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Response to Criticism of "Fine Particulate Matter and Total Mortality in Cancer Prevention Study Cohort Reanalysis"

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Keywords
epidemiology, PM2.5, deaths, CPS II, reanalysis

Response to Criticism by CPS II Investigators

Drs C. Arden Pope III (Pope), Daniel Krewski (Krewski), Susan M. Gapstur (Gapstur), Michelle C. Turner (Turner), Michael Jerrett (Jerrett), and Richard T. Burnett (Burnett),[1] as well as Gapstur and Otis W. Brawley (Brawley)[2] strongly criticized my *Dose-Response* article, Enstrom,[3] but they did not identify a single error, particularly regarding my findings of no relationship between fine particulate matter (PM2.5) and total (all-cause) mortality. Thus, my peer-reviewed findings showing no PM2.5-related deaths during 1982 to 1988 in the 1982 American Cancer Society (ACS) Cancer Prevention Study (CPS II) cohort stand unchallenged. In particular, my null findings indicate that the positive findings in 3 seminal publications by these investigators: Pope[4] and Health Effects Institute, HEI (2000)[5] and HEI (2009),[6] are not robust and not supportive of the claim that PM2.5 causes premature deaths. Instead of assessing the validity of my findings, these investigators focused on other aspects of their many analyses of CPS II data.

Their "Expanded Analyses of the ACS CPS-II Cohort" section inaccurately questions the validity of my findings: "The assertion regarding selective use of the CPS-II and PM2.5 data is false." I published prima facie evidence that their 1982 to 1989 PM2.5 mortality findings were indeed sensitive to selective use of PM2.5 and CPS II data. My evidence can be easily checked with minor modifications to the SAS programs that they used to calculate the findings in Table 34 of HEI (2009).[6] Instead of confirming or refuting my evidence, these investigators reiterated their various published analyses of PM2.5 deaths in CPS II, as summarized in their Table 1 and their Figure 1. All of their analyses could be just as sensitive to selective use of PM2.5 and CPS II data as the results in Pope,[4] HEI (2000),[5] and HEI (2009).[6]

Their "Deficiencies in Enstrom's Reanalysis" section does not identify a single error in my findings and suggests that they did not examine the data and findings in my article. For instance, they state, "In contrast, Enstrom[8] asserts that he estimates smaller PM2.5-mortality associations because he uses the 'best' PM2.5 data. He provides no evidence in support of this assertion nor does he provide any measures of the relative quality of models using alternative PM2.5 data." Strong evidence supporting my assertion is clearly presented in Tables 2 and 3 of my article and is described in the "Results" section on page 4. Then, they state, "It is not clear how or why his 'IPN' PM2.5 data differ from the 'HEI' PM2.5 data—especially given that these data come from the same monitoring network." The differences between the Inhalable Particulate Network (IPN) PM2.5 and HEI PM2.5 data are clearly shown in my Appendix Table A1 and discussed in the "Conclusion" section on page 6. To make sure that these differences are fully recognized and understood, an expanded version of Appendix Table A1 is shown in Table 1.

Their "Broader Evidence" section is not relevant to the validity of my findings and diverts attention away from my challenge to the PM2.5 death findings in Pope,[4] HEI (2000),[5] and HEI (2009).[6] Their last paragraph contains the following inaccurate statement: "But the study by Enstrom does not contribute to the larger body of evidence on the health effects of PM2.5 . . . " In conclusion, the authors have not assessed the validity of my peer-reviewed evidence of no relationship between PM2.5 and total mortality in the CPS II cohort and have not been willing to engage with me in addressing the substantive points of my findings.

Response to Criticism by ACS Officials

The ACS Vice President of Epidemiology Susan M. Gapstur and ACS Executive Vice President and Chief Medical Officer

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Table 1. List of the 85 Counties Containing the 50 Cities Used in Pope,[4] HEI (2000),[5] and HEI (2009),[6] As Well As the 35 Additional Counties Used in Enstrom (2017).[a]

