Scientific Support for EPA Proposed Rule *Strengthening Transparency in Regulatory Science*

James E. Enstrom, PhD, MPH, FFACE
UCLA and Scientific Integrity Institute
http://www.scientificintegrityinstitute.org/
http://scientificintegrityinstitute.org/biography.html
jenstrom@ucla.edu

January 14, 2020

This Comment provides strong scientific support for the EPA Proposed Rule *Strengthening Transparency in Regulatory Science.* It contains evidence that is directly relevant to the October 16, 2019 Draft Report of the EPA Science Advisory Board (SAB) Consideration of the Scientific and Technical Basis of EPA Proposed Rule *Strengthening Transparency in Regulatory Science* (https://yosemite.epa.gov/sab/sabproduct.nsf/ea5d9a9b55cc319285256cbd005a472e/8a4dabc3b78f4106852584e100541a03!OpenDocument).

My Comment begins with my December 13, 2019 *Science* eLetter "Criticism of Miranda Editorial and Joint Statement in December 6, 2019 Science Magazine" (https://science.sciencemag.org/content/366/6470/1173/tab-e-letters). The December 6, 2019 *Science* Editorial "Getting the EPA back on track" by Marie Lynn Miranda was written by 2015-2019 Rice University Provost. The Miranda Editorial (https://science.sciencemag.org/content/366/6470/1173) and the Joint Statement (https://science.sciencemag.org/content/366/6470/eaba3197) misrepresent the proposed EPA rule "Strengthening Transparency in Regulatory Science." Its true purpose is to increase scientific rigor and transparency in the research findings used to justify EPA regulations. This rule is needed because certain EPA-related findings are etiologically implausible and the authors of these findings refuse to address criticism and/or to conduct requested reanalysis. I demonstrated the importance of this rule when I independently reanalyzed the ACS CPS II data underlying the seminal 1995 Pope analysis of these data. Pope 1995 provided the primary justification for establishing the 1997 PM2.5 NAAQS. My reanalysis found NO robust relationship between PM2.5 and total mortality and it directly challenges the positive relationships in Pope 1995, HEI 2000, and HEI 2009. My reanalysis did not violate subject confidentiality and is a model for data sharing. My complete eLetter contains additional evidence in support of the EPA Transparency Rule. Provost Miranda has not responded.

Next is my October 17, 2019 EPA CASAC Comment (https://yosemite.epa.gov/sab/sabproduct.nsf/F729E7D8E248A2C5852584970009565A/$File/Enstrom+Comment+to+CASAC+re+090519+EPA+PM+PA+101719.pdf) or (http://scientificintegrityinstitute.org/JEEPMPA102219.pdf). My October 17 Comment contains detailed criticism of the 2018 Draft EPA PM ISA (PM ISA) and the 2019 Draft EPA PM PA (PM PA). Specifically, it presents strong evidence that 1) there is NO causal relationship between PM2.5 and total mortality in the US, 2) the PM PA cites 'positive authors' and omits 'null authors' and their criticism, 3) the PM PA does not address the PM2.5 deaths controversy, 4) my analyses of underlying data for four key US cohorts, including H6CS and ACS CPS II, support the need for the proposed EPA Transparency Rule, and 5) the PM PA must be revised to incorporate the CASAC Review and the criticisms by me and others.

Next is my December 11, 2019 EPA CASAC Comment (https://yosemite.epa.gov/sab/sabproduct.nsf//ADCBAE726C987F6A852584D200635254/$File/Enstrom+Comment+to+EPA+CASAC+re+PM+PA+&+PM2.5+NAAQS+121119.pdf) or (http://scientificintegrityinstitute.org/JEEPMPA121119.pdf). My December 11, 2019 Comment presented strong evidence that 1) 2018 Draft EPA PM ISA and 2019 Draft EPA PM PA Violate EPA Principles of Scientific Integrity, 2) There is Deliberate Falsification of the Research Record re Enstrom Reanalysis of ACS CPS II Cohort Data, 3) *Science* and AAAS Continue to Inappropriately Oppose the Proposed EPA Transparency Rule, and 4) *BMJ* Rejected Enstrom CPS II Reanalysis and Deleted Enstrom Peer Review of Harvard PM2.5 Manuscript. The first three pages of my deleted nine-page Peer Review of the Harvard PM2.5 manuscript are included.

