Allegations of Scientific Misconduct by Former USC Professor Michael Jerrett Regarding PM2.5 Deaths

Supplement to March 5, 2019 Presentation to USC Vice President of Research

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As per our telephone conference on March 5, 2019, I am supplementing my March 5, 2019 allegations that numerous current and former USC Preventive Medicine Professors have engaged in falsification as defined by DHHS and Section 3.2 of USC's policy on scientific misconduct (https://policy.usc.edu/scientific-misconduct/). This supplement summarizes specific evidence of falsification (exaggeration) of the relationship between fine particulate matter (PM2.5) and total mortality in four publications during 2000-2009 that are co-authored by Michael Jerrett, PhD (Jerrett), a USC Associate Professor of Preventive Medicine during 2003-2006. This specific evidence is described in detail in Enstrom 2017 and Enstrom 2018, which are attached below as the bulk of my 29-page PDF of *Dose-Response* articles and letters (http://scientificintegrityinstitute.org/DRPM25JEEPope052918.pdf). Additional background is provided in the 22-page document to the USC President and Provost that I left in your office on February 22, 2019 (http://scientificintegrityinstitute.org/USCVPRes022219.pdf).

While at USC during 2003-2006, Jerrett interacted closely with current USC Preventive Medicine Professors Kiros T. Berhane (Berhane), Duncan C. Thomas (Thomas), and Rob S. McConnell (McConnell), who were involved with hiring him in 2003. My allegations of falsification by Berhane, Thomas, and McConnell are described in my March 5, 2019 submission below. These three professors have been familiar with null evidence on PM deaths since at least 2000, when Berhane and Thomas described the 2000 Dominici, Samet, and Zeger JRSS article "Combining evidence on air pollution and daily mortality from the 20 largest US cities" as "seminal and academically stimulating." This article found that PM10, which includes PM2.5, was NOT related to daily mortality in Los Angeles. The conclusion was "These analyses alone cannot establish that increased levels of particulate air pollution as measured by PM10 cause an increase in mortality." Although they acknowledged null evidence in 2000, a Google Scholar search reveals that Berhane, Thomas, and McConnell have NEVER cited any of my evidence of NO PM2.5 deaths in Los Angeles County and CA. In addition, they have refused to engage with me on PM2.5 deaths and they have not opposed the SCAQMD claims about PM2.5 deaths or the proposed new SCAQMD PM2.5 sales tax. Jerrett has NEVER cited me in any of his many journal articles that promote PM2.5 deaths. I document his falsification in four key publications below. All the publications cited below are identified by the last name of the first author and the year of publication and they can be found in Enstrom 2017, Enstrom 2018, and/or PubMed.gov.

Dr. S. Stanley Young, an ASA Fellow and EPA Science Advisory Board Member, supports my evidence of falsification of PM2.5 mortality risk and has published his own evidence of no relationship between PM2.5 and daily mortality in Los Angeles and California, which is consistent with the null JRSS evidence. He spoke to these USC professors in 2011 and 2014, but they ignore his null evidence on PM2.5 deaths.

Four Jerrett Publications That Contain Specific Evidence of Falsification (Exaggeration) of the Relationship of PM2.5 and Total Mortality:

1) HEI 2000 (Jerrett is sixth author of Part II "Sensitivity Analyses") was shown to be severely flawed by Enstrom 2017 and Enstrom 2018. Five examples of falsification of the relationship between PM2.5 and total mortality are as follows: 1) The best available 1979-1983 PM2.5 measurements as of 2000 (Hinton 1984 and Hinton 1986) were partially included in HEI 2000 Appendix Table D, but they were not used to calculate the relationship between PM2.5 and total mortality. If the Hinton PM2.5 data had been used, HEI 2000 would have found no relationship in the United States (US). 2) Enstrom 2017 found that 85 counties with ACS CPS II subjects had Hinton PM2.5 data, but only 50 counties were analyzed in HEI 2000. 3) Among the 35 counties omitted from HEI 2000 were 7 of the 11 California (CA) counties, including the county with the highest PM2.5 level (Riverside County) and the county with the lowest PM2.5 level (Santa Barbara County). 4) When the US was divided into the five Ohio Valley states and the remaining states, there was no PM2.5 mortality risk in either area. 5) There was no PM2.5 mortality risk in CA no matter what PM2.5 data was used. These findings were possible only because I gained access in 2016 to an early version of ACS CSP II data, as per proposed EPA transparency in regulatory science.

2) Jerrett 2005 "Spatial Analysis of Air Pollution and Mortality in Los Angeles" was conducted and published while Jerrett was at USC. It found that the relative risk for PM2.5 deaths within different areas of Los Angeles was unusually high, but never mentioned that the overall PM2.5 mortality risk for Los Angeles was LOW, as shown in HEI 2000 Figure 21. One month after Jerrett 2005, Enstrom 2005 found NO PM2.5 mortality risk in Los Angeles. Nevertheless, Jerrett 2005 was cited and hyped by CARB, SCAQMD, and the press in 2006, but Enstrom 2005 was totally ignored.

3) Jerrett 2007 "Geographies of uncertainty in the health benefits of air quality improvements" found NO PM2.5 mortality risk in the ACS CPS II cohort during five mortality follow-up periods from 1982 to 2000, as shown in Enstrom 2018. The null findings in Jerrett 2007 are not cited in Jerrett's subsequent publications, such as, HEI 2009. Failure to cite of his own null findings is further evidence of falsification.

4) HEI 2009 (Jerrett is second author), extended mortality follow-up of ACS CPS II cohort, was shown to be severely flawed by Enstrom 2017 and Enstrom 2018. HEI 2009 did not cite the criticism of HEI 2000 by Lipfert and Enstrom. HEI 2009 did not present any null results based on analysis of the Hinton PM2.5 data. The HEI 2000 Figure 21 evidence of geographic variation in PM2.5 mortality risk was not addressed or preserved in HEI 2009. Extensive 2000-2008 evidence of NO PM2.5 mortality risk in CA (Enstrom 2017 Appendix Table B1) was not cited in HEI 2009. HEI 2009 did not address the criticisms of PM2.5 deaths that I stated to HEI 2009 co-authors Jerrett, Pope, and Burnett during the July 11, 2008 CARB PM2.5 Premature Deaths Teleconference (http://scientificintegrityinstitute.org/CARB071108.pdf).

The above four Jerrett publications did not cite any of the major criticisms of PM2.5 deaths that were published in peer-reviewed journals during 2000-2008 by experts like Enstrom, Phalen, Lipfert, Moolgavkar, and McClellan. All these criticisms revealed null evidence and/or described flaws in the claims of PM2.5 deaths. The claim that PM2.5 *causes* premature death violates basic epidemiologic principles like the Hill criteria for establishing causality. No causal etiologic mechanism has been established. The observed relative risks for PM2.5 mortality effects are too small, given confounding variables. The PM2.5 exposure levels in the US are below the threshold for a mortality effect.

I conclude by noting that the falsification of PM2.5 deaths by Jerrett is continuing. None of the evidence of NO PM2.5 deaths in the US that I assembled from several sources as of October 1, 2018 (http://scientificintegrityinstitute.org/PM25WGJEE100118.pdf) was cited in Jerrett's September 18, 2018 PNAS article on PM2.5 deaths (https://www.pnas.org/content/pnas/115/38/9592.full.pdf).

Allegations of Scientific Misconduct by USC Preventive Medicine Professors Regarding PM2.5 Deaths

Presentation to USC Vice President of Research

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March 5, 2019

I allege that numerous current and former USC Preventive Medicine Professors have engaged in falsification as defined by DHHS and Section 3.2 of USC's policy on scientific misconduct (https://policy.usc.edu/scientific-misconduct/). My allegations involve the following words from Section 3.2: "Research misconduct is defined as falsification in reviewing research or in reporting research results." The specific allegations "omitting data or results such that the research is not accurately represented in the research record," where "The Research Record is defined as the record of data or results that embodies the facts resulting from scientific inquiry, including, for example, laboratory records, research proposals, reports, abstracts, theses, oral presentations, journal articles, and any documents or materials provided to the university by the subject of the allegations in the course of a research misconduct proceeding."

This falsification has occurred during the past 20 years when these Professors have interacted closely with and received millions of dollars in funding from the two most powerful air pollution regulatory agencies in California, CARB and SCAQMD. These Professors have published and promoted only evidence indicating harmful effects of air pollution. They have rarely or never cited null findings that show no harmful health effects of air pollution. They have unethically and consistently ignored critics of their research and their public claims, particularly as they relate to support for CARB and SCAQMD regulations. I provide three specific allegations of falsification below and there are many other allegations contained within the evidence that I have submitted to you, the USC President, and the USC Provost (http://www.scientificintegrityinstitute.org/USCVPRes022219.pdf).

Allegation 1. USC Preventive Medicine Professors Kiros T. Berhane (Berhane) and Duncan C. Thomas (Thomas) refuse to acknowledge or discuss null evidence on PM2.5-related deaths.

Berhane is Professor of Biostatistics and Director of Graduate Programs in Biostatistics and Epidemiology at the USC Department of Preventive Medicine and he has played a particularly important role in the above falsification. Berhane has extensive knowledge of the long-running PM2.5 deaths controversy dating back to his 2000 JRSS article with Thomas. Berhane and Thomas are also familiar with the extensive null evidence on PM2.5 deaths that was presented by ASA Fellow and EPA Science Advisory Board Member Dr. S. Stan Young (Young) and me at the November 13, 2014 USC Preventive Medicine Seminar that Berhane organized.

In 2017 Berhane was appointed to the Health Effects Institute (HEI) Review Committee (https://www.healtheffects.org/about/review-committee). He organized and moderated the April 30, 2018 session on "Can We Rely on Environmental Health Research?" at the April 29-May 1, 2018 Health

Effects Institute Annual Conference (https://www.healtheffects.org/meeting/annual-conference-2018). The HEI description of the session was "Awareness has grown during the last decade that many scientific studies have not been reproduced and the problem seems to be particularly widespread in certain fields. Environmental standards are health based and there have been long-standing debates about replicability and reproducibility of the studies underpinning regulations (including data access, quality, and analyses), though arguably the recent debate has given this issue greater visibility. Reproducibility has been the focus of several recent debates in scientific journals and also is reflected in congressional efforts at transparency. This session will describe the background on this issue, different perspectives on it, and approaches to addressing it."

Unfortunately, the session did not provide any meaningfully different perspectives and included only speakers with close ties to HEI. There were presentations on "Reproducibility and Replicability: Definitions and What They Imply" by Dr. Steve Goodman (Goodman) of Stanford METRICS and "Reproducibility and Air Pollution Epidemiology", by Dr. Richard Burnett (Burnett) of Health Canada. Although Enstrom 2017 found major flaws in HEI 2000 and HEI 2009, two seminal HEI publications confirming PM2.5 deaths, Berhane did not invite me or other major critics of PM2.5 deaths to participate in the session. Furthermore, Burnett totally ignored my strong null evidence on PM2.5 deaths in his meta-analysis presentation. I immediately showed that the Burnett meta-analysis was severely flawed and biased toward a positive relationship. However, Berhane and Thomas, along with Goodman and Burnett, have refused to respond to my emails and phone calls requesting their recognition of the overwhelming evidence of NO PM2.5 deaths in California and the US.

Allegation 2. USC Preventive Medicine Professor Rob S. McConnell (McConnell) and former USC epidemiology postdoctoral fellow Dr. Jo Kay Chan Ghosh (Ghosh) deliberately falsified the PM2.5 deaths evidence in the 2016 SCAQMD AQMP.

McConnell served on the 2016 SCAQMD Health Advisory Council for the 2016 SCAMQD Air Quality Management Plan (AQMP), which was headed by Ghosh, who has been SCAQMD Health Effects Officer since 2016. I sent to Ghosh detailed criticism of the draft 2016 AQMP Health Effects Chapter on January 11, July 26, and August 15, 2016, including extensive evidence of NO PM2.5 deaths. On August 18, 2016 I personally presented this evidence to the SCAQMD Health Advisory Council, including both Ghosh and McConnell. Since the final draft 2016 AQMP ignored my null evidence, I submitted seven pages of detailed comments and criticism to Ghosh on January 30, 2017 (http://scientificintegrityinstitute.org/GhoshAll013017.pdf). This criticism includes my November 11, 2016 allegations against former USC Associate Professor Michael Jerrett (Jerrett), who is now Chair of the UCLA Environmental Health Sciences. These allegations have been essentially confirmed by the DHHS Office of Research Integrity (ORI). The 2016 AQMP is socioeconomic justified ONLY if PM2.5 causes premature deaths in Southern California. Ghosh and McConnell ignored my overwhelming evidence of NO PM2.5 premature deaths and instead used the contested positive evidence of Jerrett, which the DHHS ORI agrees is null. SCAQMD is proposing to pay for implementation of the scientifically unjustified regulations in the 2016 AQMP with a 0.5-1.0 cent increase in the Southern California sales tax as per SB 732, which was introduced to the State Legislature on February 22, 2019.

Allegation 3. USC Preventive Medicine Professor McConnell and former USC Preventive Medicine Professor Jerrett deliberately falsified the PM2.5 deaths evidence in the 2012 SCAQMD AQMP.