					1979–1983		1979–1983	1980	
					IPN PM2.5	HEIDC PM2.5	HEI PM2.5		
State	ACS Division-Unit	FIPS Code	IPN/HEI County Containing IPN/HEI City	IPN/HEI City With PM2.5 Measurements	μg/m³ (Weighted Average)	μg/m³	μg/m³ (Median)	Age-Adjusted White Death Rate (DR)	HEI Figure 5 Mortality Risk (MR)
Alabama	01037	01073	Jefferson	Birmingham	25.6016	28.7	24.5	1025.3	0.760
Alabama	01049	01097	Mobile	Mobile	22.0296	22.0	20.9	1067.2	0.950
Arizona	03700	04013	Maricopa	Phoenix	15.7790	18.5	15.2	953.0	0.855
Arkansas	04071 + 2	05119	Pulaski	Little Rock	20.5773	20.6	17.8	1059.4	0.870
California	06001	06001	Alameda	Livermore	14.3882			1016.6	
California	06002	06007	Butte	Chico	15.4525			962.5	
California	06003	06013	Contra Costa	Richmond	13.9197			937.1	
California	06004	06019	Fresno	Fresno	18.3731	10.3	10.3	1001.4	0.680
California	06008	06029	Kern	Bakersfield	30.8628			1119.3	
California	06051 + 4	06037	Los Angeles	Los Angeles	28.2239	26.8	21.8	1035.1	0.760
California	06019	06065	Riverside	Rubidoux	42.0117			1013.9	
California	06020	06073	San Diego	San Diego	18.9189	18.9		943.7	
California	06021	06075	San Francisco	San Francisco	16.3522	16.4	12.2	1123.1	0.890
California	06025	06083	Santa Barbara	Lompoc	10.6277			892.8	
California	06026	06085	Santa Clara	San Jose	17.7884	17.8	12.4	921.9	0.885
Colorado	07004	08031	Denver	Denver	10.7675	10.8	16.1	967.3	0.925
Colorado	07047	08069	Larimer	Fort Collins	11.1226			810.5	
Colorado	07008	08101	Pueblo	Pueblo	10.9155	19.9		1024.1	
Connecticut	08001	09003	Hartford	Hartford	18.3949	18.4	14.8	952.0	0.845
Connecticut	08004	09005	Litchfield	Litchfield	11.6502			941.5	
Delaware	09002	10001	Kent	Dover	19.5280			959.4	
Delaware	09004 + 2	10003	New Castle	Wilmington	20.3743	20.4		1053.7	
District of Columbia	10001 + 2	11001	District of Columbia	Washington	25.9289	25.9	22.5	993.2	0.850
Florida	11044	12057	Hillsborough	Tampa	13.7337	13.7	11.4	1021.8	0.845
Georgia	12027 + 4	13051	Chatham	Savannah	17.8127	17.8		1029.6	
Georgia	12062	13121	Fulton	Atlanta	22.5688	22.6	20.3	1063.5	0.840
Idaho	13001	16001	Ada	Boise	18.0052	18.0	12.1	892.6	0.600
Illinois	14089 + 4	17031	Cook	Chicago	25.1019	23.0	21.0	1076.3	0.945
Illinois	14098	17197	Will	Braidwood	17.1851			1054.0	
Indiana	15045	18089	Lake	Gary	27.4759	27.5	25.2	1129.8	0.995
Indiana	15049	18097	Marion	Indianapolis	23.0925	23.1	21.1	1041.2	0.970
Kansas	17287	20173	Sedgwick	Wichita	15.0222	15.0	13.6	953.4	0.890
Kansas	17289	20177	Shawnee	Topeka	11.7518	11.8	10.3	933.7	0.830
Kentucky	18010	21019	Boyd	Ashland	37.7700			1184.6	
Kentucky	18055	21111	Jefferson	Louisville	24.2134			1095.7	
Maryland	21106 + 1	24510	Baltimore City	Baltimore	21.6922	21.7		1237.8	
Maryland	21101	24031	Montgomery	Rockville	20.2009			881.9	
Massachusetts	22105 + 1	25013	Hampden	Springfield	17.5682	17.6		1025.3	
Massachusetts	22136	25027	Worcester	Worcester	16.2641	16.3		1014.6	
Minnesota	25001 + 2	27053	Hennepin	Minneapolis	15.5172	15.5	13.7	905.3	0.815
Minnesota	25150 + 5	27123	Ramsey	St Paul	15.5823			935.7	
Mississippi	26086	28049	Hinds	Jackson	18.1339	18.1	15.7	1087.4	0.930
Missouri	27001 + 3	29095	Jackson	Kansas City	17.8488	17.8		1090.3	
Montana	28009	30063	Missoula	Missoula	17.6212			938.0	
Montana	28011	30093	Silver Bow	Butte	16.0405			1299.5	
Nebraska	30028	31055	Douglas	Omaha	15.2760	15.3	13.1	991.0	0.880
Nevada	31101	32031	Washoe	Reno	13.1184	13.1	11.8	1049.5	0.670
New Jersey	33004	34007	Camden	Camden	20.9523			1146.9	
New Jersey	33007	34013	Essex	Livingston	16.4775			1072.7	
New Jersey	33009	34017	Hudson	Jersey City	19.9121	19.9	17.3	1172.6	0.810
New Mexico	34201	35001	Bernalillo	Albuquerque	12.8865	12.9	9.0	1014.7	0.710
New York	36014	36029	Erie	Buffalo	25.1623	26.5	23.5	1085.6	0.960
New York	35001	36061	New York	New York City	23.9064	23.9		1090.4	
North Carolina	37033	37063	Durham	Durham	19.4092		16.8[b]	1039.2	1.000
North Carolina	37064	37119	Mecklenburg	Charlotte	24.1214	24.1	22.6	932.8	0.835
Ohio	39009	39017	Butler	Middletown	25.1789			1108.3	

