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

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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/m³ 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/m³ 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 μg/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 $PM_{2.5}$, μg/m^3, (Weighted Average)	1979-1983 HEI $PM_{2.5}$, μg/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 $PM_{2.5}$, μg/m^3, (Weighted Average)	1979-1983 HEI $PM_{2.5}$, μg/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 μg/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

[d]Jerrett M, Burnett RT, Ma R, et al. Spatial Analysis of Air Pollution and Mortality in Los Angeles. *Epidemiology.* 2005;16(6):727-736. http://www.scientificintegrityinstitute.org/Jerrett110105.pdf

[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.

[m]Ostro B, Hu J, Goldberg D, et al. Associations of Mortality with Long-Term Exposures to Fine and Ultrafine Particles, Species and Sources: Results from the California Teachers Study Cohort. *Environ Health Perspect.* 2015;123(6):549-556. http://ehp.niehs.nih.gov/1408565/, or http://dx.doi.org/10.1289/ehp.1408565

[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/

US EPA. Regulatory Impact Analysis related to the Proposed Revisions to the National Ambient Air Quality Standards for Particulate Matter EPA-452/R-12-003. 2012. http://www.epa.gov/ttn/ecas/regdata/RIAs/PMRIACombinedFile_Bookmarked.pdf

Appendix C

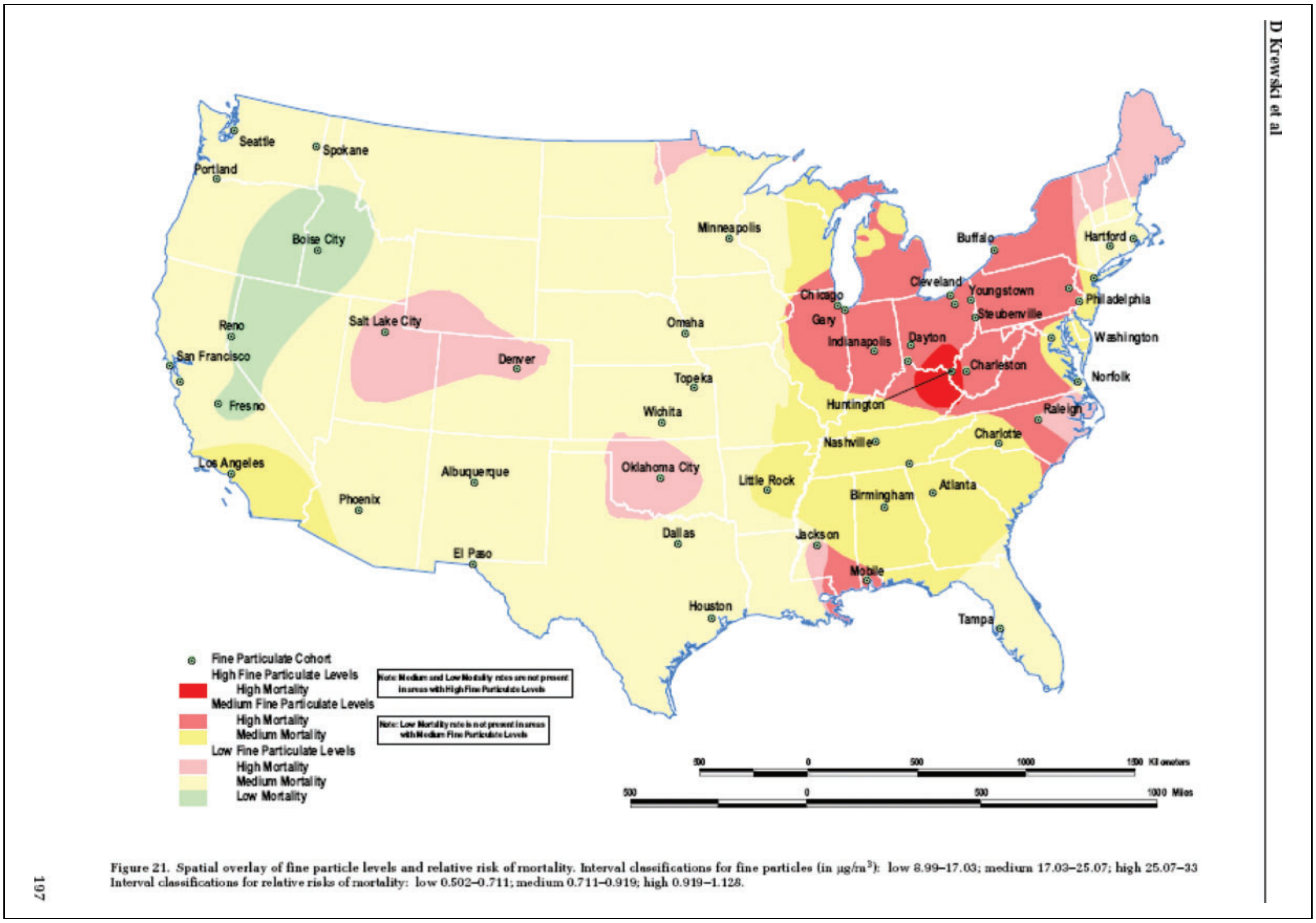

Figure C1. 1982 to 1989 $PM_{2.5}$ mortality risk (MR) in 50 cities (metropolitan areas) shown in Figure 21 on page 197 of HEI 2000[7,9] and listed in Appendix Table B1. Figure 21. Spatial overlay of fine particle levels and relative risk of mortality. Interval classifications for fine particles (in 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.

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Supplemental Material

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References

1. Pope CA III, Thun MJ, Namboodiri MM, et al. Particulate air pollution as a predictor of mortality in a prospective study of U.S. adults. *Am J Resp Crit Care Med*. 1995;151(3 pt 1):669-674. doi:10.1164/ajrccm.151.3.7881654.
2. Kaiser J. Showdown over clean air science. *Science*. 1997;277(5325):466-469.