McConnell served on the 2012 SCAQMD Health Advisory Council for the 2012 SCAQMD AQMP. I submitted extensive criticism of the draft 2012 AQMP Health Effects Chapter, including a September 17, 2012 email to McConnell regarding my August 30, 2012 criticism of the draft 2012 AQMP Health Effects Chapter (http://www.scientificintegrityinstitute.org/McConnell091712.pdf). I was particularly concerned about the inaccurate McConnell statement "In general, I think this [draft] is a good summary drawing on the key studies and reviews conducted as the foundation for regulatory decisions by EPA staff and CARB." Because McConnell did not respond to my emails about null PM2.5 evidence, I submitted September 20, 2012 criticism of SCAQMD Revised Draft 2012 AQMP Health Effects Chapter (http://www.scientificintegrityinstitute.org/AQMP092012.pdf). My criticism contains evidence of NO PM2.5 deaths in California from 26 experts, including then USC Preventive Medicine Chair Jonathan M. Samet, as well as Jerrett and Burnett. Despite its claims of an unusually strong positive relationship between PM2.5 and total mortality, there are several largely-ignored null findings in the 2005 Jerrett article "Spatial Analysis of Air Pollution and Mortality in Los Angeles." This article was conducted and published when Jerrett was a USC Preventive Medicine Professor during 2003-2006. In addition, Enstrom 2017 found serious errors in HEI 2000 and HEI 2009, which Jerrett coauthored.

On December 7, 2012 public testimony by interested individuals was given to the SCAQMD Board before it approved the 2012 AQMP. McConnell made two FALSE statements at the end of his 3:06 minute testimony (2:50-3:06): "The best available scientific evidence is that ozone and PM2.5 are making Southern Californians sick and die at greater rates that would occur otherwise. That evidence should guide how the district weighs health considerations in developing policy." (http://www.scientificintegrityinstitute.org/McConnell120712.MP3). McConnell's statement was directly contradicted by statements by me (http://www.scientificintegrityinstitute.org/Enstrom120712.MP3) and UC Irvine Professor of Medicine Robert F. Phalen (http://www.scientificintegrityinstitute.org/Phalen120712.MP3). Nevertheless, the 2012 AQMP was approved with no changes regarding its exaggerated claims about PM2.5 deaths.

After I have explained these three allegations, I will state the general nature of additional allegations. Finally, I have suggestions on how to resolve the validity of my allegations.

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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/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)				

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Appendix C

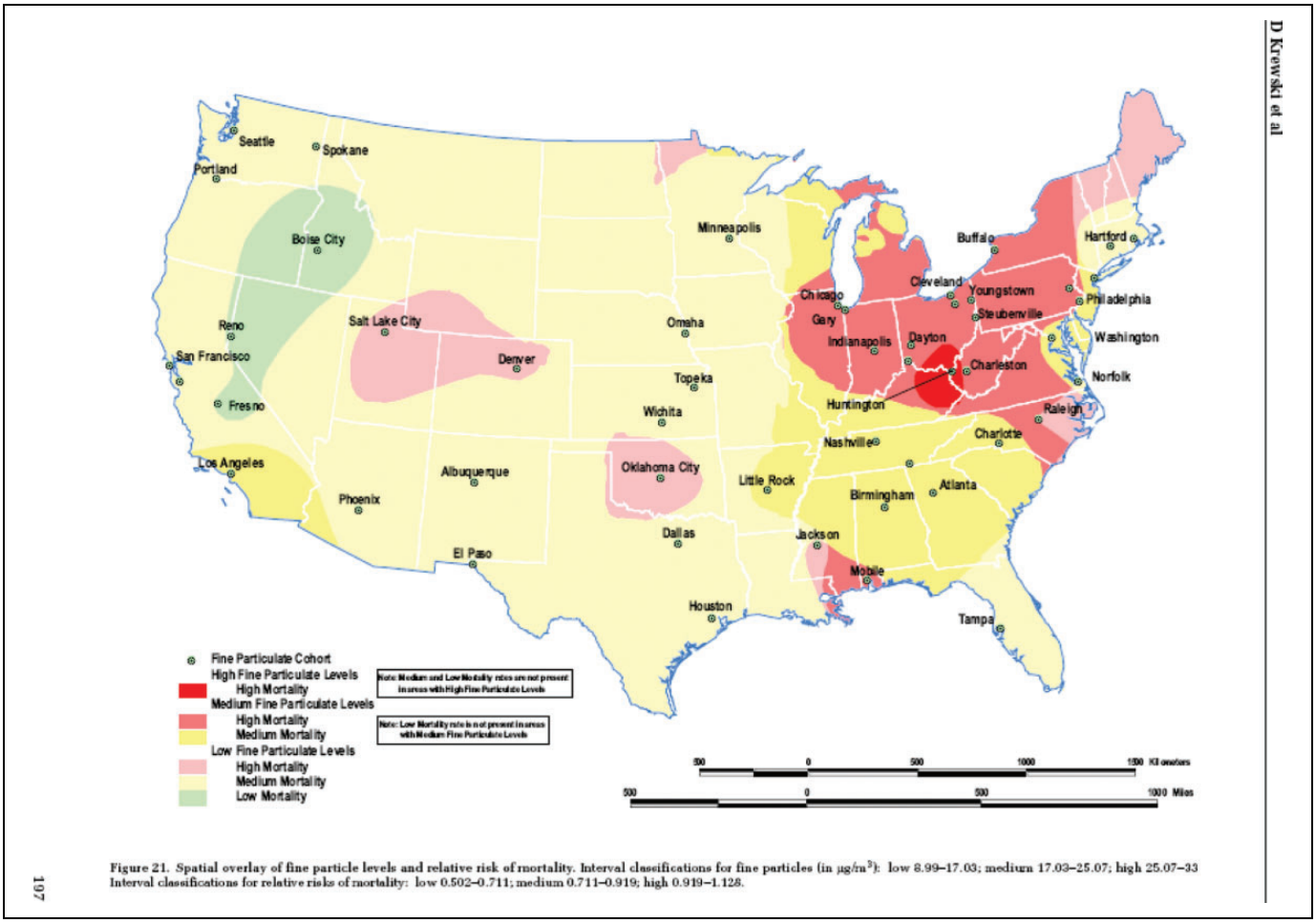

Figure C1. 1982 to 1989 $PM_{2.5}$ mortality risk (MR) in 50 cities (metropolitan areas) shown in Figure 21 on page 197 of HEI 2000[7,9] and listed in Appendix Table B1. Figure 21. Spatial overlay of fine particle levels and relative risk of mortality. Interval classifications for fine particles (in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

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Supplemental Material

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Letter to the Editor

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Fine Particulate Air Pollution and Mortality: Response to Enstrom's Reanalysis of the American Cancer Society Cancer Prevention Study II Cohort

C. Arden Pope III[1], Daniel Krewski[2,3,4], Susan M. Gapstur[5], Michelle C. Turner[2,6,7,8], Michael Jerrett[9], and Richard T. Burnett[10]

Background

The first analysis of long-term exposures to air pollution and risk of mortality using the American Cancer Society Cancer Prevention Study II (ACS CPS-II) cohort was published in 1995.[1] Subsequently, extensive independent reanalysis[2] and multiple extended analyses[3-7] were conducted. These studies have consistently demonstrated that exposure to fine particulate matter air pollution ($PM_{2.5}$) is associated with increased risk of mortality, especially cardiopulmonary or cardiovascular disease mortality. A recent analysis by Enstrom, based on early data from the ACS CPS-II cohort, reports no significant relationship between $PM_{2.5}$ and total mortality.[8] The author asserts that the original analyses, reanalyses, and the extended analyses found positive $PM_{2.5}$–mortality relationships because of selective use of CPS-II and $PM_{2.5}$ data.

Expanded Analyses of the ACS CPS-II Cohort

The assertion regarding selective use of the CPS-II and $PM_{2.5}$ data is false. The scope of analyses of the ACS CPS-II cohort conducted over more than 2 decades were explicitly expanded over time to characterize population health risks of $PM_{2.5}$ in more detail and with greater accuracy. Table 1 provides an outline of key published studies of this expansive body of air pollution research. The highlights of the obvious progress made during the course of these studies include the following:

1) increased mortality follow-up from 7 to 22 or 26 years;
2) increased number of participants included in the analyses from approximately 295 000 to 670 000;
3) increased number of deaths (a key determinant of study power) included in the analyses from approximately 21 000 to 237 000;
4) improved assessment of $PM_{2.5}$ exposures (and exposures of co-pollutants) from metro-level averages for cities with air pollution monitoring to modeled $PM_{2.5}$ exposures at geocoded residential addresses throughout the United States; and
5) improved statistical models, including improved control for individual and ecological covariates, and better representation of spatial patterns in the data.

As shown in Figure 1, estimates of the percentage increase in mortality risk per 10 $\mu g/m^3$ increase in $PM_{2.5}$ for all-cause and for cardiovascular disease mortality from studies using the ACS CPS-II cohort have been remarkably consistent across the expanded analyses over the last 20+ years. The recent analysis by Enstrom[8] shows an estimated $PM_{2.5}$–mortality association that is smaller than observed in the original analysis, the

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Table 1. Overview of Key Studies of Particulate Matter Air Pollution and Risk of Mortality Using the ACS CPS-II Cohort.

Citation	Authors	Approx. No. Participants (Deaths) for Key PM Measures	Geographic Units of Exposure	Years of Follow-Up	Comments
Am J Respir Crit Care Med. 1995;151:669-674.[1]	Pope et al	$PM_{2.5}$: 295 000 (21 000) SO_4: 550 000 (39 000)	50 metro areas 151 metro areas in the United States	7 (1982-1989)	Original analysis. Mortality, especially cardiopulmonary, associated with $PM_{2.5}$ and SO_4
Health Effects Institute 2000; HEI Special Report.[2]	Krewski et al	$PM_{2.5}$: 300 000 (23 000) SO_4: 559 000 (43 000)	50 metro areas 151 metro areas in the United States	7 (1982-1989)	Independent reanalysis that substantively reproduced original results, developed improved modeling, and provided substantial sensitivity analysis
JAMA. 2002;287:1132-1141.[3]	Pope et al	$PM_{2.5}$: 500 000 SO_4: 560 000	116 metro areas 149 metro areas in the United States	16 (1982-1998)	All-cause, lung-cancer, and cardiopulmonary mortality, associated with $PM_{2.5}$ and SO_4. Improved statistical modeling, including random effects
Circulation. 2004;109:71-77.[9]	Pope et al	$PM_{2.5}$: 500 000	116 metro areas in the United States	16 (1982-1998)	$PM_{2.5}$ associated with cardiovascular mortality. Evidence of pathophysiological pathways of disease explored
Epidemiology. 2005;16:727-736.[10]	Jerrett et al	$PM_{2.5}$: 23 000 (6000)	267 zip code areas in metro Los Angeles	18 (1982-2000)	Relatively large $PM_{2.5}$ associations with all-cause, lung-cancer, and cardiopulmonary mortality
Lancet. 2009;374:2091-2103.[11]	Smith et al	$PM_{2.5}$. SO_4, and elemental carbon: 350 000 (93 000)	86 metro areas in the United States	18 (1982-2000)	Cardiopulmonary mortality was associated with $PM_{2.5}$, SO_4, and elemental carbon. Correlations across pollutants make independent estimates difficult
Health Effects Institute 2009; Research Report Number 140.[4]	Krewski et al	$PM_{2.5}$: 500 000 SO_4: 560 000	116 metro areas 147 metro areas in the United States	18 (1982-2000)	All-cause, lung-cancer, and cardiopulmonary mortality associated with $PM_{2.5}$ and SO_4 even controlling for ecologic covariates
N Engl J Med. 2009;360:1085-1095.[5]	Jerrett et al	$PM_{2.5}$: 450 000 (118 000)	86 metro areas in the United States	18 (1982-2000)	Evaluated associations with ozone, independent of $PM_{2.5}$, however, $PM_{2.5}$–mortality associations were observed as in previous studies
Am J Respir Crit Care Med. 2011;184:1374-1381.[12]	Turner et al	$PM_{2.5}$: 178 000 never smokers (1000 lung cancer deaths)	117 metro areas in the United States	26 (1982-2008)	Long-term exposure to $PM_{2.5}$ pollution was associated with small but significant increase in risk of lung cancer mortality
Am J Respir Crit Care Med. 2013;188:593-599.[13]	Jerrett et al	$PM_{2.5}$: 74 000 (20 000)	Modeled exposures at geocoded home addresses throughout California	18 (1982-2000)	Based on individualized exposure assignments at home addresses, mortality risk was associated with air pollution, including $PM_{2.5}$
Am J Epidemiol. 2014;180:1145-1149.[14]	Turner et al	$PM_{2.5}$: 430 000	Modeled $PM_{2.5}$ exposures at geocoded home addresses throughout the United States	6 (1982-1988)	Evaluated the interactions between cigarette smoking and $PM_{2.5}$ exposures for lung cancer mortality
Circulation Res. 2015;116:108-115.[6]	Pope et al	$PM_{2.5}$: 670 000 (237 000)	Modeled $PM_{2.5}$ exposures at geocoded home addresses throughout the United States	22 (1982-2004)	The associations between all-cause and cardiovascular mortality and $PM_{2.5}$ were similar to previous studies but, given the very large cohort and large number of deaths, the statistical precision of the estimate was remarkable
Environ Health Perspect. 2016;124:785-794.[15]	Thurston et al	$PM_{2.5}$: 446 000	100 metro areas in the United States	22 (1982-2004)	Evaluated source-related components of $PM_{2.5}$. Exposures from fossil fuel combustion, especially coal burning and traffic were associated with increased ischemic heart disease mortality
Am J Respir Crit Care Med. 2016;193:1134-1142.[16]	Turner et al	$PM_{2.5}$: 670 000 (237 000)	Modeled $PM_{2.5}$ exposures at geocoded home addresses throughout the United States	22 (1982-2004)	The focus of this study was on ozone exposure but mortality was associated with $PM_{2.5}$ (both near-source and regional) as observed previously
Environ Res. 2017;154:304-310.[17]	Turner et al	$PM_{2.5}$: 429 000 (146 000) Current or never smokers	Modeled $PM_{2.5}$ exposures at geocoded home addresses throughout the United States	22 (1982-2004)	Evaluated interactions between cigarette smoking and $PM_{2.5}$. $PM_{2.5}$ was associated with all-cause and cardiovascular mortality in both smokers and never smokers with evidence for a small additive interaction
Environ Health Perspect. 2017;125:552-559.[7]	Jerrett et al	$PM_{2.5}$: 670 000 (237 000)	Modeled $PM_{2.5}$ exposures at geocoded home addresses throughout the United States	22 (1982-2004)	$PM_{2.5}$ exposures assigned to using 7 exposure models and 11 exposure estimates. $PM_{2.5}$–mortality risks were observed using all of the exposure models. Smaller associations observed using remote sensing exposure estimates; larger effects observed using exposure models that included ground-based information
Dose-Response. 2017;15(1):1-12.[8]	Enstrom	$PM_{2.5}$: 270 000 (16 000)	85 counties in the United States	6 (1982-1988)	Asserted no significant mortality associations using "best" $PM_{2.5}$ data

Abbreviations: ACS CPS II, American Cancer Society Cancer Prevention Study II; $PM_{2.5}$, particulate matter air pollution.