(continued)

Table 1. (continued)

					1979–1983		1979–1983	1980	
					IPN PM2.5	HEIDC PM2.5	HEI PM2.5		
State	ACS Division-Unit	FIPS Code	IPN/HEI County Containing IPN/HEI City	IPN/HEI City With PM2.5 Measurements	μg/m³ (Weighted	μg/m³ Average)	μg/m³ (Median)	Age-Adjusted White Death Rate (DR)	HEI Figure 5 Mortality Risk (MR)
Ohio	39018	39035	Cuyahoga	Cleveland	28.4120	27.9	24.6	1089.1	0.980
Ohio	39031	39061	Hamilton	Cincinnati	24.9979	25.0	23.1	1095.2	0.980
Ohio	39041	39081	Jefferson	Steubenville	29.6739	29.7	23.1	1058.6	1.145
Ohio	39050	39099	Mahoning	Youngstown	22.9404	22.9	20.2	1058.4	1.060
Ohio	39057	39113	Montgomery	Dayton	20.8120	20.8	18.8	1039.5	0.980
Ohio	39077	39153	Summit	Akron	25.9864	26.0	24.6	1064.0	1.060
Oklahoma	40055	40109	Oklahoma	Oklahoma City	14.9767	15.0	15.9	1050.4	0.985
Oregon	41019 + 1	41039	Lane	Eugene	17.1653	17.2		885.5	
Oregon	41026	41051	Multnomah	Portland	16.3537	19.8	14.7	1060.8	0.830
Pennsylvania	42101 + 1	42003	Allegheny	Pittsburgh	29.1043	30.0	17.9[b]	1115.6	1.005
Pennsylvania	42443	42095	Northampton	Bethlehem	19.5265			998.6	
Pennsylvania	43002 + 11	42101	Philadelphia	Philadelphia	24.0704	24.1	21.4	1211.0	0.910
Rhode Island	45001 + 6	44007	Providence	Providence	14.2341	14.2	12.9	1006.1	0.890
South Carolina	46016 + 1	45019	Charleston	Charleston	16.1635			1023.5	
Tennessee	51019 + 5	47037	Davidson	Nashville	21.8944	22.6	20.5	981.9	0.845
Tennessee	51088	47065	Hamilton	Chattanooga	18.2433	20.4	16.6	1087.9	0.840
Texas	52811 + 2	48113	Dallas	Dallas	18.7594	18.8	16.5	1024.9	0.850
Texas	52859 + 3	48141	El Paso	El Paso	16.9021	16.9	15.7	903.5	0.910
Texas	52882 + 2	48201	Harris	Houston	18.0421	18.0	13.4	1025.7	0.700
Utah	53024	49035	Salt Lake	Salt Lake City	16.6590	17.5	15.4	954.3	1.025
Virginia	55024	51059	Fairfax	Fairfax	19.5425			925.7	
Virginia	55002	51710	Norfolk City	Norfolk	19.5500	19.5	16.9	1139.3	0.910
Washington	56017	53033	King	Seattle	14.9121	14.9	11.9	943.6	0.780
Washington	56032	53063	Spokane	Spokane	13.5200	13.5	9.4	959.2	0.810
West Virginia	58130	54029	Hancock	Weirton	25.9181			1094.8	
West Virginia	58207	54039	Kanawha	Charleston	21.9511	21.7	20.1	1149.5	1.005
West Virginia	58117	54069	Ohio	Wheeling	23.9840		33.4[b]	1117.5	1.020
Wisconsin	59005	55009	Brown	Green Bay	20.5462			931.0	
Wisconsin	59052	55105	Rock	Beloit	19.8584			1019.4	

Abbreviations: ACS, American Cancer Society; HEI, Health Effects Institute; IPN, Inhalable Particulate Network; PM, particulate matter.

[a]Each location includes State, primary ACS Division-Unit number and an indication of additional numbers, Federal Information Processing Standards (FIPS) code, IPN/HEI county, IPN/HEI city with PM2.5 measurements, 1979-1983 IPN-weighted average PM2.5 level, 1979-1983 HEIDC [PM2.5 (DC)] weighted average PM2.5 level, 1979-1983 HEI [PM2.5 (OI, MD)] median PM2.5 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). All 85 counties have IPN PM2.5 data, 58 counties have HEIDC PM2.5 data, and 50 counties have HEI PM2.5 data. However, 3 cities used in HEI, (2000)[5] (Raleigh, North Carolina; Allentown, Pennsylvania; and Huntington, West Virginia) were not part of IPN and origin of the HEI PM2.5 data in HEI (2000)[5] Appendix D for these 3 cities (indicated with superscript letter "b") is unknown. As an approximation, the Raleigh NC PM2.5 value has been assigned to Durham, North Carolina; the Allentown, Pennsylvania, PM2.5 value to Pittsburgh, Pennsylvania, and the Huntington, West Virginia, PM2.5 value to wheeling West Virginia.