My Comment concludes with the December 1, 2019 *Environment International* article: "Mortality burdens in California due to air pollution attributable to local and nonlocal emissions" by Tianyang Wang, Bin Zhao, Kuo-Nan Liou, Yu Gu, Zhe Jiang, Kathleen Song, Hui Sue, Michael Jerrett, and Yifang Zhu (https://doi.org/10.1016/j.envint.2019.105232). This article has eight Chinese authors and one Canadian author (Michael Jerrett) and NO American authors. Jerrett and Zhu are senior Professors at the UCLA School of Public Health, where I spend my academic career. This article claims that there are at least 12,700 annual PM2.5 premature deaths in California and it was published 14 years after I published unrefuted evidence of NO PM2.5 premature deaths in California (Enstrom 2005). The *EI* article contains NO citation of Pope 1995, Enstrom 2005, Enstrom 2006, HEI 2000, Jerrett 2007, Enstrom 2008, Enstrom 2009, Enstrom 2010, Jerrett 2010, Enstrom 2011, Enstrom 2012, Enstrom 2017, Young 2017, Enstrom 2018, and numerous other published findings of NO PM2.5 deaths in California (see Enstrom 2017). This article is an excellent example of the deliberate falsification of evidence regarding PM2.5 premature deaths in the United States that is continuing up to the present time.

Finally, based on the evidence contained in this Comment, I make the following recommendation for the final version of the EPA Transparency Rule. Before requiring release of de-identified raw data, require an investigator using Federal funding to conduct research and to publish findings that are used for EPA rule making to 1) voluntarily cooperate with legitimate peer critics in conducting additional analysis or reanalysis in order to resolve any legitimate controversy regarding the investigator's published findings, and 2) reveal the names and comments of the peer reviewers who recommended publication of the investigator's findings (similar to the *BMJ* model of open peer review). The details of this recommendation must be worked out.

Criticism of EPA-452/P-19-001 September 2019 Policy Assessment for the Review of the National Ambient Air Quality Standards for Particulate Matter, External Review Draft

James E. Enstrom, PhD, MPH, FFACE
UCLA and Scientific Integrity Institute
http://www.scientificintegrityinstitute.org/
http://scientificintegrityinstitute.org/biography.html
jenstrom@ucla.edu

October 17, 2019

I am herewith submitting to the EPA Clean Air Scientific Advisory Committee (CASAC) detailed criticism of EPA-452/P-19-001 EPA Policy Assessment for the Review of the National Ambient Air Quality Standards for Particulate Matter (External Review Draft - September 2019) (2019 PM PA). The 2019 PM PA is severely flawed because it does not address the concerns of the April 11, 2019 CASAC Review of the EPA's Integrated Science Assessment for Particulate Matter (External Review Draft – October 2018) (Cox 2019) regarding EPA/600/R-18/179 US EPA Integrated Science Assessment (ISA) for Particulate Matter (External Review Draft) October 2018 (2018 PM ISA). To illustrate the severe flaws in 2019 PM PA, I focus on the "All-cause mortality" portion of Figure 3-3 within Section 3.2.3 PM2.5 Concentrations in Key Studies Reporting Health Effects of Chapter 3 REVIEW OF THE PRIMARY STANDARDS FOR PM2.5 of the 2019 PM PA. A key sentence on page 3-52 states "To evaluate the PM2.5 air quality distributions in key studies in this review, we first identify the epidemiologic studies assessed in the draft ISA that have the potential to be most informative in reaching conclusions on the primary PM2.5 standards." Unfortunately, Figure 3-3 on page 3-54 does not properly describe the results from the nine US prospective cohort studies of PM2.5 and total mortality. As I document below, the answer is NO to the question in the title of this essential 2017 article: "Do causal concentration–response functions exist? A critical review of associational and causal relations between fine particulate matter and mortality" in *Critical Reviews in Toxicology* by CASAC Chair Louis Anthony (Tony) Cox Jr (Cox 2017). My criticism is divided into the five sections below.