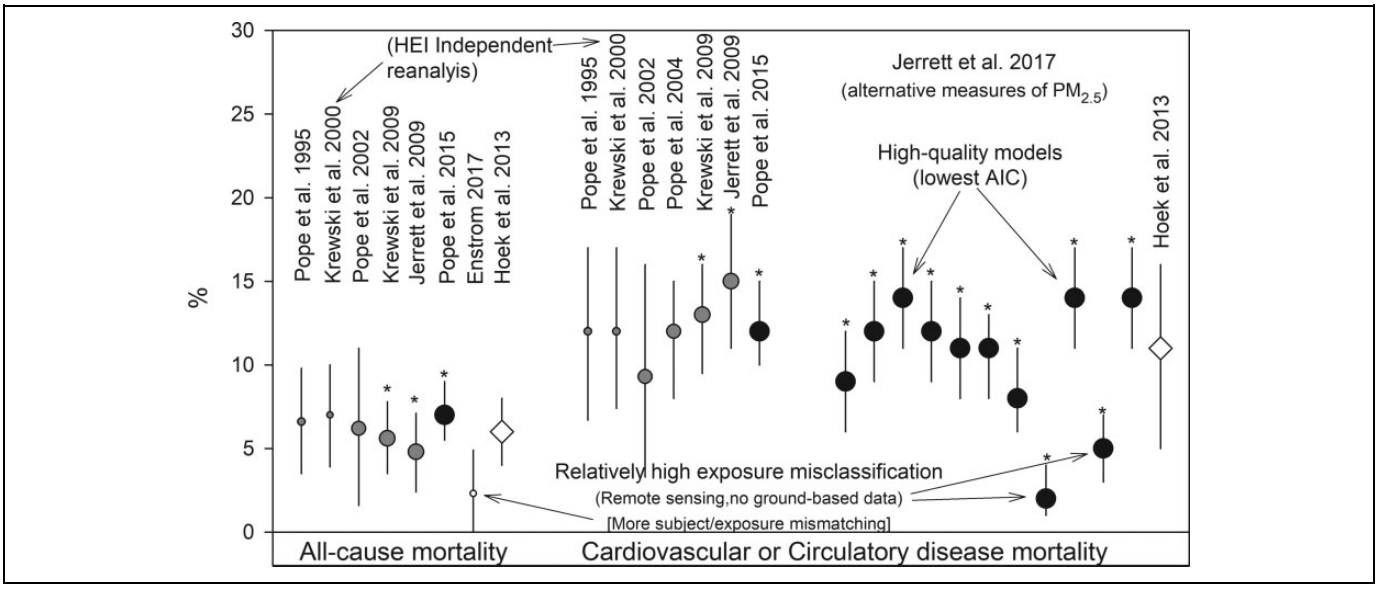

Figure 1. Nationwide estimates of percentage increase in mortality risk per 10 $\mu g/m^3$ increase in $PM_{2.5}$ from various published studies using the ACS CPS-II cohort (indicated by circles) with comparison estimates from meta-analysis of the literature (indicated by diamonds). The size of the circles is relative to the length of the follow-up period. Gray and white circles indicate metro-level and county-level geographic units of exposure, respectively. Black circles indicate that exposures were modeled at geocoded residential addresses. Asterisks indicate that, in addition to controlling for individual covariate, the models also controlled for ecological covariates. Note. (1) Krewski et al[2] report the results of an independent, confirmatory reanalysis of the ACS cohort organized by the Health Effects Institute. (2) In the investigation of alternative measures of $PM_{2.5}$ conducted by Jerrett et al,[7] the highest quality models (those with the lowest AIC) produced the highest risk estimates; remote sensing models with no ground-based data produced the lowest risk estimates, likely because of greater exposure misclassification. (3) The lowest risk estimate reported by Enstrom[8] is based on a dated and short follow-up of the ACS cohort and is likely subject to exposure mismatching. ACS CPS II indicates American Cancer Society Cancer Prevention Study II; $PM_{2.5}$, particulate matter air pollution.

reanalysis, multiple subsequent extended analyses, or meta-analyses of studies throughout the world.[18]

Deficiencies in Enstrom's Reanalysis

Enstrom's recently published analysis[8] is the least advanced analysis of the ACS CPS-II cohort to date (see Table 1). The Enstrom's analysis uses a data set with a shorter follow-up period, fewer participants, and fewer deaths than any previous $PM_{2.5}$–mortality analyses that used the CPS-II cohort, including the original 1995 analysis. He controls for a relatively limited number of individual-level covariates and does not control for any ecologic covariates. Moreover, the key deficiency in the Enstrom's reanalysis is the absence of advanced modeling approaches for exposure assessment that have been developed over the last 2 decades. Estimates of $PM_{2.5}$–mortality associations are affected by the quality of the $PM_{2.5}$ data and the accuracy of matching participants and exposures. In a recent analysis,[7] we evaluated $PM_{2.5}$ exposures using multiple exposure assessment methods. Figure 1 illustrates that there were significant $PM_{2.5}$–mortality risk associations for all $PM_{2.5}$ measures, but the associations were lower for the presumably less accurate measures that used remote sensing without ground-based data. Based on measures of model quality, the $PM_{2.5}$ exposure values that best fit (lowest Akaike Information Criteria, AIC) the data resulted in relatively larger $PM_{2.5}$–mortality associations (see Figure 1). In contrast, Enstrom[8] asserts that he estimates smaller $PM_{2.5}$–mortality associations because he uses the "best" $PM_{2.5}$ data. He provides neither evidence in support of this assertion nor any measures of the relative quality of models using alternative $PM_{2.5}$ data. It is not clear how or why his "IPN" $PM_{2.5}$ data differ from the "Health Effects Institute" $PM_{2.5}$ data—especially given that these data come from the same monitoring network.

Furthermore, Enstrom's $PM_{2.5}$ exposure assessment is likely subject to greater exposure misclassification because of inadequate assignment of geographic units of exposure. Although other published ACS CPS-II studies assigned geographic areas of exposure based on participants' residence information, the Enstrom's analysis used the ACS Division and Unit numbers to assign $PM_{2.5}$ exposures (see letter from ACS). The ACS Division and Unit numbers, however, were for the ACS volunteers that recruited the participants. These volunteers did not always live in the same area or even in the same state as the participants. Enstrom does not document the extent of this participant-exposure mismatching, but it has the potential for substantial exposure misclassification and resultant attenuation bias. Our published research using the ACS CPS-II data is based on participant-exposure matching that is accurate, includes highly spatially resolved exposure models, and utilizes ground-based monitoring and land use data.

An inexplicable deficiency of the Enstrom's article is its inadequate documentation of the relevant and extensive peer-reviewed literature. References provided in the article largely

include an unconventional mix of unpublished and non-peer-reviewed correspondence (including letters, e-mails, and transcript of a teleconference call), presentation slides, press releases, and a compilation of manuscript rejections. Key published extended analyses of the ACS CPS-II cohort,[3,5,6,7,9-17] studies of other cohorts,[18-31] or even major reviews and evaluations of the literature[32,33] are not cited or discussed.

Broader Evidence

The $PM_{2.5}$–mortality associations observed from the various analyses of the ACS CPS-II cohort are consistent with a much broader body of evidence from other studies. As examples, these include studies of other cohorts from the United States[19-26] Europe,[27-29] and Canada.[30,31] In addition, meta-analytic estimates of the $PM_{2.5}$–mortality associations based on a 2013 meta-analysis of the overall literature[18] are also provided for comparison purposes in Figure 1.

Previous studies of the ACS CPS-II cohort consistently demonstrated $PM_{2.5}$–mortality associations with cardiovascular mortality.[7,9] There has also been substantial work in exploring and understanding the biological pathways and mechanisms linking $PM_{2.5}$ exposures and cardiovascular disease and death.[32-35] Similarly, the ACS CPS-II cohort has demonstrated $PM_{2.5}$–mortality associations with lung cancer mortality,[3,12,14] and recently, the International Agency for Research on Cancer concluded, based on multiple sources of evidence, that particulate matter in outdoor air pollution is a cause of human lung cancer (group 1).[36] Enstrom[8] presents no results for cardiovascular or lung cancer mortality and largely dismisses the substantial and growing literature regarding relevant pathophysiological pathways and related biological mechanisms.

The Global Burden of Diseases, Injuries, and Risk Factors Study 2015 (conducted by the Institute for Health Metrics and Evaluation) identified ambient $PM_{2.5}$ air pollution as the 5th leading risk factor for global mortality, contributing to approximately 4.2 million deaths in 2015.[37,38] These results are based on recent and comprehensive estimates from ACS CPS-II cohort studies and 23 other peer-reviewed studies of long-term exposure to $PM_{2.5}$ and mortality from cause-specific cardiovascular and respiratory disease and lung cancer. These results underscore the importance of $PM_{2.5}$ as a substantial determinant of mortality in the general population. Consequently, these results also suggest substantial health benefits from further reductions in ambient air pollution.

In summary, we welcome thoughtful criticism of our research. But the study by Enstrom does not contribute to the larger body of evidence on the health effects of $PM_{2.5}$, as it does not utilize adequate approaches for exposure assessment, suitable methods for linking participants to exposure, and sufficient statistical control for potential confounding factors and fails to recognize the larger body of evidence on $PM_{2.5}$ exposure and disease risk.

Declaration of Conflicting Interests

The author(s) provided the following declaration of interests with respect to the research, authorship, and/or publication of this article: Daniel Krewski reports to serving as Chief Risk Scientist and CEO at Risk Sciences International (http://www.risksciences.com), a Canadian company established in 2006 in partnership with the University of Ottawa conducting work in air quality risk assessment for both public and private sector clients. He also holds an Industrial Research Chair in Risk Science under a peer-reviewed university–industry partnership program administered by the Natural Sciences and Engineering Research Council of Canada, which involves methodological research in air pollution risk assessment. He also recently served as Chair of the US Health Effects Institute Diesel Epidemiology Panel, which conducted an evaluation of recent epidemiological evidence on quantitative risk assessment of diesel emissions and lung cancer. Michelle C. Turner reports personal fees from ICF Incorporated, LLC, outside this work.

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

James E. Enstrom[1]

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]

State	ACS Division-Unit	FIPS Code	IPN/HEI County Containing IPN/HEI City	IPN/HEI City With PM2.5 Measurements	1979–1983 IPN PM2.5 $\mu g/m^3$ (Weighted Average)	1979–1983 HEIDC PM2.5 $\mu g/m^3$ (Weighted Average)	1979–1983 HEI PM2.5 $\mu g/m^3$ (Median)	1980 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)

State	ACS Division-Unit	FIPS Code	IPN/HEI County Containing IPN/HEI City	IPN/HEI City With PM2.5 Measurements	1979–1983 IPN PM2.5 $\mu g/m^3$ (Weighted Average)	1979–1983 HEIDC PM2.5 $\mu g/m^3$ (Weighted Average)	1979–1983 HEI PM2.5 $\mu g/m^3$ (Median)	1980 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 $\mu g/m^3$ 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

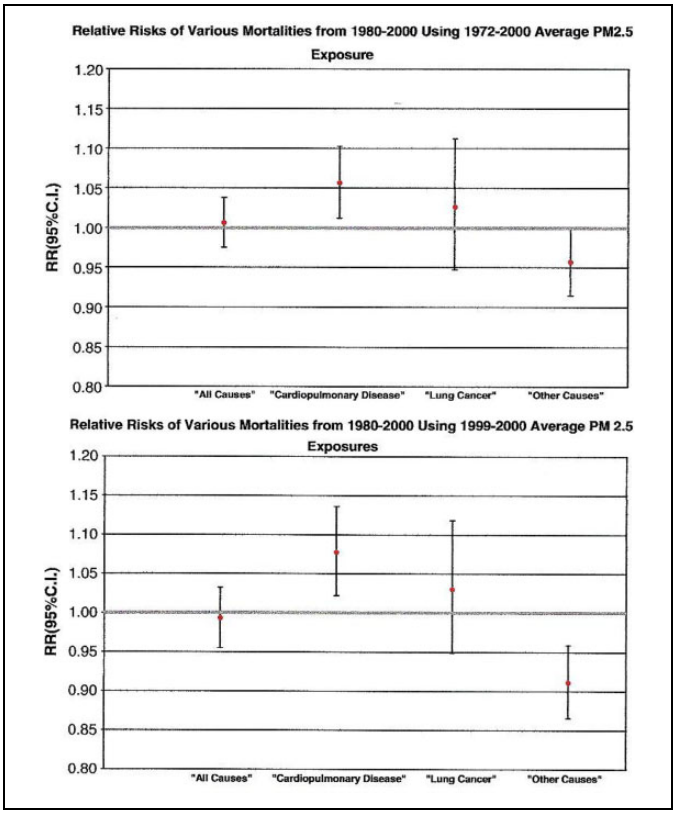

Figure 2 (Jerrett[7]). Summary of risks for different exposures over the entire follow-up.