Otis W. Brawley have not assessed the validity of my peer-reviewed findings that challenge the validity of 3 seminal CPS II-based publications: Pope,[4] HEI (2000),[5] and HEI (2009)[6]. They can easily check the accuracy of the results in Tables 1 to 3 of Enstrom[3] and they can determine whether I have correctly identified 85 counties using the ACS Division-Unit numbers shown in Appendix Table A1. Instead, they have made statements about my article like, "we cannot confirm the data are from the CPS-II cohort" and "we cannot substantiate the claim that we provided funding for the preparation of the computerized files and documentation for this research."

I want to address the statements that ACS officials Gapstur and Brawley made about my article. In my acknowledgments, I have never stated or implied that the current ACS endorsed or participated in my article or my use of CPS II data, because they did not endorse or participate. However, former ACS staff made it possible for me to obtain access to individual level data on both CPS I and CPS II participants, as I stated in my article. I received ACS external research support during the period 1973 to 1994. None of this ACS external research support was used for this article. However, ACS internal research support paid for all aspects of the 1982 to 1988 CPS II data that I possess: 1982 questionnaire data collection, 1982 to 1988 mortality follow-up, preparation of computer files, and preparation of detailed documentation.

The genuine version of the 1982 to 1988 CPS II data and detailed documentation that I possess did not come from the current ACS. My version was prepared by ACS many years ago, and I obtained it from a source with appropriate access to

Table 2. ACS CPS II Cohort Participants in Unit 41 (Jefferson County) of Division 39 (Ohio) Showing the Number of Researchers, Families, Participants, and Confirmed 1982 to 1988 Deaths for Each Group and for Each Researcher in Group 1.

Group Number	Researcher Number(s)	Number of Researchers	Family Codes	Number of Families	Number of Participants	Number of Confirmed 1982-1988 Deaths
1	5		1-15	15	29	2
1	6		1-17	14	20	3
1	7		1-15	15	30	1
1	8		1-10	9	19	3
1	9		1-16	15	26	1
1	10		1-14	14	27	2
1	5-10	6		82	151	12
2	1-8	7		41	78	1
3	1-4	3		25	36	1
4	1-9	8		91	168	7
5	1-9	8		82	105	16
6	4-10	4		36	37	9
Total		36		357	575	46

Abbreviations: ACS, American Cancer Society.; CPS, Cancer Prevention Study.

Table 3. Fully Adjusted Relative Risk (RR) 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 PM2.5 for CPS II Participants Residing in 47 to 85 Counties in the Continental United States With 1979-1983 IPN PM2.5, HEIDC PM2.5, and HEI PM2.5 Measurements.[a,b]

PM2.5 Years and Source	Number of Counties	Number of Participants	Number of Deaths	RR	95% CI (Lower-Upper)	Average PM2.5
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 HEIDC	58	216 897	12 505	1.024	(0.987-1.061)	21.09
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
1979-1983 HEIDC, N = 47	47	189 676	10 836	1.023	(0.984-1.064)	20.95
1979-1983 IPN, N = 47	47	189 676	10 836	1.021	(0.984-1.058)	21.13
1979-1983 HEI, N = 47	47	189 676	10 836	1.081	(1.036-1.128)	18.01
Fully adjusted RR for the Ohio Valley Continental United States						
1979-1983 IPN	17	53 026	3293	1.096	(0.978-1.228)	25.51
1979-1983 HEIDC	10	43 945	2749	1.048	(0.922-1.191)	25.78
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
Fully adjusted RR for the non-Ohio Valley Continental United States						
1979-1983 IPN	68	216 740	12 300	0.994	(0.967-1.023)	20.09
1979-1983 HEIDC	48	172 952	9756	0.960	(0.919-1.003)	19.90
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: CPS, Cancer Prevention Study; CI, confidence interval; HEI, Health Effects Institute; IPN, Inhalable Particulate Network; PM, particulate matter.
[a]Analysis includes continental United States, 5 Ohio Valley states, and remainder of the States. Table 1 lists up to 85 cities and counties with PM2.5 measurements
[b]1979-1983 PM2.5 data source: IPN = EPA Inhalable Particulate Network → yields insignificant RRs; HEIDC = HEI (2000)[5] Appendix D "PM2.5 (DC)" → yields insignificant RRs (apparently conducted but not reported in HEI 2000[5]); and HEI = HEI (2000)[5] Appendix D "PM2.5 (OI, MD)" → yields significant RRs, used in HEI (2000)[5].