1. 2019 PM PA Obscures the Null Relationship Between PM2.5 and Total Mortality in the US

Figure 3-3 of 2019 PM PA deliberately misrepresents the US epidemiologic evidence on the relationship of PM2.5 to total (all cause) mortality and obscures the null relationship that exists in a proper meta-analysis of the nine major US cohort studies with published findings. Particularly troubling to me is the unjustified omission from the 2019 PM PA of my March 28, 2017 "Fine Particulate Matter and Total Mortality in Cancer Prevention Study Reanalysis" in *Dose-Response* (Enstrom 2017) and my May 29, 2018 "Response to Criticism" in *Dose-Response* (Enstrom 2018). My seminal reanalysis of ACS CPS II identified major flaws in Pope 1995, the key study underlying the 1997 PM NAAQS. Instead of properly examining the detailed findings in my reanalysis, SECTION 11.2: Long-Term PM2.5 Exposure and Total Mortality of the 2018 PM ISA dismissed my reanalysis in two *inaccurate* sentences: "A recent reanalysis of early ACS results observed a null association between county-level averages of PM2.5 measured by the Inhalable Particle Network between 1979 and 1983 and deaths between 1982 and 1988 (HR: 1.01; 95% CI: 1.00, 1.02) (Enstrom, 2017). Inconsistencies in the results could be due to the use of 85 counties in the ACS analysis by Enstrom (2017) and 50 Metropolitan Statistical Areas in the original ACS analysis (Pope et al., 1995)."

A proper meta-analysis of the relationship between PM2.5 and total mortality in nine US cohort studies is given in the September 28, 2018 Intrepid Insight (II) article **"**Statistical Review of Competing Findings in Fine Particulate Matter and Total Mortality Studies".

II Table B3: Intrepid Insight Computation of Fixed and Random Effects Meta-Analysis

Nine US Cohorts That Analyzed Ambient Fine Particulate Matter (PM2.5) and Total (All-cause) Mortality
Relative Risk (RR and 95% CI) of Total Mortality Associated with Increase of 10 $\mu g/m^3$ in PM2.5

US Cohort Studies	Author Year	RR Table	F-U Years	RR	95%CI(L)	95%CI(U)
Veterans Study	Lipfert 2000	T6	1986-1996	0.890	0.850	0.950
Medicare (MCAPS) Eastern US	Zeger 2008	T3	2000-2005	1.068	1.049	1.087
Medicare (MCAPS) Central US	Zeger 2008	T3	2000-2005	1.132	1.095	1.169
Medicare (MCAPS) Western US	Zeger 2008	T3	2000-2005	0.989	0.970	1.008
ACS Cancer Prevention Study (CPS II)	HEI RR140 2009	T34	1982-2000	1.028	1.014	1.043
Nurses Health Study	Puett 2009	T3	1992-2002	1.260	1.020	1.540
Health Professionals FU Study	Puett 2011	T2	1989-2002	0.860	0.720	1.020
Harvard Six Cities Study (H6CS)	Lepeule 2012	T2	1974-2009	1.140	1.070	1.220
Agricultural Health Study	Weichenthal 2015	T2	1993-2009	0.950	0.760	1.200
NIH-AAPR Diet and Health Study	Thurston 2016	T2 F3	2000-2009	1.025	1.000	1.049
National Health Interview Survey	Parker 2018	T3corr	1997-2011	1.016	0.979	1.054
Intrepid Insight Random Effects Meta-Analysis Summary RR				**1.031**	**0.997**	**1.066**

Q Test Statistic = 109.5100704 **I^2 90.87%**
Cochrane's Q Test for Homogeneity of Studies (Null Hypothesis: Studies are Homogenous)
P-Value = 6.69843E-19 → Since Studies fail Test for Homogeneity, Random Effects Meta-Analysis Yields Summary RR = 1.031 (0.997-1.066), which is statistically consistent with 1.000 (NO relationship)

The original Zeger 2008 analysis of the Medicare cohort (MCAPS) was included in this meta-analysis rather than the Di 2017 analysis, because of the serious concerns about Di 2017 that I stated in my October 12, 2017 *NEJM* letter. Dominici, the key author on both studies, does not explain how the overall RR increased from 1.044 in the Zeger 2008 analysis to 1.073 in the Di 2017 analysis. Di 2017 does not even cite Zeger 2008. If the Medicare cohort is removed from the meta-analysis because it does not properly control for confounders, II Table B4 shows that the Summary RR = 1.014 (0.973-1.057), which is also NO relationship.