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 $\mu g/m^3$). 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

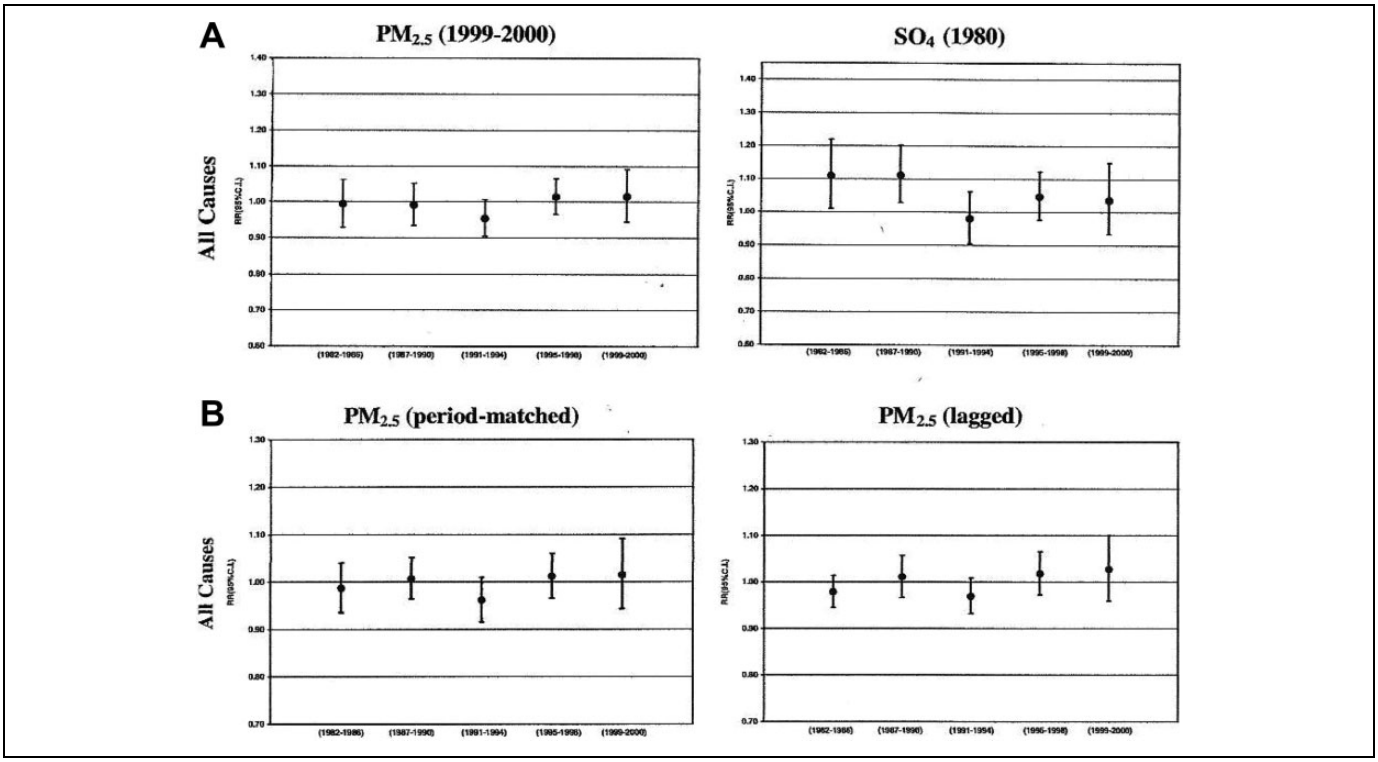

Figure 3 (Jerrett[7]). (A) Relative risks for all-cause, cardiopulmonary and lung cancer deaths estimated for five time periods of the follow-up (1982–1986, 1987–1990, 1991–1994, 1995–1998, and 1999–2000) with measured exposures. (B) Relative risks for all-cause, cardiopulmonary and lung cancer deaths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

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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Scientific Distortions in Fine Particulate Matter Epidemiology

James E. Enstrom, Ph.D., M.P.H.

ABSTRACT

The theoretical prevention of premature deaths from the inhalation of fine particulate matter is being used by the U.S. Environmental Protection Agency (EPA) to justify the National Ambient Air Quality Standard (NAAQS) and multibillion dollar regulations across the U.S., including the EPA Clean Power Plan and the California Air Resources Board (CARB) Truck and Bus Regulation. The epidemiology is severely flawed. Fine particulates probably make no significant contribution to premature mortality in the U.S. The publication of null findings has been blocked or marginalized and studies claiming excess mortality need to be reassessed.

Basics of Fine Particulate Matter

Fine particulate matter ($PM_{2.5}$) is defined by its size (≤2.5 μm diameter), not its composition. Major sources in the U.S. are forest fires, commercial and residential burning, and diesel engines. In California, a major source is China; on some days up to 30% of fine particulates had crossed the Pacific Ocean.

Of these invisible particles, the average adult in the U.S., based on actual 2015 exposure levels, would inhale about 1 gram in an 80-year lifespan, assuming that he breathes about 10,000 liters of air a day at rest. For comparison, the amount inhaled while smoking 100 cigarettes is about 4 grams.[1]

In 1997, the EPA established the NAAQS for $PM_{2.5}$ as 15 μg/m³. This was lowered to 12 μg/m³ in 2012. This standard has been largely justified on the basis of secret science epidemiology. These regulations are very powerful and impose huge costs on American businesses. The $PM_{2.5}$ NAAQS, has been used to justify several multi-billion-dollar rules, such as the EPA Clean Power Plan and the CARB Truck and Bus Regulation.

Although a significant effect from such extremely low levels is on its face highly implausible, the stringent EPA regulations are justified primarily by a claim of preventing premature deaths, assuming a value of $10 million per statistical life saved. The controversy over the issue was brought to general attention in 2002 by Professor Robert Phalen.[2]

Epidemiology of Fine Particulate Matter

The EPA claim that $PM_{2.5}$ causes "premature deaths" is based on epidemiologic cohort studies purporting to show that the relative risk (RR) for total mortality is slightly greater than 1.0 in U.S. populations exposed to higher levels of $PM_{2.5}$. No etiologic mechanism has been established, and there is no experimental evidence that inhalation of 1 g or 5 g of $PM_{2.5}$ can cause death. Weakly positive RRs do not prove causality. Major difficulties include: (1) geographic and temporal variation in $PM_{2.5}$ mortality risk; (2) exaggeration of actual human exposure by $PM_{2.5}$ monitors, which measure ambient outdoor levels far from the subjects; and (3) confounding variables such as co-pollutants. Moreover, the key study relied on by EPA, the American Cancer Society (ACS) 1982 Cancer Prevention Study (CPS II)[3] is seriously flawed.

Reanalysis of the American Cancer Society Cancer Prevention Study II (ACS CPS II)

CPS II began in 1982 and is similar to the original CPS I, which began in 1959. The seminal paper published by Pope et al. in 1995[3] was so controversial that the Health Effects Institute (HEI) sought applications from teams consisting of two to four epidemiologists, statisticians , and air pollution exposure experts to conduct a reanalysis, including "sensitivity analyses to test the robustness of the original findings and interpretations to alternative analytic approaches."[4] The HEI Reanalysis published in 2000 did not complete the mandated sensitivity analysis to assess the effect of alternate data.[5] HEI published a report in 2009,[6] which extended the mortality follow-up of the study from 1989 to 2000, but it did not incorporate the EPA Inhalable Particulate Network (IPN) $PM_{2.5}$ data[7,8] that I had called to the authors' attention in my 2005 paper.[9]

In 2016 I was able to obtain access to data in an original 1982-1988 version of CPS II. The data had been previously inaccessible since 1995 despite a congressional subpoena and repeated requests by different agencies. I am the only independent scientist who has gained access to the individual level data in both CPS I and CPS II. I was able to reproduce the same key results as Pope et al. by doing exactly what the authors did in 1995.[3] However, their results were sensitive to the $PM_{2.5}$ data that they used and to their particular analysis.

HEI did not follow its own mandate to conduct a comprehensive reanalysis. In particular, their sensitivity analysis was not done properly. Of the 13 teams that submitted reanalysis applications, HEI selected a 31-member team based in Canada, headed by statistician Daniel Krewski. It included a geographer, Michael Jerrett, and another statistician, Richard Burnett, but only had one epidemiologist, Yue Chen. Chen's degree was from Shanghai Medical University, and he was not a coauthor on either the 2000 HEI report[5] or the 2009 HEI report.[6] Thus, to reanalyze a major U.S. epidemiological study, HEI used a Canadian team that had essentially no epidemiologist.

An early clue to the existence of problems is seen in Figure 21 in the 2000 HEI Reanalysis Report.[5] (Figure 1 in this article.) This map shows that in 50 cities across the U.S. the level of $PM_{2.5}$ mortality risk varies. Higher risks were found mainly in the Rust Belt or the Ohio Valley, and levels were actually reasonably low in California and throughout most of the western part of the U.S. Beginning in 2002, I asked the head of HEI, Daniel Greenbaum, and its principal scientist, Aaron Cohen, to send me the underlying data for that map. For 16 years, they have consistently refused to reveal this data to me.

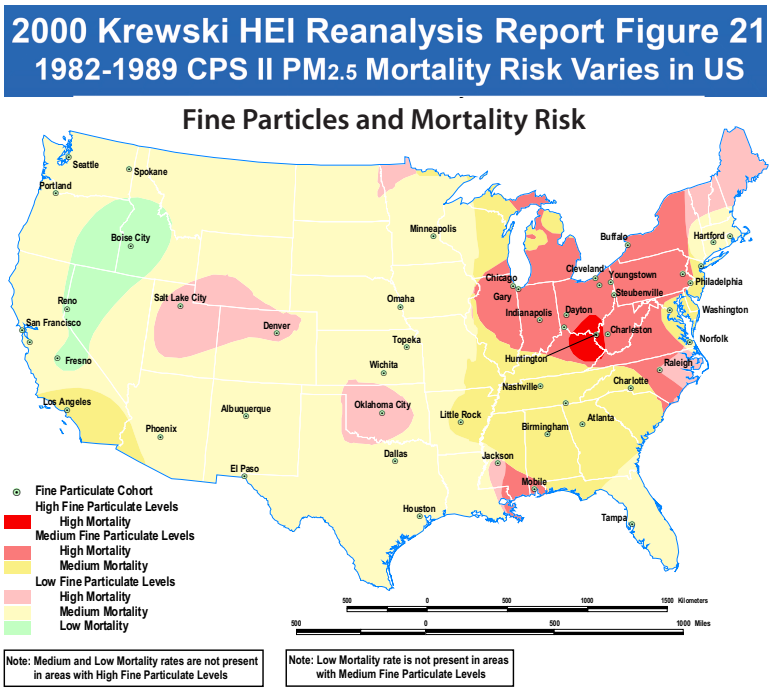

Figure 1. $PM_{2.5}$ Levels and Mortality Risk in the U.S. [Reprinted from 2000 HEI Reanalysis Report,[5] with permission.]

My analysis of the CPS II data revealed that the county of residence of subjects could be approximated based on the ACS Division and Unit numbers. The CPS II data were collected by about 70,000 researchers, including myself, who enrolled 1.2 million subjects in Fall 1982. I performed an analysis comparable to the HEI Reanalysis, as shown in Table 1. The $PM_{2.5}$ data labeled IPN in the table was published in EPA reports from the Inhalable Particulate Network (IPN) by David Hinton et al. in 1984[7] and 1986.[8] Because of the evasions that I have experienced in attempting to obtain information from HEI, I took a closer look at the 2000 HEI Reanalysis Report and found it actually contains the data that I used, although in a mislabeled and somewhat altered form. I have designated that data as HEIDC, which is labeled $PM_{2.5}$ DC in the 2000 Report. This data was indirectly referred to in a couple of places in the 2000 HEI report, although it was not analyzed.

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

1979-83 $PM_{2.5}$	Subjects	Relative Risk (95% CI)
Fully Adjusted for 50 Counties in Continental US		
IPN [Hinton]	195,215	1.025 (0.990-1.061)
HEIDC [PM2.5 DC]	216,897	1.024 (0.987-1.061)
HEI [PM2.5 OI MD]	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)
HEIDC	43,945	1.048 (0.922-1.191)
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)
HEIDC	172,952	0.960 (0.919-1.003)
HEI	153,041	1.025 (0.975-1.078)

Table 1. Enstrom Analyses of ACS CPS II Data Using Three Sources of $PM_{2.5}$ Data

Thus, using the HEI $PM_{2.5}$ data of Pope et al.,[3] there is a statistically significant slight increase in RR of 1.082. That means that if the $PM_{2.5}$ level increases by 10 µg/m³, the risk of dying goes up by about 8%. But, using the IPN $PM_{2.5}$ data, the effect is nonsignificant, RR = 1.025 (95% CI, 0.990-1.061). Note that if one divides the U.S. into the Ohio Valley (Indiana, Kentucky, Ohio, Pennsylvania, and West Virginia) and the rest of the country, the RR is indistinguishable from 1.0, no matter what $PM_{2.5}$ data is used. Only by combining the Ohio Valley, which has both a higher mortality risk and a higher level of $PM_{2.5}$, with the rest of the country can HEI show a statistically significant effect.

My reanalysis[10] has been published online since Mar 28, 2017, and so far its validity has not been challenged.

The selection of data by HEI was also very interesting, as seen in Table 2. There were actually 11 counties in California that were part of the IPN network, and the HEI analyses omitted 7 of the 11 counties for reasons the authors have not explained. HEI had data from 50 different cities, and the only ones they included from California were Fresno, Los Angeles, San Francisco, and San Jose (in Santa Clara County). Two other counties that represent the extremes in $PM_{2.5}$ levels are highlighted in the table. The Pope 1995 paper[3] was based primarily on these extremes. HEI had Albuquerque, N.M., at 9 µg/m³, as the lowest value, and Huntington, W.V., at 34.4 µg/m³, as the highest value. This is curious because the data that comes from the IPN network actually shows different high and low values. In fact, there is no measurement in the IPN for Huntington, W.V., but rather for Wheeling, W.V., listed in the IPN column. From the table, both the low and the high values are in California, both of which omitted from the HEI analysis. The low value is 10.6 µg/m³ in Santa Barbara County, and the high value is 42.0 µg/m³ in Riverside County. The $PM_{2.5}$ DC data that I found in the 2000 HEI Report appendix table, labeled HEIDC by me, had more than 50 cities, but only five of the 63 total cities were from California. The IPN network as a whole has about 85 cities. These major inconsistencies need to be addressed by these investigators. And so far, there is nothing but silence. This is only one of the issues that must be addressed if the investigators want to maintain any credibility.

