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

Journal:	*Dose-Response*
Manuscript ID	17-047-DR
Manuscript Type:	Letter to the Editor
Date Submitted by the Author:	31-Jul-2017
Complete List of Authors:	Enstrom, James E; UCLA and Scientific Integrity Institute,
Keywords:	epidemiology, PM2.5, deaths, CPS II, reanalysis

"Fine Particulate Matter Does Not Cause Premature Deaths in Cancer Prevention Study"

Enstrom Response to "Fine Particulate Air Pollution and Mortality: Response to Enstrom's Re-analysis of the American Cancer Society Cancer Prevention Study II Cohort" By Pope-Krewski-Gapstur-Turner-Jerrett-Burnett

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July 31, 2017

Critique of Response 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) strongly criticized my *Dose-Response* article, Enstrom 2017 (2), 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 1982-1988 in the 1982 American Cancer Society (ACS) Cancer Prevention Study (CPS II) cohort stand as correct and unchallenged. In particular, my null findings show that the positive findings in three seminal publications by these investigators (Pope 1995 (3), HEI 2000 (4), and HEI 2009 (5)) are not robust and do not support the claim that PM2.5 *causes* premature deaths. Instead of professionally assessing the validity of my findings, these investigators complained about what was not in my article and focused on their many unverifiable analyses of CPS II data.

Their "Expanded analyses of the ACS CPS-II cohort" section begins with a statement that is not true "The assertion regarding selective use of the CPS-II and PM2.5 data is false." I published prima facie evidence that their 1982-1989 PM2.5 mortality findings were indeed sensitive to selective use of PM2.5 and CPS II data. They have refused to confirm or refute my evidence even though my evidence can be easily checked with minor modifications to the SAS programs used to calculate the findings in Table 34 of HEI 2009. Instead, they diverted attention to their various published analyses of PM2.5 deaths in CPS II, as summarized in their Table 1 and Figure 1. All of their analyses involve unverifiable 'secret science' findings that could be just as sensitive to selective use of PM2.5 and CPS II data as the results in Pope 1995, HEI 2000, and HEI 2009.

Their "Deficiencies in Enstrom's re-analysis" section does not identify a single error in my findings and indicates that they made no effort to examine the data and findings in my study.

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 text 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 IPN PM2.5 and HEI PM2.5 data are clearly shown in my Appendix Table A1 and discussed in the Conclusion text on page 6. To make sure that these differences are fully recognized and understood, an expanded version of Appendix Table A1 is shown below as Table 1.

Their "Broader evidence" section is totally irrelevant to the validity of my findings and diverts attention away from my challenge to the validity of the PM2.5 death findings in Pope 1995, HEI 2000, and HEI 2009. Their concluding paragraph beings with this disingenuous sentence "In summary, we welcome thoughtful criticism of our research." This sentence is followed by a false statement "But the study by Enstrom does not contribute to the larger body of evidence on the health effects of PM2.5 . . ." In summary, the authors have entirely evaded my peer reviewed evidence of no relationship between PM2.5 and total mortality in the CPS II cohort and have indicated no willingness to engage in a collegial dialog on this important subject.

Additional Evidence of No PM2.5 Deaths in CPS II

Since they inaccurately criticized my article and did not assess my null findings, I searched their three seminal publications for more evidence that supports my null findings. I found evidence in HEI 2000 that I had not previously recognized. Table 29 and Appendix D in HEI 2000 describe two key sets of 1979-1983 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 1995. I now realize that most of the HEIDC PM2.5 [PM2.5 (DC)] values are the same to one decimal point as the IPN PM2.5 values in my *Dose-Response* article.

Table 1 below shows that the IPN PM2.5 and HEIDC PM2.5 are identical for 45 cities and somewhat different for 13 cities in HEI 2000 Appendix D. Three cities with PM2.5 (OI MD) values (Raleigh NC, Allentown PA, and Huntington WV) were not part of IPN and it is not clear how the PM2.5 values for these three cities were measured. As an approximation, the Raleigh NC PM2.5 value has been assigned to Durham NC, the Allentown PA PM2.5 value has been assigned to Pittsburgh PA, and the Huntington WV PM2.5 value has been assigned to Wheeling WV. Two cities in HEI 2000 Appendix D (Boston MA and St Louis MO) were not used because of unclear ACS Division Unit numbers. Table 1 is an expanded version of Appendix Table B2 in my *Dose-Response* article. Table 2 below shows relative risks (RRs) based on IPN, HEIDC, 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 my *Dose-Response* article. I believe the null RRs based on the HEIDC PM2.5 values were known to the HEI Reanalysis Team and were suppressed from HEI 2000. The support for this belief is based on their overall evasive and dishonest behavior since 2002 is described below in great deal.

The HEI 2000 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. " This section reveals that the investigators were well 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 μg/m³. One reason I did not previously recognize the similarity between the PM2.5 (DC) values and the IPN PM2.5 values was because the only mention of Inhalable Particulate Network (IPN) in HEI 2000 occurs in the footnote at end of Appendix D Table D.1. Everywhere else in HEI 2000 the term Inhalable Particulate Monitoring Network (IPMN) is used. A second reason I did not previously recognize their similarity was because the investigators have absolutely refused to cooperate in clarifying their findings or in confirming what I have done.