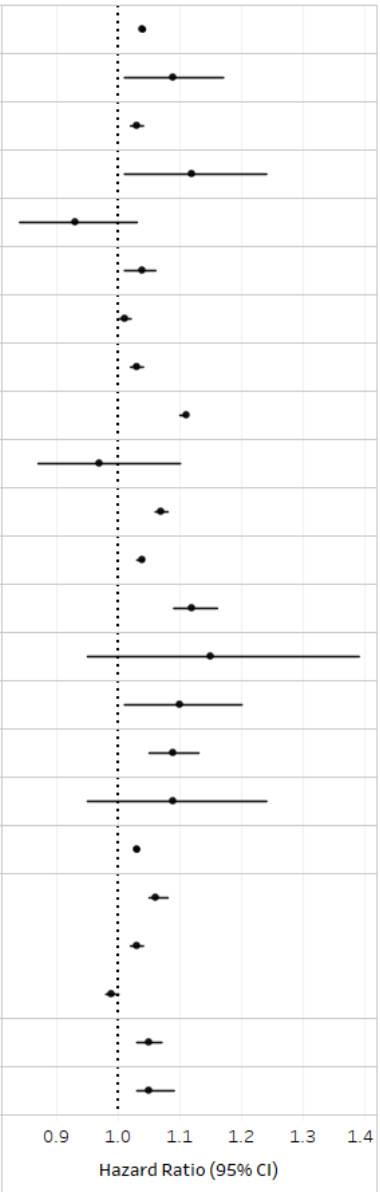
Contrary to the evidence in the detailed II Table B3, the 2019 PM PA Figure 3-3 misrepresents the US evidence and inappropriately includes Canadian evidence. For instance, Figure 3-3 omits the null findings in the original Veterans Study (Lipfert 2000), as shown in II Table B3. In addition, Figure 3-3 includes results from the CPS II cohort twice (Pope 2015 and Turner 2016) and does not mention that my reanalysis found serious flaws in Pope 1995, HEI 2000, and HEI 2009. These flaws raise doubts about the validity of subsequent 'secret science' CPS II analyses by Pope and Turner. Figure 3-3 includes results from the Medicare cohort five times (Di 2017, Shi 2016, Wang 2017, Kiomourtzoglou 2016, Zeger 2008). There is no mention that the original Medicare study (Zeger 2008) is not consistent with the recent study (Di 2017). Figure 3-3 includes results from the Nurses Health Study twice (Puett 2009 and Hart 2015) and there is no mention that Puett 2009 and Puett 2011 omitted California subjects, who most likely had null findings. Inclusion of multiple hazard ratio (RR) results from the same cohort is inappropriate and gives the misleading impression that the RRs in most of the US cohorts are positive.

Inclusion in Figure 3-3 of results from Canadian studies is totally inappropriate because these positive Canadian RRs are not relevant to PM2.5 findings and policy assessment in the US. To show how the 2019 PM PA presented these results, Figure 3-3 on page 3-54 of the 2019 PM PA is reproduced below.

2019 PM PA Figure 3-3. Epidemiologic studies examining associations between long-term PM2.5 exposures and [all-cause] mortality.