CA NM WV Counties with $PM_{2.5}$ Values Used in Pope 1995, HEI 2000, HEI 2009, Enstrom 2017

State	ACS Div-Unit	County	1979-83 $PM_{2.5}$ (µg/m³) IPN (N=85)	HEIDC (N=63)	HEI (N=50)
CA	06001	Alameda	14.3882		
CA	06002	Butte	15.4525		
CA	06003	Contra Costa	13.9197		
CA	06004	Fresno	18.3731	10.3	10.3
CA	06008	Kern	30.8628		
CA	06051	Los Angeles	28.2239	26.8	21.8
CA	06019	Riverside	42.0117		
CA	06020	San Diego	18.9189	18.9	
CA	06021	San Francisco	16.3522	16.4	12.2
CA	06025	Santa Barbara	10.6277		
CA	06026	Santa Clara	17.7884	17.8	12.4
NM	34201	Bernalillo	12.8865	12.9	9.0
WV	58117	Ohio	23.9840		[33.4]

Table 2. Comparison of Data on $PM_{2.5}$ and Mortality from Enstrom and HEI[9]

Relationship between $PM_{2.5}$ and Mortality in California

Because of the Feb 26, 2010, conference in Sacramento, which I attended along with Professor Robert Phalen, other prominent scientists, and impacted business groups, we were able to get an analysis done by HEI that dealt with the California portion of the national CPS II results. The California data was partitioned out from the national analysis in the 2009 HEI Report.[6] Based on the four HEI California counties shown in Table 2, the RR is about 0.9, significantly below 1.0, as shown in Table 3. This inverse relationship was reproduced using either the HEI data or the IPN data. Of course, this relationship cannot be etiologically correct, but it shows what can result from data omission and manipulation.

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)

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Table 3. Relative Risk for $PM_{2.5}$ and Mortality in California Based on Four Counties

There are actually six California cohorts that have been used to analyze the relationship between $PM_{2.5}$ and total mortality, as shown in Table 4. The cohort that I initially used is labeled CA CPS I;[9] the cohort used by Jerrett et al.[11] is labeled CA CPS II. The Adventist Health Study of Smog (AHSMOG) was the original cohort study in California.[12] There are also the California Teachers Cohort,[10] the "West" portion of the Medicare Cohort Air Pollution Study (MCAPS),[13] and the National Institutes of Health-American Association of Retired Persons (NIH AARP) cohort, which was published in 2016 by Thurston et al.[14] The NIH AARP cohort is supposed to be an open access database, but is apparently currently controlled by Thurston. I have been able to get access to only the California portion of the data, and my analysis shows no effect in California. Averaging all six cohorts gives an RR of exactly 1.00, which means no relationship between $PM_{2.5}$ and total mortality.

The lack of an effect in California might explain why Pope et al.[3] omitted seven California cities from the national analysis. As Figure 1 shows, there is tremendous variation across the country. Yet the most severe regulations are in California, despite the clear absence of mortality risk there!

$PM_{2.5}$ 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/ORI111116.pdf) 6

Table 4. $PM_{2.5}$ and Total Mortality in Six California Cohorts

Both my analysis and that by Thurston et al. on the NIH AARP cohort,[14] summarized in Table 5, show no effect nationwide or in California.

$PM_{2.5}$ 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)

Table 5. Comparison of Enstrom and Thurston Analyses for U.S. and California

An International Perspective on $PM_{2.5}$

Despite the null effect shown by their own data and analyses, prominent advocates of drastic measures to reduce $PM_{2.5}$ levels state in a major paper in the May 13, 2017, *Lancet* that ambient $PM_{2.5}$ was the fifth-ranking mortality risk factor worldwide in 2015. Aaron J. Cohen, until recently HEI Principal Scientist, is the lead author, and Pope is a coauthor. The study is part of the World Health Organization (WHO) Global Burden of Disease (GBD) Project and was largely funded by HEI. The article claims that $PM_{2.5}$ causes 4.2 million deaths annually worldwide, with 88,000 deaths in the U.S. (see Table 6). The mean $PM_{2.5}$ level is 8.4 μg/m³ in the U.S. and 58.4 μg/m³ in China. Clearly, the $PM_{2.5}$ level and premature deaths are low in the U.S. and high in China, India, and Africa.

May 13, 2017 (on line April 10, 2017) *Lancet*
'Global Burden of Disease' by Cohen & Pope

2015 Deaths Attributed to $PM_{2.5}$

Table 2

Country	Deaths	Death Rate (per 100,000)	Mean $PM_{2.5}$ ($\mu g/m^3$)
USA	88,400	18.5	8.4
China	1,108,100	84.3	58.4
India	1,090,400	133.5	74.3
Pakistan	135,100	136.3	65.0
Bangladesh	122,400	133.2	89.4
World	4,200,000		

8

Table 6. Global Deaths Attributed to $PM_{2.5}$[15]

Agenda-driven Science

Since publishing my 2005 critique of the relationship between $PM_{2.5}$ and total mortality[9] and my 2017 critique,[10] I have sent numerous requests to Pope, ACS, HEI, and others, inviting a rebuttal. I have received no response that confirms or refutes any of my analyses. It has, however, been incorrectly asserted that, "The study by Enstrom does not contribute to the larger body of evidence on the health effects of $PM_{2.5}$." ACS has criticized me for having CPS II data that they have deliberately tried to keep secret. My invitations to authors and ACS officials to attend meetings, teleconferences, and symposia have simply been ignored. They even ignored an August 1, 2013, subpoena from the U.S. House Science, Space, and Technology Committee.

The control over air pollution research and assessments that is recognized by EPA is not based on special expertise in epidemiology. Pope, the self-proclaimed "world's leading expert on the effects of air pollution on health," is a professor of economics at Brigham Young University and holds a 1981 Ph.D. in agricultural economics from Iowa State University, where he studied the dynamics of crop yields. Michael Jerrett, who is one of the most prolific publishers and a member of the HEI reanalysis team, has a 1996 Ph.D. in geography from the University of Toronto, and no formal training in epidemiology. Aaron J. Cohen, until recently HEI's Principal Scientist, does hold a 1991 D.Sc. degree in epidemiology from Boston University, but he has badly misused the principles and standards of epidemiology. Although he supervised the 1998-2000 HEI Reanalysis Project, he has refused to clarify findings from this project and has refused to confirm or refute the findings in my 2017 CPS II reanalysis. It is very disturbing that ACS has allowed CPS II data to be used for more than 20 years for research that misuses the principles and standards of epidemiology and that has nothing significant to do with cancer.

The principal qualification for admission to the elite circle of influence appears to be dedication to the agenda of global controls on economic activity via air pollution regulations. The conclusion reached by researchers is apparently predetermined, as stated in the last paragraph of the GBD study on ambient air pollution: "As the experience in the U.S. suggests, changes in ambient $PM_{2.5}$ associated with aggressive air quality management programmes, focused on major sources of air pollution including coal combustion, household burning of solid fuels, and road transport, can lead to increased life expectancy over short timeframes."[15]

What is the state of scientific integrity? It is very dangerous to one's career to criticize views backed by powerful interests, and I do it only because I believe current trends are anti-science and dangerous to our country. Simply being a passive observer is no longer acceptable.

To disclose my own background, I obtained a Ph.D. in physics in 1970, but I became an epidemiologist starting in 1973 in order to apply the rigorous principles of physics to observational epidemiology. I had a long career as a research professor and researcher at the UCLA School of Public Health. My research has examined the influence of environmental and lifestyle factors on mortality, and has on occasion reached politically incorrect conclusions. My research in air pollution epidemiology has been strongly influenced by Dr. Frederick Lipfert and Professor Robert Phalen. In February 2010 I was terminated from UCLA without warning and told that my "research is not aligned with the academic mission of the Department." In February 2015 I settled a three-year federal whistleblower retaliation lawsuit against UCLA and my termination was reversed. My case and some of the issues related to my air pollution epidemiology research have been discussed in this journal.[16]

My background and publications, including rejections of my research, often without peer review, are documented on my website, www.scientificintegrityinstitute.org. I believe that major journals simply will not accept articles that challenge the established view. Moreover, authors of the papers promoting $PM_{2.5}$ premature deaths omit null results, even their own. For example, Jerrett is the lead author of a 2007 study that shows no increased mortality associated with $PM_{2.5}$ in the CPS II cohort if the results are divided into five time periods.[17] Although researchers are paid millions of dollars, they're not under any obligation to address any of the concerns about their work. Those who disagree with the agenda are denied research funding.

We must prevent American science from following historical examples like that of Trofim Denisovich Lysenko. He was a phony plant geneticist, who gained the favor of Joseph Stalin because he didn't believe in Mendelian genetics. Lysenko's views controlled much of Soviet agriculture in the 1930s, 1940s, and 1950s, with devastating effect. False crop statistics were published, and dissenting scientists were purged. Nikolai Vavilov, a renowned plant geneticist, was imprisoned by Stalin and died of malnutrition.

Concerns about integrity in Western science are being raised. Richard Horton, editor of *The Lancet*, writes: "The case against science is straightforward: much of the scientific literature, perhaps half, may simply be untrue. Afflicted by studies with small sample sizes, tiny effects, invalid exploratory analyses, and flagrant conflicts of interest, together with an obsession for pursuing fashionable trends of dubious importance, science has taken a turn towards darkness."[18]

A U.S. House of Representatives bill called the Secret Science Reform Act was passed in 2014 and 2015 in order "to prohibit the Environmental Protection Agency from proposing, finalizing, and disseminating regulations or assessments based upon science that is not transparent or reproducible." The bill was revived in 2017 as the Honest and Open New EPA Science Treatment (HONEST) Act, labeled H.R. 1430, and was passed by the U.S. House of Representatives.

American science needs to guard against the heirs of Sinclair Lewis's protagonist in his 1927 novel *Elmer Gantry*, an itinerant preacher who is able to sell false religion to gullible people. We have prominent scientists who have successfully sold the notion that inhaling 1 g of invisible particles over an 80-year lifetime can cause premature death.

Conclusions

There is strong evidence from two large national cohorts that $PM_{2.5}$ does not cause premature deaths in the US. There is strong evidence that this relationship has been falsified by EPA, the Health Effects Institute, and leading researchers for more than 20 years. Better oversight to assure scientific integrity, such as access to data, transparency, and consideration of opposing views, is imperative.

James E. Enstrom, Ph.D., M.P.H., a physicist and epidemiologist, is a retired research professor from the University of California, Los Angeles, and president of the Scientific Integrity Institute in Los Angeles. Contact: jenstrom@ucla.edu

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From: Edward Calabrese <edwardc@schoolph.umass.edu>
Date: February 22, 2019 at 9:07:32 AM PST
To: "uscprovost@usc.edu" <uscprovost@usc.edu>
Cc: "James Enstrom (jenstrom@ucla.edu)" <jenstrom@ucla.edu>
Subject: Enstrom Request

Dear Provost Quick:

I have followed the set of email exchanges between you and Professor James Enstrom. As you know they deal with Critical issues of scientific evidence, public health policy, scientific integrity, academic freedom and the role of Universities in public leadership. His letters focused on the critical question of air pollution and PM2.5. My interest principally stems from the fact that as editor in chief of the journal Dose Response I encouraged The public scientific debate on the PM2.5 issue, involving Professor Enstrom and others across the broad scientific spectrum. This issues are complex and critical and they need the leadership and engagement of academic leaders at the Provost level. You need to see the issues and the role of your University in these debates, even when people are critical. Let me urge you to constructively meet with Professor Enstrom on these matters. He is knowledgeable, honest, an Excellent researcher and one committed to the public good. He also can challenge the status quo, which is good. Please choose to engage with him. I could tell from the letter exchange that you were not inclined to do to so. I believe this is a mistake….you and he can learn much from each other, helping USC, California, the USA and the world. I have had a long career in academia and my own disputes and debates…..constructive dialogue really helps…..Please show your leadership now.

Sincerely,

Ed Calabrese Ph.D
UMass/Amherst

How a scientist's disputed views about pollution may change EPA

Los Angeles Times 2-19-19

Ed Calabrese's theory that low doses of toxic chemicals are good for people could soon become U.S. policy.

By Susanne Rust

In early 2018, a deputy assistant administrator in the EPA, Clint Woods, reached out to a Massachusetts toxicologist best known for pushing a public health standard suggesting that low levels of toxic chemicals and radiation are good for people.

"I wanted to check to see if you might have some time in the next couple of days for a quick call to discuss a couple items," Woods wrote to Ed Calabrese.

Less than two weeks later, Calabrese's suggestions on how the Environmental Protection Agency should assess toxic chemicals and radiation were introduced, nearly word for word, in the U.S. government's official journal, the Federal Register.

"This is a major big time victory," Calabrese wrote in an email to Steve Milloy, a former coal and tobacco lobbyist who runs a website, junkscience.com, that seeks to discredit mainstream climate science.

"Yes. It is YUGE!" wrote Milloy, in response.

It was a glorious moment for Calabrese, who had been snubbed for decades by mainstream public health scientists because of his controversial research and theories.

It also signified the major shift the EPA has taken under the Trump administration.More than any before it, this White House has actively sought out advice from industry lobbyists and the scientists they commission in setting pollution rules.