Direct evidence that the investigators themselves have found no relationship between PM2.5 and total mortality in CPS II is contained in the 2007 *SERRA* article co-authored by Jerrett, Burnett, Pope, and Krewski, and ACS (Thun) (6). Although they cited 16 of their CPS II analyses in their Table 1, they did not cite the 2007 *SERRA* article. Figure 2 from the SERRA article shows no relationship between PM2.5 and Total (All Cause) Deaths during 1982-2000 in the CPS II cohort. This 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 (Krewski et al. 2000; Pope et al. 2002). 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, Figures 3a and 3b from the *SERRA* article show no relationship between PM2.5 and Total (all cause) Deaths during 1982-1986, 1987-1990, 1991-1994, 1995-1998, and 1999-2000. Furthermore, they found low RRs outside of the Ohio Valley, as they state in the Discussion 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, 3a, and 3b from the *SERRA* article are shown below.

Evasion and Scientific Misconduct by CPS II Investigators and HEI

Since 2002 HEI senior staff, HEI-funded investigators, and ACS epidemiologists have not addressed my evidence of geographic variation in PM2.5 mortality risk and have not conducted

my requested analyses in order to clarify PM2.5 mortality risk in the CPS II cohort. The impasse has existed since August 9, 2002 when HEI President Daniel Greenbaum and HEI Principal Scientist Aaron J. Cohen first refused to provide city-specific mortality risks from HEI 2000 Figures 5 and 21 (http://www.scientificintegrityinstitute.org/Cohen080902.pdf). Additional HEI refusals through October 4, 2013 are fully described in this Greenbaum link (http://www.scientificintegrityinstitute.org/Greenbaum100413.pdf), which is Reference 15 of my *Dose-Response* article.

Since the July 11, 2008 CARB PM2.5 Premature Deaths Teleconference involving Pope, Jerrett, Burnett, and myself, these investigators have ignored my detailed and serious concerns that Pope 1995 and HEI 2000 did not use the IPN PM2.5 data that I used in my 2005 *Inhalation Toxicology* article, which found no PM2.5-related deaths in the California CPS I cohort (http://www.scientificintegrityinstitute.org/CARB071108.pdf). This Teleconference is cited as Reference 24 in my *Dose-Response* article.

In addition, Pope, Krewski, Jerrett, Greenbaum, and Cohen, as well as others, have ignored extensive evidence and criticisms that were raised by me and others during the February 26, 2010 CARB Symposium on PM2.5 and Premature Deaths (https://www.arb.ca.gov/research/health/pm-mort/pm-mort-ws_02-26-10.htm). This day-long conference was a particularly important event because we all made our contributions in front of a large audience of California businessmen who were being adversely impacted by CARB diesel regulations. These regulations were justified in large part by the evidence of PM2.5-related deaths in the CPS II cohort and by the claim of CARB Scientific Advisor Pope that PM2.5 was associated with 18,000 premature deaths annually in California. For a full and balanced discussion of the PM2.5 deaths controversy, please watch the six hour webcast of this CARB meeting (http://cal-span.org/unipage/?site=cal-span&owner=CARB&date=2010-02-26).

Because of the above events and other related evidence, I have meticulously documented PM2.5 scientific misconduct from 2005 through 2013 by Pope, Krewski, Jerrett, and other CPS II-related investigators. The misconduct includes extensive falsification of the research record involving their own findings, my findings, and other findings relating PM2.5 to mortality in the US. This misconduct Is described on pages 81-90 of my May 12, 2017 Comments to EPA requesting reform of the National Ambient Air Quality (NAAQS) for PM2.5, as per Executive Order 13777 (http://www.scientificintegrityinstitute.org/EPA051217.pdf). These investigators have intensified their evasion and scientific misconduct since my *Dose-Response* article became a peer-reviewed journal publication.

On March 10, 2017 I requested that Greenbaum and Cohen confirm my *Dose-Response* findings (http://www.scientificintegrityinstitute.org/Greenbaum031017.pdf), as follows: "In order to test the validity of my evidence, I request that you conduct a sensitivity analysis that produces tables similar to the California tables presented with your September 7, 2010 letter to CARB. Specifically, please produce tables which describe the PM2.5 and mortality relationship in the CSP II cohort for the Ohio Valley states (Indiana, Kentucky, Ohio, Pennsylvania, and West

Virginia) and for the remainder of the Continental United States. Also, please produce these same tables using the 1979-1983 EPA IPN PM2.5 data, which I used in my 2005 *Inhalation Toxicology* article, instead of the PM2.5 data used in the 2000 and 2009 HEI Reports."

I received a March 17, 2017 response from Greenbaum with no commitment to test the validity of my evidence (http://www.scientificintegrityinstitute.org/Greenbaum031717.pdf) and since then Greenbaum has done nothing meaningful other than determine that Pope, Krewski, and ACS refuse to test the validity of my evidence.