an authorized copy of this version. I have confirmed the validity of this version by showing that (1) the numbers of participants by ACS Division agree almost exactly with the numbers shown in the Fall 1984 CPS II Newsletter (Volume 2, Number 2) Table "Final Numbers of Researchers and Participants by Division"; (2) Table 1 of Enstrom[3] has age at enrollment, sex, race, and education distributions of CPS II participants that agree almost precisely with the same distributions shown in Pope[4] and HEI (2000)[5]; and (3) the CPS II data file information on the participants that I personally enrolled in CPS II agrees with the data that I submitted to ACS in 1982. The ACS epidemiologists can confirm the version of the CPS II data used in my article by confirming my findings in Tables 1 to 3 and Appendix Table A1.[3]

They claim that "when classified using the Division and Unit numbers, the geographically-defined exposure measure will be highly inaccurate for some participants." Actually, the Division-Unit number accurately identifies the county of residence for most CPS II participants. 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 PM2.5 measurements were made. Based on information I have obtained, at least 90% of the 575 CPS II participants in Unit 041 lived in Jefferson County as of September 1, 1982, and ACS can confirm this. In addition, ACS can confirm the detailed information that I have shown in Table 2, regarding the 575 CPS II participants in ACS Unit 041 of ACS Division 39. Table 2 shows the number of researchers, families, participants, and confirmed 1982 to 1988 deaths for the 6 ACS groups within ACS Unit 041. In addition, Table 2 shows these same numbers for each of the 6 researchers in ACS group 1. Thus, as of now, all of the findings in Enstrom[3] stand unchallenged. The ACS has not produced any evidence that invalidates my CPS II cohort findings.

Additional Evidence of No PM2.5 Deaths in CPS II

Since the above investigators criticized my article and did not assess my null findings, I searched their 3 seminal publications for more evidence that supports my null findings. I found evidence in HEI (2000)[5] that I had not previously recognized. Table 29 and Appendix D in HEI (2000)[5] describe 2 key sets of 1979 to 1983 PM2.5 measurements: (1) PM2.5 (OI MD), which is "median fine particle mass from Original Investigators" for 50 cities and designated by me as HEI PM2.5 and (2) PM2.5 (DC), which is "mean fine particle fraction from dichotomous sampler" values for 58 IPN cities and designated by me as HEIDC PM2.5. The PM2.5 (OI MD) values are the ones used in Pope.[4] I now realize that most of the HEIDC PM2.5 [PM2.5 (DC)] values are the same to 1 decimal point as the IPN PM2.5 values in Enstrom.[3]

Table 1 shows that the IPN PM2.5 and HEIDC PM2.5 are identical for 45 cities and somewhat different for 13 cities in HEI (2000)[5] Appendix D. Three cities with PM2.5 (OI MD) values (Raleigh, North Carolina; Allentown, Pennsylvania; and Huntington, West Virginia) were not part of IPN and it is not clear how the PM2.5 values for these 3 cities were measured. As an approximation, the Raleigh NC PM2.5 value has been assigned to Durham, North Carolina, and the Allentown, Pennsylvania, PM2.5 value has been assigned to Pittsburgh, Pennsylvania, and the Huntington, West Virginia, PM2.5 value has been assigned to Wheeling, West Virginia. Two cities in HEI (2000)[5] Appendix D (Boston, Massachusetts and St Louis, Missouri) were not used because of unclear ACS Division-Unit numbers. Table 1 is an expanded version of Appendix Table A1 in Enstrom.[3] Table 3 shows relative risks (RRs) based on IPN PM2.5, HEIDC PM2.5, and HEI PM2.5 values for 85, 58, 50, and 47 cities/counties. The RRs based on the HEIDC PM2.5 values are essentially identical to the null RRs based on the IPN PM2.5 values. Only the RRs based on HEI PM2.5 values are significantly positive, as shown in Enstrom.[3] I find it surprising that the null RRs based on the HEIDC PM2.5 values were not included in HEI (2000)[5] or HEI (2009).[6]

The HEI (2000)[5] Sensitivity Analysis "Risk Estimates Based on Alternative Air Quality Data" section states on page 170, "The means or medians of various indices of air pollution are summarized in Table 30." The data included in this section reveal that the investigators seemed to be aware of the differences in mortality risk associated with PM2.5 (OI MD) and PM2.5 (DC). Table 31 shows RR (all causes) = 1.18 (1.09-1.26) based on PM2.5 (OI MD) values for 50 cities. This value is reduced to RR (all causes) = 1.12 (1.06-1.19) based on PM2.5 (DC) values for 63 cities. Both of these RRs are based on a maximum change in PM2.5 of 24.5 $\mu g/m^3$. I did not previously recognize the similarity between the PM2.5 (DC) values and the IPN PM2.5 values because the only mention of IPN in HEI (2000)[5] occurs in the footnote at the end of Appendix D of Table D.1. Everywhere else in HEI (2000),[5] the term Inhalable Particulate Monitoring Network is used.