All-cause mortality

Exposure Proxy	Country	Citation	Cohort	Health Data	Air Quality Data	Reported PM Mean (Range)(ug/m3)
Modelled	U.S.	Di et al., 2017b	Medicare	2000-2012	2000-2012	11 (5th and 95th: 6.21- 15.64)
		Hart et al., 2015	Nurses Health	2000-2006	1999-2006	12.0 (NR)
		Pope et al., 2015	ACS CPS-II	1982-2004	1999-2004	12.6 (1.0–28.0)
		Puett et al., 2009	Nurses Health	1992-2002	1988-2002	13.9 (5.8–27.6)
		Puett et al., 2011	Health Pro fessionals	1989-2003	1988-2003	17.8 (NR)
		Shi et al., 2016	Medicare	2003-2008	2003-2008	8.12 (0.8-20.22)
		Thurston et al., 2016	NIH-AARP	2000-2009	2000-2008	12.2 (2.9-28.0)
		Turner et al., 2016	ACS CPS-II	1982-2004	1999-2004	12.6 (1.4-27.9)
		Wang et al., 2017	Medicare	2000-2013	2000-2013	NR (Median: 10.7) (6.0-20.6)
		Weichenthal et al., 2014	Ag Health	1993-2009	2001-2006	Iowa: 8.8; North Carolina: 11.1 (NR)
	Canada	Crouse et al., 2012	CanCHEC	1991-2001	2001-2006	8.7 (1.9- 19.2)
		Crouse et al., 2015	CanCHEC	1991-2006	1984-2006	8.9 (0.9- 17.6)
		Pinault et al., 2016	CCHS	2000-2011	1998-2011	6.3 (1.0-13.0)
Monitor	U.S.	Goss et al., 2004	U.S. Cystic Fibrosis	1999-2000	2000	13.7 (NR)
		Hart et al., 2015	Nurses Health	2000-2006	2000-2006	12.7 (NR)
		Kiomourtzoglou et al., 2016	Medicare	2000-2010	2000-2010	12.0 (Mean Range: 9-13) (NR)
		Lepeule et al., 2012	Harvard Six-City	2001-2009	1979-2009	1974-2009: 15.9; 2000 onwards mean range: <15-<18 (NR)
		Lipfert et al., 2006	Veterans	1997-2001	1999-2001	14.3 (NR)
		Zeger et al., 2008	MCAPS	2000-2005	2000-2005	Central region: NR (Median: 10.7) (NR) Eastern region: NR (Median: 14.0) (NR) Western region: NR (Median: 13.1) (NR)
	Canada	Crouse et al., 2012	CanCHEC	1991-2001	1987-2001	11.2 (NR)
		Weichenthal et al., 2016a	CanCHEC	1991-2009	1998-2009	9.8 (4.74-13.62)



2. 2019 PM PA Cites 'Positive Authors' and Omits 'Null Authors' and Their Criticism

Based on my extensive PM2.5 epidemiologic research and related knowledge since February 2002, I have strong evidence that the 2019 PM PA almost exclusively cites the research of 'positive authors,' investigators who publish positive relationships emphasizing the adverse health effects of PM2.5, and omits the 'null authors,' investigators who publish evidence of no health effects of PM2.5 and criticism of the adverse health effects findings. Prime evidence of this bias is my above critique of Figure 3-3 and the failure of the 2019 PM PA to address the serious issues raised in Cox 2017 and Cox 2019. In addition, the evidence of extreme bias toward 'positive authors' extends to the EPA 452/R-11-003 April 2011 Policy Assessment for the Review of the Particulate Matter National Ambient Air Quality Standards (2011 PM PA) and the annual publication of the American Lung Association "State of the Air" (ALA SOTA) (https://www.lung.org/our-initiatives/healthy-air/sota/). To document the magnitude of this bias, I tabulated the first author names of the publications cited in the 2019 PM PA, the 2011 PM PA, the 2019 ALA SOTA, and the 2011 ALA SOTA.

Table 1 shows the 2019 PM PA citations of 45 'positive authors' separated into: Group 1) 21 authors associated with the Harvard TH Chan School of Public Health (HTHCSPH) and/or other northeastern universities; Group 2) 10 Canadian authors; and Group 3) 14 authors associated with the American Cancer Society or California universities. Group 1 authors are cited 291 times, Group 2 authors are cited 277 times, and Group 3 authors are cited 142 times. This is a grand total of 710 citations of 'positive authors.'