My April 10, 2017 request directly to Pope and Krewski that they confirm or refute my findings has yielded no evidence regarding the validity of my findings (http://www.scientificintegrityinstitute.org/Pope041017.pdf). However, Pope was quoted in the April 16, 2017 Bakersfield Californian by Lois Henry "We need people to be skeptical and pick apart our work. It forces us to be more rigorous." (http://www.scientificintegrityinstitute.org/Henry041617.pdf). Also, Pope wrote the May 9, 2017 letter to the editor that I commented on above (1).

My May 12, 2017 email to HEI Board Chairman Richard Celeste regarding the evasive HEI and Pope responses to my *Dose-Response* article yielded a May 12, 2017 response from Celeste to Greenbaum, the HEI Board and Committee Members, and me acknowledging that HEI senior staff brought my article to the attention of the HEI Board and were preparing further comments for me, (http://www.scientificintegrityinstitute.org/Celeste051217.pdf). I have received no further comments from HEI addressing the validity of my *Dose-Response* findings.

My May 26, 2017 request to HEI 2009 co-author Turner, who based her 2004 MSc dissertation and her 2012 Ph.D. dissertation on analyses of CPS II data, has not been answered (http://www.scientificintegrityinstitute.org/Turner052617.pdf). Thus, she is in violation of her 2017 authorship agreement as per the ICMJE Uniform Requirements "to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved" (9).

On June 12, 2017 Greenbaum provided me with the July 25, 1997 HEI Reanalysis Project Request for Qualifications (http://www.scientificintegrityinstitute.org/Greenbaum061217.pdf). This RFQ specifies the background and requirements for the HEI Reanalysis Project. The Objectives and Scope include this sentence: "2) Conduct sensitivity analyses to test the robustness of the original findings and interpretations to alternative analytic approaches." (http://www.scientificintegrityinstitute.org/HEIRFQ072597).

My *Dose-Response* findings make it clear that the robustness of the Pope 1995 findings were not 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. According to Greenbaum, responses to the RFQ were received from 13 teams and HEI selected the Krewski team based at the University of Ottawa in Canada. The 31-member Krewski team was apparently the only

team based outside of the United Status. Amazingly, the Krewski team had no qualified epidemiologist who recognized and examined the selective nature of the Pope 1995 epidemiologic findings and then conducted the mandated sensitivity analyses, as I have done.

My June 15, 2017 request to Cohen yielded a July 6, 2017 response that did not assess my findings regarding PM2.5 deaths in the CPS II cohort (http://www.scientificintegrityinstitute.org/Cohen070617). Thus, he, like Turner, is in violation of his 2017 authorship agreement as per the ICMJE Uniform Requirements "to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved" (9).

My July 4, 2017 request to William Ryan Diver, ACS Epidemiology Data Analysis Core Director, to confirm or refute my findings has yielded no response (http://www.scientificintegrityinstitute.org/Diver070417.pdf). He has had authorized access to CPS II data since 2002 and can easily perform the verification tasks that I have requested, but he has refused to do so. Thus, he is in violation of his 2017 authorship agreement as per the ICMJE Uniform Requirements (9). Indeed, Turner, Cohen, Pope, Krewski, Gapstur, Jerrett, and Burnett are all in violation of the ICMJE Uniform Requirements as of 2017 (9).

As a result of the above requests, I did receive a June 30, 2017 email message from Pope that includes this slight concession in support of my *Dose-Response* findings "Briefly, our work to date addresses the fact that the PM2.5-mortality association can be sensitive to the method of exposure assignment in any cohort." (http://www.scientificintegrityinstitute.org/Pope063017.pdf). In addition, Cohen, Pope, and Burnett provided indirect evidence that supports my findings in their May 13, 2017 Lancet "Global Burden of Disease" article, which went online April 10, 2017 (7). The reprinted Table 2 from this article shows that, based on their own exaggerated PM2.5 deaths evidence, the US as of 2015 had a very low annual PM2.5-related death rate (18.5 deaths per 100,000 persons) and low PM2.5 exposure (8.4 μg/m³). This table also shows that PM2.5 pollution is concentrated in other parts of the world, particularly China and India, and not in the US. Once there is full confirmation of the evidence of no PM2.5-related deaths in the CPS II cohort and other national cohorts, like the NIH AARP cohort (8), EPA and other regulatory agencies, like CARB, will be required to acknowledge that PM2.5 does not cause premature deaths in the US.

Lack of Epidemiologic Qualifications of CPS II Investigators

Since 1995 the above CPS II investigators have shown no respect for transparent reproducible science or for the limits of epidemiology, as explained in detail in my *Dose-Response* article (2). I believe their unprofessional behavior is due in large part to their lack of formal training in epidemiology and to their lack of respect for the methods and limitations of epidemiology, particularly regarding the definition of causality. Only one investigator (Gapstur) has doctoral level training in epidemiology. Another one (Turner) has doctoral level training in population

health, received under the direction of Krewski and Pope. The Ph.D. dissertations of the six investigators who wrote the response (1) are described below.