It appears that the investigators themselves found no relationship between PM2.5 and total mortality in CPS II in the 2007 *SERRA* article authored by Jerrett et al.[7] Although they cited 16 of their CPS II analyses in their Table 1, they did not cite Jerrett.[7] Figure 2 from Jerrett[7] shows no relationship between PM2.5 and total (all-cause) deaths during 1982 to 2000 in the CPS II cohort. The following quote accompanies Figure 2 "3.1 Health effects The RRs of mortality across the period of follow-up based on the subset of the 51 cities considered were smaller than in the full air pollution cohort considered in the previously full ACS cohort . . . . For example, all-cause mortality was significantly elevated by 6% in the larger cohort, but generally was not significantly elevated in these sub analyses." In addition, Figure 3 (A and B) from Jerrett[7] shows no relationship between PM2.5 and total (all-cause) deaths during 1982 to 1986, 1987 to 1990, 1991 to 1994, 1995 to 1998, and 1999 to 2000. Furthermore, they found low RRs outside the Ohio Valley, as they state in the Discussion section on page 518, "Overall estimated RRs in the 51 cities used in this study were lower than in previous national studies. The lower RR estimates probably resulted from the exclusion of cities in the Ohio River Valley, which tended to demonstrate larger RRs from air pollution than other geographic regions . . . ." Figures 2 and 3 (A and B) from Jerrett[7] are reprinted here.

On June 12, 2017, HEI President Daniel Greenbaum (Greenbaum) provided me with the July 25, 1997 HEI Reanalysis Project Request for Qualifications (RFQ) (http://www.scientificintegrityinstitute.org/Greenbaum061217.pdf). This RFQ specifies the background and requirements for the HEI Reanalysis Project: "HEI is seeking applications representing teams consisting of 2-4 epidemiologists, statisticians and air pollution exposure experts." According to Greenbaum, responses to the RFQ were received from 13 teams and HEI selected the 31-member Krewski team based at the University of Ottawa in Canada, apparently the only foreign-based team. The RFQ objectives and scope include this sentence: "(2) Conduct sensitivity analyses to test the robustness of the original

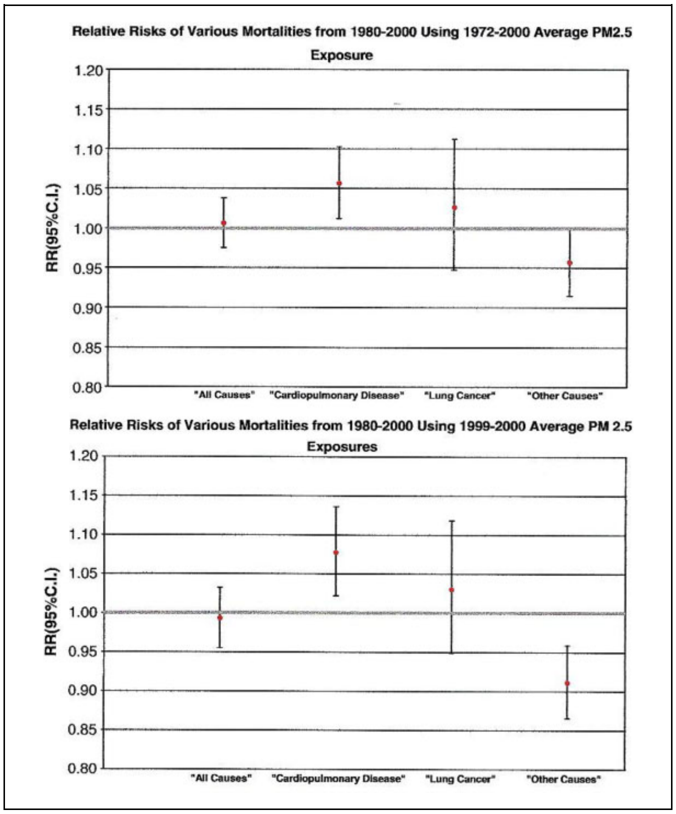

Figure 2 (Jerrett[7]). Summary of risks for different exposures over the entire follow-up.

findings and interpretations to alternative analytic approaches" (http://www.scientificintegrityinstitute.org/HEIRFQ072597.pdf). The Enstrom[3] findings challenge whether the robustness of the Pope[4] findings was properly tested with alternative PM2.5 data, such as IPN PM2.5 data, or alternative cities and counties and metropolitan areas within the CPS II cohort. I first published in 2005 the total mortality RRs for all 11 California counties in the CPS I cohort with IPN PM2.5 data.[8]