Denouncing the Obama-era EPA as an agency beholden to environmental extremists, the administration has not only dismissed mainstream science but embraced widely discredited alternatives that critics say are not consistent with the agency's focus on improving public and environmental health.

Calabrese's role illustrates a different side of this shift: the potential removal of long-standing public health practices and the incorporation of industry-backed and disputed science into federal environmental policy.

Calabrese spent decades advancing his ideas, facing skepticism and criticism from peers in the toxicology community while winning funding from companies whose bottom lines conformed to his views.

He says most of the pushback he receives comes from left-of-center toxicologists who see him as "the devil incarnate" for accepting industry funding and challenging their ideology. He maintains his science is solid and will be vindicated in time.

"These environmental regulatory people are very closed-minded," he said. They won't reconsider their standards, and see that some of the agents they call harmful "actually can induce adaptive responses," Calabrese said.

This view — that pollution and radiation can be beneficial — has many experts worried. The fact that such a position might become EPA policy, they say, portends a future in which corporate desires outweigh public and environmental health.

"Industry has been pushing for this for a long time," said David Michaels, former assistant secretary of labor for the Occupational Safety and Health Administration who's a professor of environmental and occupational health at George Washington University. "Not just the chemical industry, but the radiation and tobacco industries too."

If the EPA ultimately adopts Calabrese's proposed new regulations, researchers say it could change decades of standards and guidelines on clean air, water and toxic waste. It could also fundamentally alter the way the government assesses new chemicals and pesticides entering the marketplace.

"This is industry's holy grail," Michaels said.

Can pollution be healthy?

For decades, federal agencies charged with investigating and regulating carcinogens, toxic chemicals and radiation have been guided by the assumption that if a substance is dangerous at some level, it is harmful at any level. The higher the exposure, the more harm done. The lower the dose, the less. And the risk doesn't entirely disappear until the substance is removed.

This is known as the linear no-threshold model, and industry dislikes it because it generally assumes that there is no level, or threshold, of exposure that can be considered totally safe.

But research done on low exposures to toxins has been less than definitive. Experiments designed to test carcinogens and radiation at low levels often produce conflicting results — with, for example, some studies of a chemical showing harm, other studies showing no effect, and a few suggesting a net benefit. In other cases, there is no information at all to guide regulators.

In the face of such uncertainty, the EPA and other agencies have taken a cautious approach by relying on the linear no-threshold model. Where data are absent or uncertain, they assume some level of risk.

It is an imperfect but protective approach, many public health specialists say. They argue that in a human population that varies widely in age, health and levels of chemical exposures, it is imperative that the agency cast a wide, conservative and protective net.

For decades, national and international scientific bodies have upheld this approach. It has been reviewed and re-reviewed dozens of times, including most recently by the congressionally chartered National Council on Radiation Protection and Measurements, the National Academy of Sciences, Engineering and Medicine and the EPA.

At the same time, industry has funded scientists to conduct and promote research designed to poke holes in the linear no-threshold model.

And that is where Calabrese comes in. He has long argued that regulators "erred on the side of being protective" at the cost of billions of dollars a year to industry.

Calabrese is a proselytizer of hormesis, the idea that dangerous chemicals and radiation are beneficial at low doses. He says they have a stimulating effect.

Polluting industries have promoted hormesis as an alternative to linear no-threshold for decades, but they had gotten little traction until the EPA embraced it in April.

"It's clearly not mainstream," said Thomas Burke, professor and director of the Risk Sciences and Public Policy Institute at Johns Hopkins' Bloomberg School of Public Health.

Burke and other experts say there are clearly scenarios in which toxic chemicals can have beneficial effects in clinical and pharmacological settings, such as in the case of tamoxifen, which at low doses is effective at preventing and treating breast cancer but at higher doses can lead to blood clots, stroke and uterine cancer.

But, they say, what happens in a clinical setting can't and shouldn't be immediately applied to a regulatory, public health setting.

In the clinical case, "you have a doctor controlling and administering the medication to an individual," said David Jacobs, a professor of public health at the University of Minnesota, who has published studies showing hormetic effects in some industrial pollutants. "The doctor can pull the medication at any time.

"There is no way to control the dose a person gets from an industrial or agricultural chemical," he said. "It's not being doled out in pills and monitored by a physician who can lower it if the patient isn't responding well."

Therefore, Jacobs said, it would be dangerous to use hormesis as a framework for protecting public and environmental health.

"It really doesn't pass the sniff test" when applying it to public health, Burke said, while allowing for its place in the forum of ideas. "I always teach my classes that there are other theories. It's like any part of science, there are different points of view. Whether it's about climate change or low doses."

But he also teaches that one needs to know who has skin in the game. And in the case of hormesis, he said, that's industry.

Big bucks from Big Tobacco

Then Donald Trump was elected president.

Active pursuit by White House

On Sept. 5, 2017, nearly nine months after Trump was sworn in as president and seven months after Scott Pruitt was confirmed as administrator of the EPA, Calabrese wrote an email to Milloy, the former coal lobbyist who is a Fox news commentator. The Times obtained the emails through a public records request to the University of Massachusetts.

"I wanted to connect with you on whether and how it may be possible to get the EPA to consider changing the LNT [linear no-threshold model] to something far better," Calabrese wrote.

Milloy had served on Trump's EPA transition team and was still in touch with high-ranking officials in then-Secretary Pruitt's agency.

A few months later, Calabrese wrote to Milloy again, letting him know that he'd corresponded with Ryan Jackson, Pruitt's chief of staff, and sensed interest in a move against linear no-threshold.

Not long after Woods, the EPA's deputy assistant of the Office of Air and Radiation, emailed Calabrese asking if he wanted to talk about "default linear assumptions" and other items.

The two arranged a call, and on April 19, 2018, Woods sent Calabrese draft language for a small section in the EPA's proposed new ruling on transparency, called "Strengthening Transparency in Regulatory Science."

"It is good what you have but you need a little more," wrote Calabrese, who then suggested a line, which he altered twice, in email exchanges with Woods, before settling on this: "EPA shall also incorporate the concept of model uncertainty when needed as a default to optimize low dose risk estimation based on the major competing models (LNT, Threshold, and Hormesis)."

In other words, if the EPA is uncertain about a particular chemical's impact at low doses, it would abandon linear no-threshold as a default, and try other models instead, including hormesis.

On April 25, Milloy sent Calabrese the final wording for the draft proposal, which included Calabrese's line nearly word for word.

"I am almost passing out with surprise and euphoria," Calabrese wrote Milloy after seeing the document.

The rule was posted for comment in the Federal Register on April 30, although a final ruling has not been announced.

John Konkus, an EPA spokesman, said the input and perspective from "the editor-in-chief of the journal Dose Response" was welcomed and reflected the perspective of "a wide variety of scientific experts" the agency reached out to when drafting the proposal.

Public health specialists outside the agency say that if the final language is adopted, it is likely to tie the EPA in knots as it tries and then debates all the alternative models. It could also have profound effects on current and future standards for drinking water, air and toxic waste sites.

"EPA tries to be conservative in its setting of risks," said Jan Beyea, a retired radiation physicist who has worked with the National Academies of Science. "Calabrese and collaborators think that most pollutants are good for you at low doses, so no need to be conservative."

EPA spokeswoman Molly Block declined to speculate on whether the rule would be passed and how it would affect environmental rules that were set based on the linear no-threshold model.

Industry groups have praised the proposed change.

"We support moving away from over-reliance on the linear no-threshold default," wrote a spokesman for the American Chemistry Council, the trade group for the chemical industry. It's a method, he says, that "frequently results in inflated health risk estimates and unwarranted, costly risk management decisions."

Milloy also seemed pleased with the proposed ruling.

"The EPA should be open and transparent about how and what they are basing their decisions on," he said, "and they should be using the best science available."

In any case, he said, "we're winning."

In the early 1980s, Calabrese was a tenured professor at the University of Massachusetts, stringing together public agency and industry-funded grants to study chemicals in drinking water and the effects of ozone on mice.

His funders included the EPA, the state of Massachusetts, the Hoffmann-La Roche pharmaceutical company and semiconductor giant Digital Corp.

Then in 1985, he reached out to the Council for Tobacco Research, the research arm of the tobacco industry, seeking a grant to examine "a possible inherited and metabolic susceptibility to lung cancer in smokers." His proposal was declined.

Sheldon Sommers, a physician at New York's Lenox Hill Hospital and scientific director of the council, wrote in response to the grant application that Calabrese's proposal "is a mad hatter's tea party sort of epidemiologic approach, and a total $2.1 million-plus would likely be frittered away, in my opinion," according to documents from the UC San Francisco Truth Tobacco Industry Documents archive.

But by the 1990s, Calabrese had solidly established himself as a trusted scientist with the tobacco industry. He found it was interested in research that questioned the methods that regulatory agencies use to assess risk.

In a 1994 proposal to R.J. Reynolds, Calabrese offered to investigate a new kind of smokeless cigarette for the company, but also incorporate into his research "the loss of current benefits associated with smoking, such as protection from certain types of cancers and other illnesses."

It was when he began his work on hormesis that Calabrese got attention from a broader range of industries.

With seed money from R.J. Reynolds, Dow Chemical, Procter & Gamble and others, as well as the EPA, Calabrese established a hormesis working group at the University of Massachusetts, which he called the Biological Effects of Low Level Exposures, or BELLE. Minutes from a 1990 advisory board meeting show the group chose not to use the word "hormesis" in its official name.

According to documents, Calabrese and his funders also held off on pushing a hormesis regulatory agenda until they'd built a sizable base of published scientific research.

Between 1990 and 2013, Calabrese received more than $8 million from companies and institutions, including R.J. Reynolds, Exxon Mobil, Dow Chemical, General Electric, the Department of Energy and the U.S. Air Force, to conduct research on hormesis.

Spokesmen from Exxon Mobil and the Air Force say they no longer fund Calabrese's work.

Calabrese established his own scientific society, the International Dose Response Society, and hormesis journal — now called Dose Response — where he served as editor-in-chief.

He wrote hundreds of articles, in his journal and in others (including "Should hormesis be the default model in risk assessment?" and "The importance of hormesis to public health"), organized dozens of conferences and delivered scores of talks.

His publication portfolio is vast and broad. It includes not just studies of hormesis, but research on soil ingestion, opinion pieces on law and regulatory policy, historical treatise on science,scathing and a few , posthumous rebukes of revered scientists, such as Hermann Muller, a Nobel Prize winner and supporter of linear no-threshold.

Calabrese insists his funding does not influence his work.

"My job involves finding financial support to do studies in my field," Calabrese said. "I seek support from the private and public sectors. The university independently evaluates each of these for compliance with the rules."

Not all of his money comes from industry or government agencies with extensive toxic waste sites. Between 2000 and 2013, Calabrese received $50,000 from the EPA to hold a conference on soil ingestion, and $50,000 from the California Environmental Protection Agency for a reference database he built on cancer publications. He also received a $750,000 joint grant from the EPA and the American Chemistry Council, the chemical industry's trade group, to study soil ingestion by construction workers.

Yet, despite his prolific career, he has instigated criticism and rebuke from many of his peers for his push on public and environmental health policy. He has been described as a "prominent industry consultant," having "outlying views" whose science is "way out there."

For years he failed to get regulatory agencies to take him seriously.

16Mar2019

S. Stanley Young
genetree@bellsouth.net
919 219 2030

Randolph Hall
Vice President of Research, USC
rwhall@research.usc.edu.

Dear Dr. Hall:

I am an applied statistician and I have been examining environmental epidemiology methods and claims for several years. See attached short bio, A01.

Dr. James Enstrom sent me a three-page statement on evidence of misconduct, which I fully support, A00.

From the very beginning, 1993 or so, the linking of air quality to health effects has been very tenuous. There is no doubt that under very special circumstances that air pollution can kill: Meuse Valley 1930, Denora PA 1948, London 1952. But the circumstances are very special, requiring a combination of conditions: temperature inversion lasting several days, small particles in the air and some form of acid in the air. That combination of circumstances is very rare and not replicated in 1st world countries today. A paper in Lancet 2001 described the very special circumstances that occurred in the Meuse Valley, attached, A02.

Indeed, I secured all the death certificates for California for the years 2000 to 2012, ~2M certificates. We have done extensive analysis of that data set and find no association between current air quality, PM2.5 and ozone, and deaths. I presented a seminar at USC Nov 13, 2014 on that material. The seminar was advertised and well-attended. Dr Gauderman was invited. Dr Thomas attended. See the slides presented in that lecture, attached A03.

I placed a technical report of that work on arXiv in 2015: https://arxiv.org/abs/1502.03062. Also, the analysis data set was made public in 2015. The work is well-known and interested individuals can download the data set and do their own analysis.

I also made a listing of air quality/health effects that are negative. It is attached A04.

In my opinion, researchers at USC are fulling informed of many negative results, but they do not cite them.

Sincerely,

S. Stanley Young, PhD, FASA, FAAAS

Short Bio 2018c

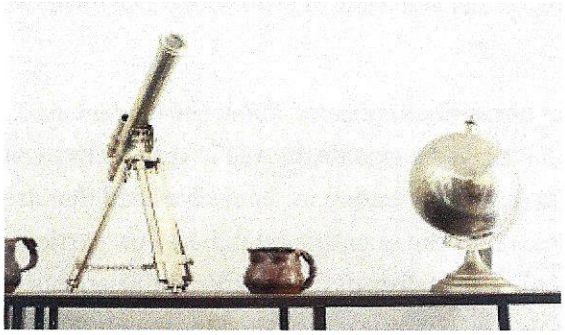
Dr. S. Stanley Young is currently the CEO of CGStat and previously worked at Eli Lilly, GlaxoSmithKline and the National Institute of Statistical Sciences on questions of applied statistics. His current interest is studying methods used in the evaluation of observational studies. He also works on bioinformatics problems.