Clive Arden Pope, III: 1981 Ph.D. in Agricultural Economics from Iowa State University
"The Dynamics of Crop Yields in the U.S. Corn Belt as Effected by Weather and Technological Progress"

Daniel Richard Krewski: 1977 Ph.D. in Statistics from Carleton University, Canada
"Linearization and Replication Methods in Finite Population Sampling"

Susan Mary Gapstur: 1993 Ph.D. in Epidemiology from University of Minnesota
"Alcohol and cancer: Relationship with site-specific cancers and steps toward a biochemical marker for alcohol intake"

Michelle Catherine Turner: 2012 Ph.D. in Population Health from University of Ottawa, Canada
"Environmental Risk Factors for Lung Cancer Mortality in the Cancer Prevention Study-II"

Michael Leo Jerrett: 1996 Ph.D. in Geography from University of Toronto, Canada
"Green cost, red ink: An environmental accounting of the defensive expenditures made by municipal governments in Ontario"

Richard Thomas Burnett: 1982 Ph.D. in Statistics from Queen's University, Canada
"The Piecewise Proportional Hazards Model"

Conclusions

Because of their extensively documented pattern of evasion and misrepresentation, I have strong evidence that Pope, Krewski, and ACS (Thun and Gapstur) have deliberately exaggerated the relationship between PM2.5 and total mortality in the CPS II cohort since 1995. In particular, they have falsified the PM2.5 and total mortality relationship within the US by misrepresenting their own findings and ignoring the null findings of several other investigators. They have now refused to acknowledge the significance of the null findings in my *Dose-Response* article, knowing that I have directly analyzed an original version of the CPS II cohort data with six-year mortality follow-up. Furthermore, they do not realize that my independent analysis of the CPS II cohort data brings into question all of their unverifiable 'secret science' analyses of CPS II data. Every effort is being made force ACS, HEI, and these investigators to professionally cooperate in transparent and verifiable analyses of the CPS II cohort data. Also, every effort is being made to have EPA reassess all CPS II evidence relating PM2.5 to mortality. Finally, every effort is being made to have the EPA PM2.5 NAAQS entirely reassessed.

References

1. Pope CA III, Krewski D, Gapstur SM, Turner MC, Jerrett M, Burnett RT. "Fine Particulate Air Pollution and Mortality: Response to Enstrom's Re-analysis of the American Cancer Society Cancer Prevention Study II Cohort." Submitted to *Dose-Response* May 9, 2017

2. Enstrom JE. Fine particulate matter and total mortality in Cancer Prevention Study Cohort Reanalysis. *Dose-Response* 2017;15:1-12 doi/10.1177/1559325817693345

3. Pope CA III, Thun MJ, Namboodiri MM, et al. Particulate air pollution as a predictor of mortality in a prospective study of U.S. adults. *Am J Resp Crit Care Med* 1995;151:669-674. doi: 10.1164/ajrccm.151.3.7881654

4. Krewski D, Burnett RT, Goldberg MS, et al. Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality: Special Report. Cambridge, MA: Health Effects Institute, July 2000. Part I. Replication and Validation (http://www.healtheffects.org/Pubs/Rean-part1.pdf) and Part II. Sensitivity Analyses (http://www.healtheffects.org/Pubs/Rean-part2.pdf), particularly Figure 5 on page 161, Figure 13 on page 89, and Figure 21 on page 197 and Appendix D (http://pubs.healtheffects.org/getfile.php?u=988)

5. Krewski D, Jerrett M, Burnett RT, et al. Extended Follow-Up and Spatial Analysis of the American Cancer Society Study Linking Particulate Air Pollution and Mortality. HEI Research Report 140, Health Effects Institute, Boston, MA, June 2009, particularly Table 34 (http://pubs.healtheffects.org/view.php?id=315)

6. Jerrett M, Newbold KB, Burnett RT, et al. Geographies of uncertainty in the health benefits of air quality improvements. *Stoch Environ Res Risk Assess* 2007;21:511-522.

7. Cohen AJ, Brauer M, Burnett R, et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet* 2017;389(10082):1907-1918 (May 13, 2017).

8. Thurston GD, Ahn J, Cromar KR, et al. Ambient particulate matter air pollution exposure and mortality in the NIH-AARP Diet and Health Cohort. *Environ Health Perspect* 2016;124(4):484-490.

9. Turner MC, Cohen AJ, Burnett RT, Jerrett M, Diver WR, Gapstur SM, Krewski D, Samet JM, Pope CA III. Interactions between cigarette smoking and ambient $PM_{2.5}$ for cardiovascular mortality. *Environ Res* 2017;154:304-310 (April 2017). https://doi.org/10.1016/j.envres.2017.01.024

https://www.elsevier.com/journals/environmental-research/0013-9351/guide-for-authors