Table 2 shows the 2019 PM PA citations of 50 authors who have published null findings and/or criticisms of the relationship between air pollution (particularly PM2.5) and mortality. These 'null authors' include CASAC members, CASAC consultants, four doctors representing 112 German pulmonary physicians (https://www.dw.com/en/nitrogen-oxide-is-it-really-that-dangerous-lung-doctors-ask/a-47202076), myself, and many other distinguished MDs and PhDs dating back more than 30 years. The 2019 PM PA cited these 50 'null authors' a grand total of 10 times: 9 citations were to Cox 2019 and 1 citation was to Lipfert 2006. There were NO citations to 48 'null authors.'

Table 3 shows that 2019 PM PA cited the 7 CASAC members 9 times and cited the 12 CASAC consultants 8 times. All 9 of the CASAC member citations refer to the April 11, 2019 CASAC Review of the 2018 PM ISA submitted to EPA by Chair Tony Cox (Cox 2019).

In summary, the 2019 PM PA contained 710 'positive author' and 10 'null author' citations. The 2011 PM PA contained 529 'positive author' citations and 8 'null author' citations. The 2019 ALA SOTA contained 217 'positive author' citations and 0 'null author' citations. The 2011 ALA SOTA contained 165 'positive author' citations and 0 'null author' citations. In other words, both the EPA PM PA and the ALA SOTA are extremely biased toward 'positive author' findings and against 'null author' findings. Furthermore, the 2019 PM PA citation results in Table 1 reveal a dramatic increase since the 2011 PM PA in the citation of Group 2 Canadian authors and their Canadian studies. This shift toward Canadian authors and Canadian evidence is totally inappropriate because the 2019 PM PA is supposed to use the particulate matter evidence in the US as the basis for policy assessment in the US!

Table 1. 'Positive Author' Citations in 2011 & 2019 EPA PM Policy Assesment and 2011 & 2019 ALA State of the Air October 17, 2019

'Postive Authors' Who Publish and/or Promote Positive PM2.5 Death Findings				EPA PM PA	EPA PM PA	ALA SOTA	ALA SOTA
First Name	Last Name	Institution (HTHCSPH training shown)	State	2019	2011	2019	2011
Group 1) Harvard TH Chan School of Public Health & Other NE Investigators							
Michelle L	Bell	Yale U (2002 PhD Enviro Eng JHU)	CT	25	39	7	5
Robert D	Brook	University of Michigan	MI	12	0	0	1
Patricia F	Coogan	Boston University	MA	4	0	0	0
Douglas W	Dockery	HTHCSPH (1979 ScD Env Health at HTHCSPH)	MA	7	20	8	8
Francine	Dominici	JHBSPH-->HTHCSPH	MA	27	29	12	6
Jaime E	Hart	HTHCSPH (2008 ScD Env Health at HTHCSPH)	MA	9	0	0	5
Francine	Laden	HTHCSPH (1998 ScD Env Health at HTHCSPH)	MA	14	18	5	6
Joanne	Lepeule	HTHCSPH	MA	14	0	3	0
Morton	Lippmann	NYU	NY	6	2	1	1
Marianthi-Anna	Kioumourtzoglou,	Columbia MSPH (2013 ScD Env Health Sci HTHCSPH)	NY	8	0	1	0
Murray A	Mittleman	HTHCSPH (1994 DrPH HTHCSPH)	MA	4	2	4	5
C Arden	Pope III	BYU (1992-1993 IPH Env Health at HTHCSPH)	UT	20	27	11	13
Robin C	Puett	University of Maryland SPH	MD	12	0	1	1
Zev	Ross	ZevRoss Spacial Analysis	NY	6	0	0	0
Jonathan M	Samet	JHBSPH->USC DPM->CO SPH (1977 MS Epi HTHCSPH)	CO	28	88	9	5
Joel D	Schwartz	US EPA-->HTHCSPH	MA	40	70	37	21
Frank E	Speizer	HTHCSPH	MA	3	3	3	3
Helen H	Suh	HTHCSPH-->Tufts U (1993 ScD Env Health HTHCSPH)	MA	5	3	2	1
George D	Thurston	NYU (1983 ScD Env Health Sci HTHCSPH)	NY	16	9	6	5
Annette	Zanobetti	HTHCSPH	MA	24	51	18	10
Scott L	Zeger	JHBSPH	MD	7	15	4	4
Total Citations				291	376	132	100
Group 2) Canadian Investigators							
Jeffrey R	Brook	University of Toronto DLSPH	CN	13	5	1	1
Richard T	Burnett	Health Canada, Ottawa	CN	38	33	7	5
Daniel L	Crouse	University of New Brunswick, Fredericton	CN	20	0	0	0
Daniel	Krewski	University of Ottawa	CN	19	34	6	4
Randall V	Martin	Dalhousie University, Halifax	CN	33	0	0	0
Lauren	Pinault	Statistics Canada, Ottawa	CN	16	0	0	0
Michelle L	Turner	University of Ottawa	CN	33	1	2	0
Aaron	van Donkelaar	Dalhousie University, Halifax	CN	56	0	0	0
Paul J	Villeneuve	University of Toronto SPH	CN	14	10	2	1
Scott	Weichenthal	Health Canada, Ottawa	CN	35	0	0	0
Total Citations				277	83	18	11
Group 3) American Cancer Society and California Investigators							
W Ryan	Diver	ACS National	GA	13	0	1	0
Susan M	Gapstur	ACS National	GA	14	0	1	0
Michael J	Thun	ACS National (1983 MS Epi HTHCSPH)	GA	4	5	5	4
Edward L	Avol	USC DPM	CA	7	6	7	6
Bernard S	Beckerman	UC Berkeley SPH	CA	10	0	0	0
Kiros T	Berhane	USC DPM	CA	6	5	6	4
W James	Gauderman	USC DPM	CA	9	11	9	6
Frank D	Gilliland	USC DPM	CA	8	5	7	5
Michael	Jerrett	CN-->USC DPM-->UCB SPH-->UCLA SPH	CA	52	5	8	6
Rob S	McConnell	USC DPM	CA	7	9	7	5
John M	Peters	USC DPM	CA	3	11	5	7
Edward B	Rappaport	USC DPM	CA	4	4	3	3
Duncan C	Thomas	USC DPM	CA	1	5	4	4
Hita	Vora	USC DPM	CA	4	4	4	4
Total Citations				142	70	67	54
Grand Total Citations				710	529	217	165