Dr. Young graduated from North Carolina State University, BS, MES and a PhD in Statistics and Genetics. He worked in the pharmaceutical industry on all phases of pre-clinical research. He has authored or co-authored over 70 papers including six “best paper” awards, and a highly cited book, *Resampling-Based Multiple Testing*. He has three issued patents. He is interested in all aspects of applied statistics. He conducts research in data mining.

Dr. Young is a Fellow of the American Statistical Association and the American Association for the Advancement of Science. He is an adjunct professor of statistics at North Carolina State University, the University of Waterloo, and the University of British Columbia where he has co-directed thesis work. He is also an adjunct professor of biostatistics in the Jiann-Ping Hsu College of Public Health at Georgia Southern University. Dr. Young is on the Scientific Advisory Board of the U.S. Environmental Protection Agency.

Concerns about National Academy of Sciences and Scientific Dissent

Dec 15, 2015 | Peter Wood



Introductory note: NAS president Peter Wood sent the following letter by email on December 9, 2015 to California members of the National Academy of Sciences.

Dear Members of the National Academy of Sciences,

This is an NAS to NAS letter—which requires some "disambiguation." I am president of the National Association of Scholars, founded in 1987, and whose organizers apparently didn't give much thought to the space already occupied by those initials by the National Academy of Sciences, founded 124 years earlier. I'll defer to the Academy's seniority by reserving NAS in what follows for the body of scientists who incorporated during President Lincoln's tenure. The National Association of Scholars is a broad-based group of academics that includes professors in the humanities and social sciences (I'm an anthropologist) as well as the natural sciences.

The occasion for this letter is Dr. Marcia K. McNutt, Editor-in-Chief of *Science*. We are concerned that she is the only official candidate to be the next NAS president. To be clear, the National Association of Scholars does not oppose Dr. McNutt's candidacy. We simply believe

that members of an important national organization like NAS should have at least two candidates to consider when voting for your next president. Indeed, the American Association for the Advancement of Science (AAAS), which publishes *Science*, always has two candidates for president and its other elected positions. Other scientific organizations also have two candidates for their elected positions.

Also, we want to bring to your attention our serious concerns about the current state of discourse in the sciences. Dr. McNutt has played a significant role in three active controversies involving national regulatory policy that deserve attention in themselves and that are also part of a larger problem. The larger problem is how the scientific establishment, particularly *Science* and NAS, should evaluate and respond to serious dissent from legitimate scientists. This is an especially important consideration for NAS, which was established to provide "independent, objective advice on issues that affect people's lives worldwide."

The three controversies are:

1. The status of the **linear no-threshold (LNT) dose-response model** for the biological effects of nuclear radiation. The prominence of the model stems from the June 29, 1956 *Science* paper, "Genetic Effects of Atomic Radiation," authored by the NAS Committee on the Biological Effects of Atomic Radiation. This paper is now widely questioned and has been seriously critiqued in many peer-reviewed publications, including two detailed 2015 papers. These criticisms are being taken seriously around the world, as summarized in a December 2, 2015 *Wall Street Journal* commentary. In August 2015 four distinguished critics of LNT made a formal request to Dr. McNutt to examine the evidence of fundamental flaws in the 1956 paper and retract it. However, on August 11, 2015 Dr. McNutt rejected this request without even reviewing the detailed evidence. Furthermore, Dr. McNutt did not even consider recusing herself and having independent reviewers examine evidence that challenges the validity of both a *Science* paper and an NAS Committee Report.

This is a consequential matter that bears on a great deal of national public policy, as the LNT model has served as the basis for risk assessment and risk management of radiation and chemical carcinogens for decades, but now needs to be seriously reassessed. This reassessment could profoundly alter many regulations from the Nuclear Regulatory Commission, Environmental Protection Agency, and other government agencies. The relevant documents regarding the 1956 *Science* paper and Dr. McNutt can be examined at www.nas.org/images/documents/LNT.pdf.

2. Extensive evidence of scientific misconduct in the epidemiology of **fine particulate air pollution** (PM2.5) and its relationship to mortality. Since 1997 EPA has claimed that lifetime inhalation of about a teaspoon of particles with diameter less than 2.5 microns *causes* premature death in the United States and it established an national regulation based on this claim. *Science* has provided extensive news coverage of this issue and its regulatory significance, but has never published any scientific criticism of this questionable claim, which is largely based on nontransparent research.

Earlier this year, nine accomplished scientists and academics submitted to *Science*

well-documented evidence of misconduct by several of the PM2.5 researchers relied upon by EPA. The evidence of misconduct was first submitted to Dr. McNutt in a detailed June 4, 2015 email letter, then in a detailed July 20, 2015 Policy Forum manuscript "Transparent Science is Necessary for EPA Regulations," and finally in an August 17, 2015 Perspective manuscript "Particulate Matter Does Not Cause Premature Deaths." Dr. McNutt and two *Science* editors immediately rejected the letter and the manuscripts and never conducted any internal or external review of the evidence. This a consequential matter because many multi-billion dollar EPA air pollution regulations, such as, the Clean Power Plan, are primarily justified by the claim that PM2.5 is killing Americans. The relevant documents regarding this controversy can be examined at https://www.nas.org/images/documents/PM2.5.pdf.

3. *Science* promotes the so-called **consensus model of climate change** and excludes any contrary views. This issue has become so polarized and polarizing that it is difficult to bring up, but at some point the scientific community will have to reckon with the dramatic discrepancies between current climate models and substantial parts of the empirical record. Recent evidence of *Science* bias on this issue is the June 26, 2015 article by Dr. Thomas R. Karl, "Possible artifacts of data biases in the recent global surface warming hiatus"; the July 3, 2015 McNutt editorial, "The beyond-two-degree inferno"; the November 13, 2015 McNutt editorial, "Climate warning, 50 years later"; and the November 25, 2015 AAAS News Release, "AAAS Leads Coalition to Protest Climate Science Inquiry."

Dr. McNutt's position is, of course, consistent with the official position of the AAAS. But the attempt to declare that the "pause" in global warming was an illusion has not been accepted by several respected and well-informed scientists. One would not know this, however, from reading *Science*, which has declined to publish any dissenting views. One can be a strong supporter of the consensus model and yet be disturbed by the role which *Science* has played in this controversy. Dr. McNutt and the journal have acted more like partisan activists than like responsible stewards of scientific standards confronted with contentious claims and ambiguous evidence. The relevant documents and commentary regarding the Karl paper and McNutt editorials can be examined at https://www.nas.org/images/documents/Climate_Change.pdf.

All three of these controversies have arisen on issues in which a strong degree of scientific consensus became intertwined with public policy and institutional self-interest. That intertwining can create selective blindness.

Dr. McNutt has in her career found herself faced more than once with the challenge of what to do when an entrenched orthodoxy meets a substantial scientific challenge. The challenge in each case could itself prove to be mistaken, but it met what most scientists would concede to be the threshold criteria to deserve a serious hearing. Yet in each case Dr. McNutt chose to reinforce the orthodoxy by shutting the door on the challenge.

The three areas that I sketched above, however, seem to have such prominence in public policy that they would warrant an even greater investment in time, care, and attention than would be normally the case. In that light, Dr. McNutt's dismissive treatment of scientific criticisms is disturbing.

I bring these matters to your attention in the hope of accomplishing two things: raise awareness that the three issues represent threats to the integrity of science arising from the all-too-human tendency to turn ideas into orthodoxies; and suggest that it might be wise for NAS to nominate as a second candidate for president someone who has a reputation for scientific objectivity and fairness and who does not enforce orthodoxy.

I welcome your responses. The National Association of Scholars will present an open forum on these matters with a section reserved specifically for NAS members. Furthermore, I will put you in contact with NAS members who are concerned about Dr. McNutt becoming the next NAS president.

Thank you for your consideration.

Yours sincerely,

Peter Wood
President
National Association of Scholars
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New York, NY 10018
www.nas.org
(917) 551-6770

EMBARGOED UNTIL 2:00PM US ET, THURSDAY 21 MARCH 2019

Science

POLICY FORUM

Cite as: G. T. Goldman and F. Dominici, *Science* 10.1126/science.aaw9460 (2019).

Don't abandon evidence and process on air pollution policy

Gretchen T. Goldman[1] *and* Francesca Dominici[2]

[1]Center for Science and Democracy, Union of Concerned Scientists, Cambridge, MA, USA. [2]Harvard T. H. Chan School of Public Health, Boston, MA USA.
Email: ggoldman@ucsusa.org

Who decides how to establish causality?

Air pollution kills—scientists have known this for many years. But how do they know? The global scientific community has developed and agreed upon a framework that draws on multiple lines of evidence across different scientific disciplines to assess the existence and strength of links between air pollution and health. In the United States, federal policies require use of this science-based framework to ensure that air pollution standards protect the public's health. But now this science-based policy process—and public health—are at risk. Recent developments at the U.S. Environmental Protection Agency (EPA) stand to quietly upend the time-tested and scientifically backed process the agency relies on to protect the public from ambient air pollution (*1*). One of these developments—changes in how the EPA handles causality between air pollutants and health effects—has received less attention but, if enacted, would alter the approach that the EPA has used for more than a decade to set health-based air pollutant standards. At the March meeting of the EPA's Clean Air Scientific Advisory Committee (CASAC) (*2*), these changes may begin to unfold. The agency now faces a dilemma. If the EPA leadership embraces the process proposed by the current CASAC chair, it will fundamentally change the EPA's process for scientific assessment. If the EPA leadership ignores the CASAC recommendations, then the agency would be declining to listen to (what should be) its top science advisers, thus eroding the foundational concept of peer review as central to ensuring the use of strong science in policy decisions.

WEIGHT OF THE EVIDENCE

Consistent with how the broader scientific community builds consensus on a topic, the EPA for decades has methodically assessed the strength of the relationship between air pollution and health outcomes, and has determined the need for strengthening pollutant protections. These determinations have been made only after robust, transparent peer review with public input. The Clean Air Act–mandated CASAC, a group of experts that operates independently from the EPA, has provided science advice on ambient air pollutant standards since the law's enactment. Their input is supplemented by pollutant-specific panels of experts that span scientific disciplines and have long histories of peer-reviewed publications. These review panels provide pollutant-specific, evidence-based advice needed for EPA to set air pollution standards. Even in the face of enormous political and financial pressures to roll back pollution controls, this process has worked remarkably well across both Republican and Democratic administrations and has been upheld in the courts, where several legal challenges to its use in past pollutant reviews have been defeated [see supplementary materials (SM), section 1). Political decisions haven't always aligned with the science, but the process for developing and communicating policy-relevant scientific assessments has remained largely intact (*3*).

Within these scientific assessments, the EPA has applied a weight-of-the-evidence approach for causality determination using a five-level hierarchy, ranging from a "causal relationship" to "no evidence of a causal relationship," to assess links between air pollutants and health effects. This approach is rooted in the scientific community's decades-long effort to evaluate the relationship between cause and effect, beginning with work by Sir Bradford Hill in 1965 and a 1964 report from the U.S. Surgeon General, and then with approaches later developed by leading scientific bodies such as the National Academy of Medicine and International Agency for Research on Cancer (see SM, section 2).

To assess the independent effect of a pollutant on human health and welfare, the EPA's approach considers multiple lines of evidence gathered from various scientific fields, spanning atmospheric physics and chemistry, exposure science, dosimetry, toxicology, statistics, data science, clinical medicine, and epidemiology. The agency systematically identifies, evaluates, and summarizes the relevant peer-reviewed scientific evidence. In this process, the EPA assesses whether there is consistency of effects within a discipline, coherence of effects across disciplines, and evidence of biological plausibility. Thus, the causality determinations developed for an air pollutant and a specific health outcome, such as respiratory effects or mortality, reflect the assessment of the collective body of evidence, rather than a single line of evidence or the use of a single statistical method (*4*). This multidisciplinary

Summary of Comments on uzSpyx-Goldman-03-22-19-SJM-comments.pdf

Page: 1

Number: 1 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:05:27 AM

False. This claim is thoroughly and definitively debunked in my 2016 book "Scare Pollution: Why and How to Fix the EPA."

Number: 2 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:10:16 AM

False. No statistical study correlates air quality and death beyond the noise range. They are really all negative studies. There is no toxicological or clinical study evidence supporting the notion that air quality kills.

Number: 3 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:11:55 AM

Yes. At risk of being brought back into reality.

Number: 4 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:25:33 AM

False. I can't think of any effort to "roll back" air pollution controls. Of course, people have opposed the mindless and pointless tightening of air quality standards, but no rollbacks -- although the standards could be rolled back without causing harm.

Number: 5 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:14:10 AM

There is no public health threat from air quality anywhere in the world, let along in the US. Our air is clean and safe as it has always been except for three days in October 1948 in Donora, Pennsylvania.

Number: 6 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:26:58 AM

Until the Trump administration came to town, the corrupt forces of junk science had a lock-down on EPA.

Number: 7 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:16:20 AM

This is actually true. For the past 20 years, EPA scientists and grantees have been relying on junk science to advance the canard that air quality kills. That is about to change.

Number: 8 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:29:23 AM

Weight-of-the-evidence is NOT a scientific method. It is a political method for determining regulatory standards.

Number: 9 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:17:08 AM

Yes. Stick with junk science or get rid of it?

Number: 10 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:17:27 AM

For the better.

Number: 11 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:30:22 AM

Ironically, no air quality study passes muster under the Bradford-Hill criteria.

Number: 12 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:18:34 AM

The "top science advisers" referred to here are part of the the biggest collection of science frauds in the history of science.

Number: 13 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:21:52 AM

False. CASAC determined in 1997 that PM2.5 was not associated with death. So EPA replaced those CASAC members with new CASAC members who were pretty much all paid EPA stooges.

Number: 14 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:23:05 AM

Uh... except for the CASAC members who received hundreds of millions of dollars in grant payola from EPA.

Number: 15 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:33:17 AM

This is not how the process works in reality. In reality, statistical studies are rigged to produce crappy results that are then heralded as the greatest science since Newton's Laws.

framework has been embraced widely by the scientific community as the appropriate process for public health applications (*5*).