Table 1. List of the 85 counties containing the 50 cities used in Pope 1995, HEI 2000, and HEI 2009, as well as the 35 additional counties used in Enstrom 2017. 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, 1979-83 IPN weighted average PM2.5 level, 1979-83 HEIDC [PM2.5 (DC)] weighted average PM2.5 level, 1979-83 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, three cities used in HEI 2000 (Raleigh NC, Allentown PA, and Huntington WV) were not part of IPN and origin of the HEI PM2.5 data in HEI 2000 Appendix D for these three cities (indicated with *) is unknown. As an approximation, the Raleigh NC PM2.5 value has been assigned to Durham NC, the Allentown PA PM2.5 value has been assigned to Pittsburgh PA, and the Huntington WV PM2.5 value has been assigned to Wheeling WV. [Editorial Note: the column headings and data need to be properly aligned as per *D-R* Appendix Table A1]

State	ACS Div-Unit	FIPS Code	IPN/HEI County containing IPN/HEI City	IPN/HEI City with $PM_{2.5}$ Measurements	1979-83 IPN $PM_{2.5}$ ($\mu g/m^3$) (weighted average)	1979-83 HEIDC $PM_{2.5}$ ($\mu g/m^3$)	1979-83 HEI $PM_{2.5}$ ($\mu g/m^3$) (median)	1980 Age-Adj White Death Rate (DR)	HEI Fig 5 Mort-ality Risk (MR)
AL	01037	01073	JEFFERSON	Birmingham	25.6016	28.7	24.5	1025.3	0.760
AL	01049	01097	MOBILE	Mobile	22.0296	22.0	20.9	1067.2	0.950
AZ	03700	04013	MARICOPA	Phoenix	15.7790	18.5	15.2	953.0	0.855
AR	04071+2	05119	PULASKI	Little Rock	20.5773	20.6	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	10.3	1001.4	0.680
CA	06008	06029	KERN	Bakersfield	30.8628			1119.3	
CA	06051+4	06037	LOS ANGELES	Los Angeles	28.2239	26.8	21.8	1035.1	0.760
CA	06019	06065	RIVERSIDE	Rubidoux	42.0117			1013.9	
CA	06020	06073	SAN DIEGO	San Diego	18.9189	18.9		943.7	
CA	06021	06075	SAN FRANCISCO	San Francisco	16.3522	16.4	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	17.8	12.4	921.9	0.885
CO	07004	08031	DENVER	Denver	10.7675	10.8	16.1	967.3	0.925
CO	07047	08069	LARIMER	Fort Collins	11.1226			810.5	
CO	07008	08101	PUEBLO	Pueblo	10.9155	19.9		1024.1	
CT	08001	09003	HARTFORD	Hartford	18.3949	18.4	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+2	10003	NEW CASTLE	Wilmington	20.3743	20.4		1053.7	

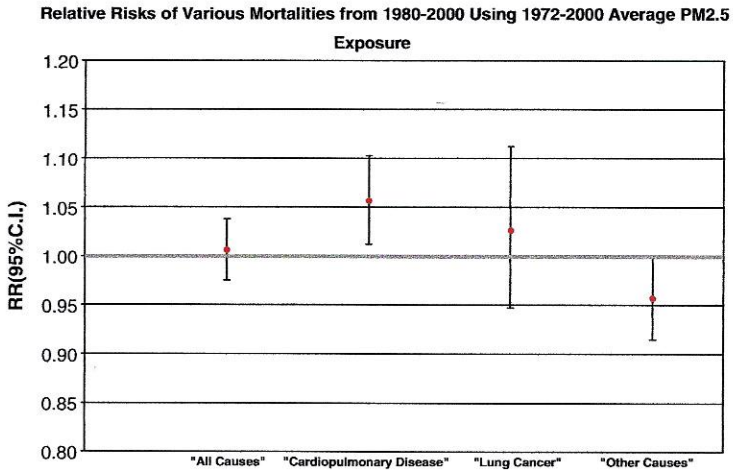
DC	10001+2	11001	DIST COLUMBIA	Washington	25.9289	25.9	22.5	993.2	0.850
FL	11044	12057	HILLSBOROUGH	Tampa	13.7337	13.7	11.4	1021.8	0.845
GA	12027+4	13051	CHATHAM	Savannah	17.8127	17.8		1029.6	
GA	12062	13121	FULTON	Atlanta	22.5688	22.6	20.3	1063.5	0.840
ID	13001	16001	ADA	Boise	18.0052	18.0	12.1	892.6	0.600
IL	14089+4	17031	COOK	Chicago	25.1019	23.0	21.0	1076.3	0.945
IL	14098	17197	WILL	Braidwood	17.1851			1054.0	
IN	15045	18089	LAKE	Gary	27.4759	27.5	25.2	1129.8	0.995
IN	15049	18097	MARION	Indianapolis	23.0925	23.1	21.1	1041.2	0.970
KS	17287	20173	SEDGWICK	Wichita	15.0222	15.0	13.6	953.4	0.890
KS	17289	20177	SHAWNEE	Topeka	11.7518	11.8	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+1	24510	BALTIMORE CITY	Baltimore	21.6922	21.7		1237.8	
MD	21101	24031	MONTGOMERY	Rockville	20.2009			881.9	
MA	22105+1	25013	HAMPDEN	Springfield	17.5682	17.6		1025.3	
MA	22136	25027	WORCESTER	Worcester	16.2641	16.3		1014.6	
MN	25001+2	27053	HENNEPIN	Minneapolis	15.5172	15.5	13.7	905.3	0.815
MN	25150+5	27123	RAMSEY	St Paul	15.5823			935.7	
MS	26086	28049	HINDS	Jackson	18.1339	18.1	15.7	1087.4	0.930
MO	27001+3	29095	JACKSON	Kansas City	17.8488	17.8		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	15.3	13.1	991.0	0.880
NV	31101	32031	WASHOE	Reno	13.1184	13.1	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	19.9	17.3	1172.6	0.810
NM	34201	35001	BERNALILLO	Albuquerque	12.8865	12.9	9.0	1014.7	0.710
NY	36014	36029	ERIE	Buffalo	25.1623	26.5	23.5	1085.6	0.960
NY	35001	36061	NEW YORK	New York City	23.9064	23.9		1090.4	
NC	37033	37063	DURHAM	Durham	19.4092		16.8*	1039.2	1.000
NC	37064	37119	MECKLENBURG	Charlotte	24.1214	24.1	22.6	932.8	0.835
OH	39009	39017	BUTLER	Middletown	25.1789			1108.3	
OH	39018	39035	CUYAHOGA	Cleveland	28.4120	27.9	24.6	1089.1	0.980
OH	39031	39061	HAMILTON	Cincinnati	24.9979	25.0	23.1	1095.2	0.980
OH	39041	39081	JEFFERSON	Steubenville	29.6739	29.7	23.1	1058.6	1.145
OH	39050	39099	MAHONING	Youngstown	22.9404	22.9	20.2	1058.4	1.060
OH	39057	39113	MONTGOMERY	Dayton	20.8120	20.8	18.8	1039.5	0.980
OH	39077	39153	SUMMIT	Akron	25.9864	26.0	24.6	1064.0	1.060
OK	40055	40109	OKLAHOMA	Oklahoma City	14.9767	15.0	15.9	1050.4	0.985
OR	41019+1	41039	LANE	Eugene	17.1653	17.2		885.5	