3. Gamble JF. $PM_{2.5}$ and mortality in long-term prospective cohort studies: cause-effect or statistical associations? *Environ Health Perspect*. 1998;106(9):535-549. doi:10.1289/ehp.98106535.
4. Phalen RF. The particulate air pollution controversy. *Nonlinearity Biol Toxicol Med*. 2004;2(4):259-292. doi:10.1080/15401420490900245. Accessed February 20, 2017.
5. Enstrom JE, Young SS, Dunn JD, et al. Particulate Matter Does Not Cause Premature Deaths. August 17, 2015. https://www.nas.org/images/documents/$PM_{2.5}$.pdf Within Wood P. Concerns about National Academy of Sciences and Scientific Dissent. National Association of Scholars. December 15, 2015. https://www.nas.org/articles/nas_letter. Accessed February 20, 2017.
6. Enstrom JE. *EPA's Clean Power Plan and $PM_{2.5}$-related Co-Benefits. Tenth International Conference on Climate Change. Panel 8. Heartland Institute*. Washington, DC: 2015. http://climateconferences.heartland.org/james-enstrom-iccc10-panel-8/, and http://www.scientificintegrityinstitute.org/JEEICCC061115.pdf. Accessed February 20, 2017.
7. Krewski D, Burnett RT, Goldberg MS, et al. Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality: Special Report. Cambridge, MA: Health Effects Institute; 2000. Part I. Replication and Validation and Part II. Sensitivity Analyses, particularly Figure 5 on page 161, Figure 13 on page 89, and Figure 21 on page 197 and Appendix D and Appendix F. https://www.healtheffects.org/publication/reanalysis-harvard-six-cities-study-and-american-cancer-society-study-particulate-air. Accessed February 20, 2017.
8. Enstrom JE. Fine particulate air pollution and total mortality among elderly Californians, 1973-2002. *Inhal Toxicol*. 2005; 17(14):803-816. PMID:16282158. http://scientificintegrityinstitute.org/IT121505.pdf
9. Enstrom JE. Response to "A Critique of 'Fine Particulate Air Pollution and Total Mortality Among Elderly Californians, 1973-2002'" by Bert Brunekreef, PhD, and Gerald Hoek, PhD. *Inhal Toxicol*. 2006;18(7):509-514. http://scientificintegrityinstitute.org/IT060106.pdf
10. Enstrom JE. Particulate Matter is Not Killing Californians. Proceedings of the American Statistical Association 2012 Joint Statistical Meeting, Section on Risk Analysis, San Diego, CA: 2012: pages 2324-2336. https://www.amstat.org/meetings/jsm/2012/proceedings.cfm, and http://www.scientificintegrityinstitute.org/ASAS092812.pdf
11. July 22, 2013 US House Science Committee Final Request to EPA for ACS CPS II Data. https://science.house.gov/news/press-releases/committee-threatens-subpoena-epa-secret-science, and https://science.house.gov/sites/republicans.science.house.gov/files/documents/07-22-2013%20Smith%20and%20Stewart%20to%20McCarthy.pdf. Accessed February 20, 2017.
12. August 1, 2013 US House Science Committee Subpoena to EPA Requesting ACS CPS II Data. https://science.house.gov/news/press-releases/smith-subpoenas-epa-s-secret-science, and https://science.house.gov/sites/republicans.science.house.gov/files/documents/Subpoena%20link.pdf. Accessed February 20, 2017.
13. Brawley OW. August 19, 2013 ACS Brawley Letter to EPA Refusing to Cooperate with August 1, 2013 US House Science Committee Subpoena of ACS CPS II Data. http://www.scientificintegrityinstitute.org/Brawley081913.pdf. Accessed February 20, 2017.
14. Gapstur SP. September 20, 2013 ACS Letter to Enstrom Denying CPS II Collaboration as Proposed in September 16, 2013 Enstrom Email. http://www.scientificintegrityinstitute.org/GapsturEns092013.pdf. Accessed February 20, 2017.