Cohen, Pope, and Burnett provided indirect support for my findings in their May 13, 2017, *Lancet* "Global Burden of Disease" article, which went online April 10, 2017.[9] Table 2 from this article shows that, based on their own PM2.5 deaths evidence, the United States had a very low 2015 annual PM2.5-related death rate (18.5 deaths per 100 000 persons) and very low average ambient PM2.5 exposure (8.4 μg/m^3). This table also shows that PM2.5 pollution is concentrated in other parts of the world, particularly China, India, and Africa, and not in the United States. In addition to the evidence of no PM2.5-related deaths in the CPS II cohort, there is null evidence in 2 other national cohorts: the NIH-AARP cohort[10] and the Veterans cohort.[11]

The null PM2.5 total mortality evidence is further described in my August 12, 2017, Doctors for Disaster Preparedness talk "Scientific Misconduct in PM2.5 Epidemiology" (https://www.youtube.com/watch?v=DaFUhJxMNco), my October 12, 2017, NEJM letter "Air pollution and mortality in the Medicare population,"[12] my November 9, 2017, America First Energy Conference talk "ACS Promotes Air Pollution

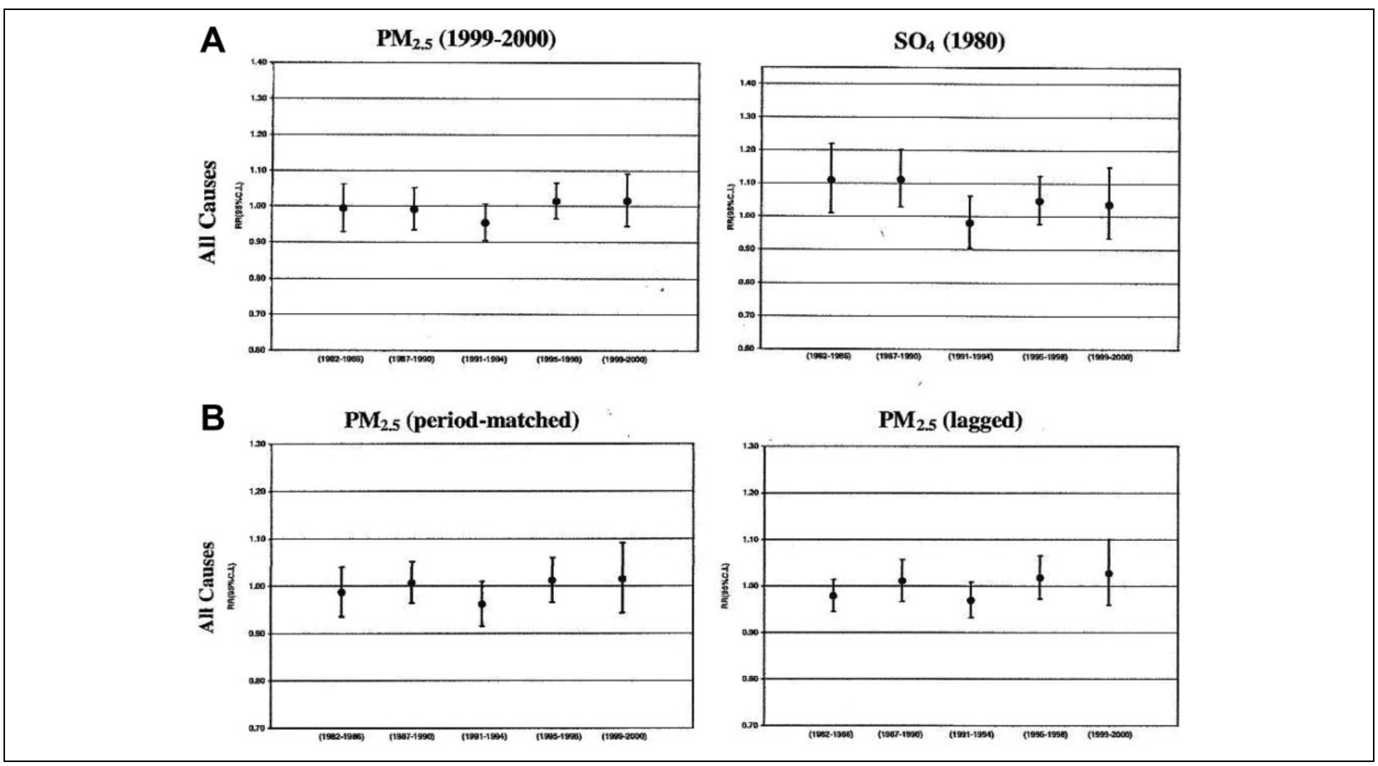

Figure 3 (Jerrett[7]). (A) Relative risks for all-cause, cardiopulmonary and lung cancer deaths estimated for five time periods of the follow-up (1982–1986, 1987–1990, 1991–1994, 1995–1998, and 1999–2000) with measured exposures. (B) Relative risks for all-cause, cardiopulmonary and lung cancer deaths estimated for five time periods of the follow-up (1982–1986, 1987–1990, 1991–1994, 1995–1998, and 1999–2000) with imputed exposures.