OR	41026	41051	MULTNOMAH	Portland	16.3537	19.8	14.7	1060.8	0.830
PA	42101+1	42003	ALLEGHENY	Pittsburgh	29.1043	30.0	17.9*	1115.6	1.005
PA	42443	42095	NORTHAMPTON	Bethlehem	19.5265			998.6	
PA	43002+11	42101	PHILADELPHIA	Philadelphia	24.0704	24.1	21.4	1211.0	0.910
RI	45001+6	44007	PROVIDENCE	Providence	14.2341	14.2	12.9	1006.1	0.890
SC	46016+1	45019	CHARLESTON	Charleston	16.1635			1023.5	
TN	51019+5	47037	DAVIDSON	Nashville	21.8944	22.6	20.5	981.9	0.845
TN	51088	47065	HAMILTON	Chattanooga	18.2433	20.4	16.6	1087.9	0.840
TX	52811+2	48113	DALLAS	Dallas	18.7594	18.8	16.5	1024.9	0.850
TX	52859+3	48141	EL PASO	El Paso	16.9021	16.9	15.7	903.5	0.910
TX	52882+2	48201	HARRIS	Houston	18.0421	18.0	13.4	1025.7	0.700
UT	53024	49035	SALT LAKE	Salt Lake City	16.6590	17.5	15.4	954.3	1.025
VA	55024	51059	FAIRFAX	Fairfax	19.5425			925.7	
VA	55002	51710	NORFOLK CITY	Norfolk	19.5500	19.5	16.9	1139.3	0.910
WA	56017	53033	KING	Seattle	14.9121	14.9	11.9	943.6	0.780
WA	56032	53063	SPOKANE	Spokane	13.5200	13.5	9.4	959.2	0.810
WV	58130	54029	HANCOCK	Weirton	25.9181			1094.8	
WV	58207	54039	KANAWHA	Charleston	21.9511	21.7	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	

Table 2. Fully adjusted relative risk of death from all causes (RR and 95% CI) from September 1, 1982 through August 31, 1988 associated with change of 10 μg/m³ increase in PM2.5 for CPS II subjects residing in 47 to 85 counties in the continental United States with 1979-83 IPN PM2.5, HEIDC PM2.5, and HEI PM2.5 measurements. Analysis includes continental United States, five Ohio Valley states, and remainder of the states. Table 1 lists the up to 85 cities and counties with PM2.5 measurements.