15. Greenbaum D. October 4, 2013 HEI Response to September 26, 2013 Enstrom Email Declining to Conduct Special Analyses of ACS CPS II re 2000 HEI Reanalysis Report.http://scientificintegrityinstitute.org/Greenbaum100413.pdf. Accessed February 20, 2017.
16. Hinton DO, Sune JM, Suggs JC, Barnard WF. Inhalable Particulate Network Report: Operation and Data Summary (Mass Concentrations Only). Volume I. April 1979-December 1982. EPA-600/4-84-088a. Research Triangle Park, NC: U.S. Environmental Protection Agency, November 1984, particularly pages 102-160 of 210 total pages. http://nepis.epa.gov/Exe/ZyPDF.cgi/20015OU3.PDF?Dockey=20015OU3.PDF. Accessed February 20, 2017.
17. Hinton DO, Sune JM, Suggs JC, Barnard WF. Inhalable Particulate Network Report: Data Summary (Mass Concentrations Only). Volume III. January 1983-December 1984. EPA-600/4-86/019. Research Triangle Park, NC: U.S. Environmental Protection Agency; April 1986: particularly pages 51-80 of 227 total pages. http://nepis.epa.gov/Exe/ZyPDF.cgi/9101R4L8.PDF?Dockey=9101R4L8.PDF
18. SAS, PHREG and REGRESSION Procedures, SAS/STAT 9.4 User's Guide. Cary, NC: SAS Institute Inc. http://support.sas.com/documentation/94/index.html. Accessed February 20, 2017.
19. Centers for Disease Control. National Center for Health Statistics. 1980 CDC WONDER On-line Database, compiled from Compressed Mortality File CMF 1968-1988. http://wonder.cdc.gov/cmf-icd9.html. Assessed April 15, 2016.
20. Krewski D, Jerrett M, Burnett RT, et al. 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: 2009, particularly Table 34. https://www.healtheffects.org/publication/extended-follow-and-spatial-analysis-american-cancer-society-study-linking-particulate. Accessed February 20, 2017.
21. Krewski D. August 31, 2010 Letter to HEI re Special Analysis of California Subjects Within ACS CPS II Cohort Based on 2009 HEI Research Report 140 Methodology. http://www.arb.ca.gov/research/health/pm-mort/HEI_Correspondence.pdf. Accessed February 20, 2017.
22. Lipfert FW, Malone RG, Daum ML, Mendell NR, Yang CC. A Statistical Study of the Macroepidemiology of Air Pollution and Total Mortality. Brookhaven National Laboratory. Upton, NY. Report No. BNL 52122, April 1988, 136 pages. http://www.osti.gov/scitech/servlets/purl/7028097. Accessed February 20, 2017.
23. Lipfert F. Commentary on the HEI reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality. *J Toxicol Environ Health A*. 2003;66(16-19):1705-1714; discussion 1715-1722. doi:10.1080/15287390306443.
24. Enstrom JE. July 11, 2008 CARB $PM_{2.5}$ Premature Deaths Teleconference Involving Enstrom, Pope, Jerrett, and

Burnett. Transcript and Audio File. http://www.scientificintegrityinstitute.org/CARB071108.pdf. Accessed February 20, 2017.

25. Enstrom JE. Analysis of HEI 2000 Figures 5 and 21 to Identify $PM_{2.5}$ Mortality Risk in 49 US Cities Used in Pope 1995 and HEI 2000. September 30, 2010. http://www.scientificintegrityinstitute.org/HEIFigure5093010.pdf
26. Enstrom JE. Submission to UCLA Research Integrity Officer Karagozian Challenging Jerrett et al. $PM_{2.5}$ Mortality Findings and Karagozian Response. December 19, 2016. http://scientificintegrityinstitute.org/RIOJerrettAll121916.pdf
27. Enstrom Compilation of Rejections of This Paper by Seven Major Journals. http://www.scientificintegrityinstitute.org/CPSIIRej122716.pdf. Accessed February 20, 2017.