krewski, Burnett, and Thun and eight other Jerrett Project investigators (http://www.atsjournals.org/doi/abs/10.1164/rccm.201303-0609OC). This paper was published exactly one month after the subpoena was issued for the CPS II data used in the paper. The paper is highly misleading and completely ignores the overwhelming null evidence in the October 28, 2011 Jerrett Final Report (http://www.arb.ca.gov/research/apr/past/06-332.pdf). The positive relationship that it does report is a based on a "conurbation" land use regression model that normalizes out the low death rates in the urban areas of California. This ad hoc model was not even mentioned in the original proposal. Furthermore, the paper does not cite the overwhelming null California PM2.5 mortality evidence that is summarized in my September 28, 2012 ASA JSM 2012 paper (http://www.scientificintegrityinstitute.org/ASAS092812.pdf). The serious flaws in the *AJRCCM* paper are discussed in detail by Dr. William Briggs in his blogs of August 6, 2013 (http://wmbriggs.com/blog/?p=8720) and September 11, 2013 (http://wmbriggs.com/blog/?p=8990). The *AJRCCM* paper and the defiance of its authors reinforces the importance of the subpoena of EPA "secret science" data and the urgent need for independent reanalysis of the ACS CPS II data that underlies this paper and the subpoenaed papers, as explained by Dr. Briggs on September 25, 2013 (http://wmbriggs.com/blog/?p=9241).

In conclusion, Dr. Pope, in collaboration with Drs. Krewski, Jerrett, Burnett, and Thun, has engaged in serious scientific misconduct (falsification) in his PM2.5 epidemiology research and reviews, particularly as it relates to geographic variation in PM2.5 mortality risk and lack of risk in California. The dishonest claim of Dr. Pope and his collaborators that there is a current substantial PM2.5 mortality rink in California has been used by EPA and CARB to justify draconian regulations designed to reduce alleged premature deaths in California due to PM2.5 when there is overwhelming epidemiologic evidence that these deaths do not actually exist.