PM2.5 Years and Source	Number of Counties	Number of Subjects	Number of Deaths	RR	95% CI Lower	95% CI Upper	Average PM2.5
Fully adjusted RR for the Continental United States							
1979-83 IPN	85	269,766	15,593	1.023	(0.997	1.049)	21.15
1979-83 HEIDC	58	216,897	12,505	1.024	(0.987	1.061)	21.09
1979-83 IPN	50	195,215	11,221	1.025	(0.990	1.061)	21.36
1979-83 HEI	50	195,215	11,221	1.082	(1.039	1.128)	17.99
1979-83 HEIDC N=47	47	189,676	10,836	1.023	(0.984	1.064)	20.95
1979-83 IPN N=47	47	189,676	10,836	1.021	(0.984	1.058)	21.13
1979-83 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							
1979-83 IPN	17	53,026	3,293	1.096	(0.978	1.228)	25.51
1979-83 HEIDC	10	43,945	2,749	1.048	(0.922	1.191)	25.78
1979-83 IPN	12	42,174	2,652	1.050	(0.918	1.201)	25.75
1979-83 HEI	12	42,174	2,652	1.111	(0.983	1.256)	22.02
Fully adjusted RR for the Non-Ohio Valley Continental United States							
1979-83 IPN	68	216,740	12,300	0.994	(0.967	1.023)	20.09
1979-83 HEIDC	48	172,952	9,756	0.960	(0.919	1.003)	19.90
1979-83 IPN	38	153,041	8,569	0.975	(0.936	1.015)	20.15
1979-83 HEI	38	153,041	8,569	1.025	(0.975	1.078)	16.89

1979-83 PM2.5 Data Source:
IPN = EPA Inhalable Particulate Network (Hinton 1984 and 1986)→ Yields Insignificant RRs
HEIDC= HEI 2000 Appendix D 'PM2.5 (DC)'→ Yields Insignificant RRs (apparently conducted but not reported in HEI 2000)
HEI = HEI 2000 Appendix D 'PM2.5 (OI,MD)'→ Yields Significant RRs (used in HEI 2000)



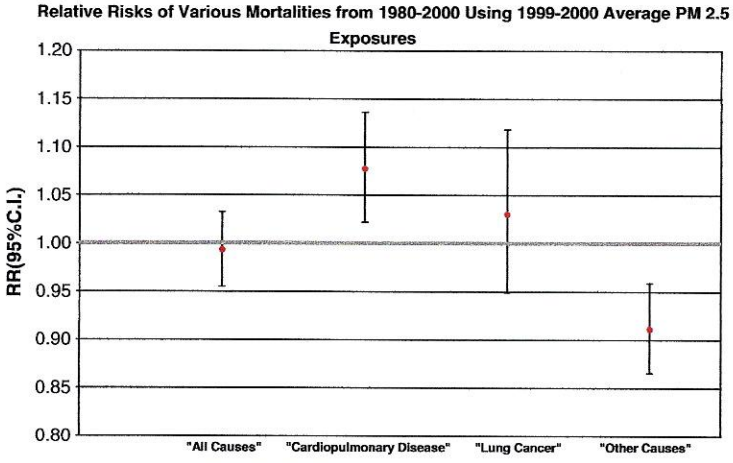
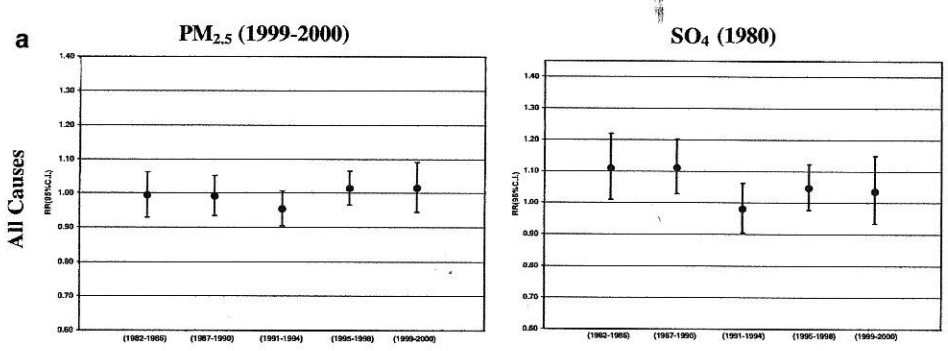


Fig. 2 Summary of risks for different exposures over the entire follow-up



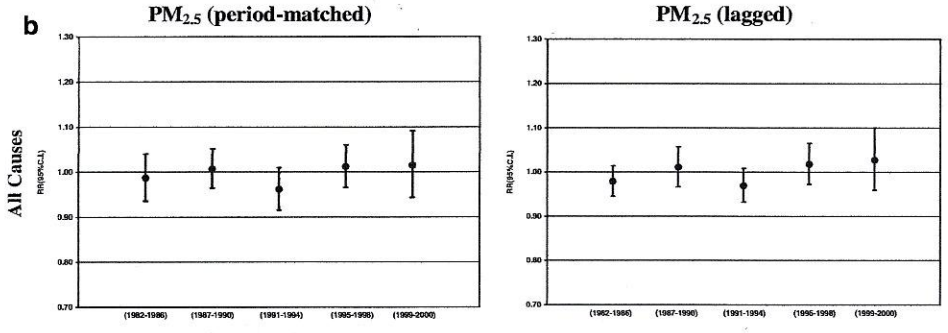


Fig. 3 **a** Relative risks for all-cause, cardiopulmonary and lung cancer deaths estimated for five time periods of the follow-up (1982–1986, 1987–1990, 1991–1994, 1995–1998, and 1999–2000) with measured exposures. **b** Relative risks for all-cause, cardiopulmonary and lung cancer deaths estimated for five time periods of the follow-up (1982–1986, 1987–1990, 1991–1994, 1995–1998, and 1999–2000) with imputed exposures

Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015

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Summary

Background Exposure to ambient air pollution increases morbidity and mortality, and is a leading contributor to global disease burden. We explored spatial and temporal trends in mortality and burden of disease attributable to ambient air pollution from 1990 to 2015 at global, regional, and country levels.