Since its inception, this causal framework rooted in the weight of the evidence has been continuously improved through extensive input from CASAC during prior pollutant reviews, involving 11 CASAC panels and 138 individuals (*6*). These improvements have come from building a base in the scientific literature over time, have allowed for newly developed statistical methods to be applied to air pollution studies, and have been supported broadly by CASAC and the scientific community.[3]

The process matters. Under the Clean Air Act's National Ambient Air Quality Standards, the causal determinations developed in the EPA science assessment are used in the risk and exposure assessment and policy assessment to evaluate the impacts of setting air pollution standards at different levels. Together, these three documents are what the EPA administrator will use to set air pollution standards at a level that will protect public health with an adequate margin of safety, as the Clean Air Act requires. Thus, it is crucial that the EPA science assessment reflect the current scientific understanding of a pollutant's effects on health and welfare.

MANIPULATIVE CAUSATION

An alternative framework for determining the linkages between air pollutants and health outcomes in the EPA process is now being promoted by the current CASAC chair, Louis Anthony (Tony) Cox Jr. Rather than look at the weight of the evidence from studies across different fields and different study designs, members of CASAC are proposing in a draft letter that the EPA instead limit the studies that inform its causality determinations to those that can pass a specific narrow approach called manipulative causality (*7*).[8] Cox will oversee the committee's review of the science assessment and related EPA documents and shepherd the development of a scientific recommendation to the EPA administrator on what level of ambient particulate matter will protect public health with an adequate margin of safety.

Under this framework, to justify regulatory action, air pollution epidemiological studies must demonstrate manipulative causation, that is, there must be direct evidence that the implementation of a regulatory action and/or a reduction in pollutant exposure leads to a health benefit.[9] As an attempt to be more precise from a statistical viewpoint, the position argues, in the context of a single epidemiological study, it is necessary to apply causality tests, such as the one implemented by the Causal Analytics Toolkit (CAT), proposed by Cox himself, and/or other existing statistical approaches (Granger causality, information relations in directed acyclic graph models, and Bayesian networks) (see SM section 3). The CASAC chair argues that the majority of current epidemiological studies considered by the EPA only provide evidence of an association (and not evidence of causation) between exposure to air pollution and health effects because, he falsely claims, they do not adjust for confounders (such as weather, demographic, or socioeconomic variables), and therefore, they are not proving manipulative causation.[1]

In principle, attempting to assess causality from observational data in air pollution epidemiology can be viewed as a reasonable framework to address the general issue of confounding bias in individual studies.[2] New statistical methods for the analysis of epidemiological studies on air pollution and health can inform and improve the EPA's approach to its science assessment.[4] Indeed, this is the value of the weight-of-the-evidence approach, which is open to new advances in all fields, including causal inference studies. But instead of allowing these ideas to be introduced, debated, peer reviewed, and advanced in the scientific literature, the CASAC chair suggests that this process be largely skipped and that one specific approach for the analysis of epidemiological data, from a field that is still in its infancy, should trump all other kinds of scientific knowledge.[5]

Further, a requirement of manipulative causation fails to recognize the full depth and robustness of existing approaches in epidemiology, statistics, and causal inference and the degree to which they deal with confounding factors. To study environmental hazards like air pollution, we must rely on analyses of observational data.[6] Randomized control trials are not possible (or ethical) when studying environmental hazards.[7] The great majority of epidemiological studies are designed to estimate how changing an exposure leads to a change in health outcomes while adjusting for confounders, that is, keeping fixed all the other variables that may affect outcomes (such as weather, income, copollutants, etc.). Many of the peer-reviewed epidemiological studies included in the EPA's science assessments rely on careful selection of the study design (e.g., time series, prospective cohorts, quasi-experiments), and these studies adjust for confounding bias to infer causality. Many of these studies use regression methods and include the confounders as covariates. Other studies use methods for causal inference and rely on matching, comparing communities or individuals that have different exposures but are matched with respect to the value of the confounders (e.g., individuals with the same education level but different air pollution exposure; see SM section 4). Other studies rely on quasi-randomization (*8*). It has not been convincingly shown that a manipulative causation framework and Cox's proposed tests for causality would be clearly superior to these rigorous and well-vetted approaches.[10]

It remains to be seen whether methods for causal inference such as proposed by CASAC members will become mainstream in air pollution epidemiology. But from the current standpoint, manipulative causation and Cox's causality tests

Number: 1 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:40:09 AM
And the CASAC chair is correct -- except that even the studies where an association is claimed are really just statistcal noise.

Number: 2 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:41:18 AM
It is not scientific to assess causality from epidemiologic studies alone. Even the Obama-run EPA admitted this in litigation with me.

Number: 3 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:34:50 AM
False. The folks being referred to here are all EPA grantees who have been paid to toe th EPA line.

Number: 4 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:41:55 AM
There is nothing new in statistics.

Number: 5 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:43:15 AM
If you regulate and there is no improvement, there is something wrong with your regulation. Duh.

Number: 6 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:43:57 AM
There is no robustness in air quality epidemiology. Just a lot of fraud.

Number: 7 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:45:32 AM
Funny. Because air quality epidemiology is so bad, EPA ran human clinical trials on air pollutants in an effort to cause harm if not death to its human guinea pigs.

Number: 8 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:36:25 AM
Wait until you see what this term means.

Number: 9 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:38:15 AM
This is part of the Bradofrd Hill criteria referred to by the author above. If you remove exposure to a poison, you should bee less poisoning. If air quality kills, there should be fewer deaths in cleaner air. But that is not observed anywhere.

Number: 10 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:47:08 AM
These studies are all junk. The foregoing description is an effort to buff turds into popsicles. No sale.

are among many tools in the analytical toolbox. It's not obvious based on current bodies of literature that these new approaches are so powerfully and obviously an indictment of other methods and conclusions, that we should abandon all that we've learned from other approaches, and dismiss all the epidemiological evidence accumulated so far from many disciplines. This all reflects a very normal phenomenon across all science: All methods come with assumptions and have their own strengths and weaknesses, so using varying methods can lead to varying views on a phenomenon.

What matters is the study design and the ability to assess in a transparent way all of the potential sources of confounding bias and error, peer review, and independent reanalyses by experts in the field (*9*). When charged with the task of assessing the weight of evidence of harmful effects from exposure to air pollution, scientists must, and indeed always have, integrate knowledge across many scientific fields and assess all the potential sources of uncertainty. The CASAC chair's proposal suggests skipping this process.

The EPA's mandate under the Clean Air Act requires the agency to protect public health, including within sensitive subgroups (such as children and the elderly), with an adequate margin of safety.[4] To achieve this, the law allows the EPA to be flexible in deciding what an adequate margin of safety is. This is crucial for ensuring that those most sensitive to harm from air pollution are truly protected. The proposed manipulative causation framework and proposed statistical tests of causality, however, place a nearly unattainable burden of proof on the scientific community, and this is unlikely to protect those who need it most.

To be clear, well-validated methods for causal inference can play a useful role: This is because they include a more transparent disclosure of all the assumptions that are needed to properly adjust for confounding compared with regression modeling and therefore can infer causality in analyses of observational data. Furthermore, causal inference approaches tend to be more robust to violation of assumptions regarding the form of the statistical model when controlling for confounding bias. There is a literature on methods for casual inference applied to air pollution studies, including the role of causality in data-driven science to inform air pollution regulatory actions (see SM section 5). Regardless, air pollution regulations must be based on existing evidence and demonstrated inference methods that arise from review of existing literature.[9]

In the case of particulate matter, the scientific community has taken several steps to increase the credibility of the results of the epidemiological studies and their ability to infer causality from analyses of observational data. The Health Effects Institute (HEI), a highly regarded independent research institute funded primarily by the EPA and the motor vehicle industry, appointed an independent panel of scientists to reanalyze the results of the landmark American Cancer Society and Harvard Six-Cities Studies that demonstrated the link between long-term particulate exposure and premature death, and indeed they validated the conclusions of the original study (see SM section 6).[1] More recently, the HEI has funded three epidemiological studies to be conducted by three separate teams on three separate populations in three separate locations (United States, Canada, and Europe) to address the defined scientific question of how low-level exposure to fine particulate matter is harmful to human health—a question that arose from the prior particulate matter review completed in 2012. The U.S. team recently published two studies of Medicare data, and used two different study designs (cohort and case cross-over) to estimate the effect of long- and short-term exposure to particulate matter on mortality for the same study population. Both studies found strong evidence of increased risk of mortality at levels well below the safety standards for particulate matter (*10*, *11*).[2]

Despite this cautious, robust, and repeated approach, in its 7 March draft letter, the current CASAC could not reach consensus on the scientific evidence for the link between particulate exposure and mortality.[3] This is perhaps unsurprising given the lack of epidemiological expertise involved. Breaking with historical CASAC member expertise, the EPA leadership declined to place an epidemiologist on the current CASAC.[5] Furthermore, the committee would benefit from the expertise of the particulate matter review panel that the EPA disbanded last October, breaking with decades of precedent of pollutant-specific review panels supplementing the expertise of the seven-member CASAC.[6] The agency also failed to convene a similar review panel for updating the ground-level ozone standard, and the agency expedited review timelines for both pollutants.[7] This means less public input and fewer opportunities for independent scientists, including experts in epidemiology and statistics, to consider and debate this new argument of manipulative causation.

Together, EPA's nixing of the pollutant review panels, the expedited timelines for review of particulate matter and ozone standards, and this narrow view of testing manipulative causation now proposed by the CASAC's chair have proven unpopular among scientists, including experts in the field of causal inference and data science.[8] Three separate letters, penned by 15 members of the dismissed particulate matter review panel, 17 former members of the previous ozone review panel, and 7 previous CASAC members, express the concern about the process and scientific substance of the particulate and ozone reviews led by Cox. Separately, 206 air pollution and public health experts have called on the EPA to reconvene the disbanded particulate matter review panel (see SM section 7).[10]

The particulate matter standard is also being targeted in other ways. The EPA-proposed rule Strengthening

Number: 1 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:51:24 AM
HEI is not independent. It is half-funded by EPA and half-funded by corrupt industry (like engine manufacturers) that want more stringent air quality standards.

Number: 2 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:52:18 AM
These studies have been spotlighted on JunkScience.com previously. They are both just more science fraud.

Number: 3 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 12:49:00 PM
Because there are still Obama dead-enders on the CASAC panel.

Number: 4 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:49:26 AM
Children are not "more" susceptible to anything in the environment than adults. If anything, children are sturdier... that's why chemotherapy works better on children. As to old people, there is no evidence that outdoor air has any effect on them whatsoever.

Number: 5 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 12:20:28 PM
Ridiculous. Epidemiology is just statistics. CASAC Chair Tony Cox is a statistician. Many/most "epidemiologists" never studied epidemiology. One of the most infamous PM2.5 "epidemiologists" -- i.e., C. Arden Pope III -- was trained as an agronomist.

Number: 6 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 12:21:09 PM
This panel was disbanded because it was corrupt.

Number: 7 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 12:50:02 PM
Ozone is 90% PM2.5 fraud. The rest is ozone fraud.

Number: 8 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 12:51:18 PM
They are unhappy because the Trump administration is ending their science fraud gravy train.

Number: 9 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 11:50:05 AM
Existing evidence shows that air quality harms no one.

Number: 10 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 12:51:58 PM
Make science fraud great again.

Transparency in Regulatory Science carries forward an idea Congress has raised for years but failed to pass (*12*). The rule would restrict the studies that the EPA can use in regulatory decisions by declaring that "the dose response data and models" that underlie regulations must be transparent and accessible to the public. Such restrictions would severely hamstring the EPA's ability to protect people from ambient air pollution.[1] Although some studies do rely on Medicare claims data and therefore would be able to comply with such a requirement, the sweeping proposal raises concerns about study subject privacy regarding medical records, intellectual property, and reproducibility, among other challenges (see SM section 8).[2]

The sum of these changes to the process and scientific approach to setting the particulate matter standard could have far-reaching effects. Avoided particulate pollution accounts for some one-third to one-half of the total monetized benefits of all major federal regulations (not just air quality regulations) (*8*). If the particulate standard is weakened, those benefits would drop in value, and the many public health protections that require cost-benefit analysis to be implemented would be at risk.[3]

Weakening the EPA's long-standing processes for assessing the health impacts of air pollutants could erode the agency's ability to obtain independent science advice on agency decisions on public health protections. In any case, this could ultimately lead to weakening of ambient air pollutant standards. A science assessment that fails to provide a comprehensive look at the relationship between an air pollutant and health effects will yield a subsequent risk and exposure assessment and policy analysis that are flawed, and these crucial documents feed into the EPA administrator's decision on where to set air pollutant standards. Without a robust process to ensure that decision-makers have access to the best available science, policy decisions are unlikely to protect public health.

If the particulate matter and ozone standards are loosened now or in future reviews, people will suffer the consequences. More than 23 million Americans live in areas that exceed the current particulate matter standard, and more than a third of the nation's population lives in areas that exceed the current ozone standard (see SM section 9). If the administration sets air pollution standards that fail to rely on the weight of the evidence on air pollution and health, not only are we casting scientific progress aside, but we risk the health of thousands breathing unhealthy air. As a policy analyst observed, "Science without policy is science, policy without science is gambling" (*13*).[4]

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SUPPLEMENTARY MATERIALS

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Number: 1 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 12:53:02 PM

Regulations should not be based on secret science. The EPA grantees hide their science because it is fraud.

Number: 2 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 12:53:50 PM

Excuses... excuses.

Number: 3 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 12:54:28 PM

The cost-benefit analysis is also fraud, as explained in "Scare Pollution."

Number: 4 Author: stevenmilloy Subject: Inserted Text Date: 3/20/19, 12:55:53 PM

Air quality was not a public health problem in the US before the Clean Air Act. It is not a problem now. Claims to the contrary are ignorance and/or lies.