Pseudoscience" (http://americafirstenergy.org), and my key 2017 correspondence with the above investigators (http://www.scientificintegrityinstitute.org/DREmails101317.pdf).

Conclusions

My findings of no PM2.5-related deaths during 1982 to 1988 in the CPS II cohort, which are based on my peer-reviewed reanalysis of the CPS II data, stand unchallenged.[3] In addition, my null findings challenge the positive findings in 3 seminal publications by Pope,[4] HEI 2000,[5] and HEI 2009[6] as not robust and not supportive of the claim that PM2.5 causes premature deaths. The responses by Pope[1] and Gapstur[2] have failed to assess the validity or significance of my null findings,[3] but letters supporting the validity of my null findings have been published by Drs S. Stanley Young,[13] Frederick W. Lipfert,[14] and John D. Dunn.[15]

Every effort is being made to encourage ACS, HEI, and the CPS II investigators to cooperate in transparent and verifiable analyses of the CPS II cohort data. However, given the unchallenged null findings in Enstrom,[3] the Environmental Protection Agency (EPA) must reassess all CPS II evidence relating PM2.5 to mortality as part of the current integrated science assessment of the PM2.5 National Ambient Air Quality Standard (NAAQS).

Declaration of Conflicting Interests

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References

1. Pope CA III, Krewski D, Gapstur SM, Turner MC, Jerrett M, Burnett RT. Fine particulate air pollution and mortality: response to Enstrom's re-analysis of the American Cancer Society Cancer Prevention Study II cohort (letter). *Dose-Response*. 2017;15(4). doi:10.1177/1559325817746303.
2. Gapstur SM, Brawley OW. Re: fine particulate matter and total mortality in cancer prevention study cohort reanalysis (letter). *Dose-Response*. 2017;15(4). doi:10.1177/1559325817749412.
3. Enstrom JE. Fine particulate matter and total mortality in cancer prevention study cohort reanalysis. *Dose-Response*. 2017;15(1): 1-12. doi:10.1177/1559325817693345.
4. Pope CA 3rd, 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
5. 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, July 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 (http://pubs.healtheffects.org/ publication/reanalysis-harvard-six-cities-study-and-american-cancer-society-study-particulate-air). Accessed April, 2018.
6. 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, June 2009, particularly Table 34 (http://pubs.healtheffects.org/publication/extended-follow-and-spatial-analysis-american-cancer-society-study-linking-particulate). Accessed April, 2018.
7. Jerrett M, Newbold KB, Burnett RT, et al. Geographies of uncertainty in the health benefits of air quality improvements. *Stoch Environ Res Risk Assess*. 2007;21(5):511-522. doi:10.1007/s00477-007-0133-2 (http://scientificintegrityinstitute.org/jerrett051707.pdf)
8. Enstrom JE. Fine particulate air pollution and total mortality among elderly Californians, 1973–2002. *Inhal Toxicol*. 2005; 17(14):803-816. doi:10.1080/08958370500240413 (http://www.arb.ca.gov/planning/gmerp/dec1plan/gmerp_comments/enstrom.pdf)
9. Cohen AJ, Brauer M, Burnett R, et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet*. 2017;389(10082):1907-1918. doi:10.1016/S0140-6736(17)30505-6.
10. 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. doi:10.1289/ehp.1509676.
11. Lipfert FW, Perry HM Jr, Miller JP, Baty JD, Wyzga RE, Carmody SE. The Washington University-EPRI Veterans' cohort mortality study: preliminary results. *Inhal Toxicol*. 2000;12(suppl 4):41-73. doi:10.1080/713856640.
12. Enstrom JE. Air pollution and mortality in the Medicare population (letter). *N Engl J Med*. 2017;377(15):1498. doi:10.1056/NEJMc1709849.
13. Young SS. Evidence supporting no dose response of mortality to air quality (letter). *Dose-Response*. 2018;16(1). doi:10.1177/1559325817750485.
14. Lipfert FW, Enstrom JE. Fine particulate and total mortality in cancer prevention study cohort reanalysis (letter). *Dose-Response*. 2018;16(1). doi:10.1177/1559325817746304.
15. Dunn JD. Enstrom's expose of air pollution epidemiology problems (letter). *Dose-Response*. 2018;16(1). doi:10.1177/1559325817749414.