Methods We estimated global population-weighted mean concentrations of particle mass with aerodynamic diameter less than 2·5 μm ($PM_{2·5}$) and ozone at an approximate 11 km×11 km resolution with satellite-based estimates, chemical transport models, and ground-level measurements. Using integrated exposure–response functions for each cause of death, we estimated the relative risk of mortality from ischaemic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, lung cancer, and lower respiratory infections from epidemiological studies using non-linear exposure–response functions spanning the global range of exposure.

Findings Ambient $PM_{2·5}$ was the fifth-ranking mortality risk factor in 2015. Exposure to $PM_{2·5}$ caused 4·2 million (95% uncertainty interval [UI] 3·7 million to 4·8 million) deaths and 103·1 million (90·8 million 115·1 million) disability-adjusted life-years (DALYs) in 2015, representing 7·6% of total global deaths and 4·2% of global DALYs, 59% of these in east and south Asia. Deaths attributable to ambient $PM_{2·5}$ increased from 3·5 million (95% UI 3·0 million to 4·0 million) in 1990 to 4·2 million (3·7 million to 4·8 million) in 2015. Exposure to ozone caused an additional 254 000 (95% UI 97 000–422 000) deaths and a loss of 4·1 million (1·6 million to 6·8 million) DALYs from chronic obstructive pulmonary disease in 2015.

Interpretation Ambient air pollution contributed substantially to the global burden of disease in 2015, which increased over the past 25 years, due to population ageing, changes in non-communicable disease rates, and increasing air pollution in low-income and middle-income countries. Modest reductions in burden will occur in the most polluted countries unless $PM_{2·5}$ values are decreased substantially, but there is potential for substantial health benefits from exposure reduction.

Funding Bill & Melinda Gates Foundation and Health Effects Institute.

Lancet 2017; 389: 1907–18

Published Online
April 10, 2017
http://dx.doi.org/10.1016/S0140-6736(17)30505-6

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	Deaths, in thousands (95% UI)	Risk factor rank for deaths	Deaths per 100 000 people (95% UI)	DALYs, in thousands (95% UI)	DALYs per 100 000 people (95% UI)	Population-weighted mean $PM_{2·5}$ (μg/m³; 95% UI)
China	1108·1 (948·7–1272·8)	1	84·3 (71·5–96·7)	21 778·7 (18 903·5–24 584·2)	1478·6 (1275·9–1675·6)	58·4 (58·1–58·7)
India	1090·4 (936·6–1254·8)	2	133·5 (112·8–154·9)	29 609·6 (25 923·3–33 562·7)	2922·1 (2527·3–3327·5)	74·3 (73·9–74·8)
USA	88·4 (66·8–115·0)	6	18·5 (14·2–23·7)	1485·9 (1166·3–1841·7)	337·1 (265·0–416·8)	8·4 (8·4–8·5)
Indonesia	78·6 (62·0–96·7)	7	49·9 (38·5–61·6)	2185·0 (1730·4–2716·2)	1081·1 (860·4–1324·2)	15·4 (15·1–15·7)
Brazil	52·3 (41·9–65·1)	9	30·9 (24·2–39·0)	1083·9 (884·0–1322·7)	573·7 (467·3–702·3)	11·4 (11·2–11·5)
Pakistan	135·1 (114·3–159·2)	4	136·3 (113·7–163·5)	4217·3 (3545·1–4916·3)	3114·2 (2651·3–3657·7)	65·0 (63·8–66·2)
Nigeria	50·9 (35·7–73·2)	10	68·9 (48·5–101·7)	2410·0 (1640·4–3387·0)	1581·0 (1107·6–2237·2)	38·0 (37·5–38·5)
Bangladesh	122·4 (103·2–144·4)	5	133·2 (111·8–158·4)	3408·0 (2920·3–3945·8)	2972·0 (2533·4–3469·1)	89·4 (87·3–91·7)
Russia	136·9 (111·3–161·1)	3	62·6 (51·8–73·2)	2601·6 (2194·8–3007·2)	1255·0 (1077·8–1431·1)	16·6 (16·2–17·0)
Japan	60·6 (44·5–81·4)	8	16·8 (12·8–21·9)	705·8 (561·2–891·0)	261·7 (212·8–319·2)	13·3 (13·1–13·6)

Countries are shown in order of population size in 2015. DALY=disability-adjusted life-year. $PM_{2·5}$=particle mass with aerodynamic diameter less than 2·5 μm. UI=uncertainty interval.

Table 2: **2015 estimates of mortality and disability-adjusted life-years attributable to ambient particulate matter pollution and population-weighted mean particulate matter pollution in the world's ten most populous countries**