Table 2. 'Null Author' Citations in 2011 & 2019 EPA PM Policy Assesment and 2011 & 2019 ALA State of the Air October 17, 2019

'Null Authors' Who Publish Null AP Findings and/or Criticize Postive AP Findings				EPA PM PA	EPA PM PA	ALA SOTA	ALA SOTA
First Name	Last Name	Institution	State	2019	2011	2019	2011
Published Critics of Air Pollution (including PM2.5) Causing Deaths							
Jerome C	Arnett	Pulmonologist & CEI Retired	WV	0	0	0	0
Daren	Bakst	Heritage Foundation & PM2.5 Working Group	DC	0	0	0	0
Lester	Breslow	CA Dept Public Health & UCLA SPH	CA	0	0	0	0
W Matt	Briggs	wmbriggs.com & Cornell U	NY	0	0	0	0
William B	Bunn	Navistar International & U So Car	SC	0	0	0	0
Edward J	Calabrese	U Massachuetts Amherst	MA	0	0	0	0
Alan	Carlin	EPA Retired	VA	0	0	0	0
L Anthony	Cox	Cox Associates & U Colorado Denver	CO	9	0	0	0
John D	Dunn	Darnall Army Medical Center	TX	0	0	0	0
Myron	Ebell	Competitive Enterprise Institute	DC	0	0	0	0
James E	Enstrom	UCLA Retired & Scientific Integrity Institute	CA	0	0	0	0
Gordon J	Fulks	Gordon Fulks and Associates & CO2 Coalition	OR	0	0	0	0
Michael	Fumento	AEI & Hudson & 'Polluted Science' Author	DC	0	0	0	0
John F	Gamble	Exxon Retired	NJ	0	0	0	0
Lawrence	Garfinkel	ACS National	NY	0	0	0	0
Julie E	Goodman	Gradient	MA	0	0	0	0
E Cuyler	Hammond	ACS National	NY	0	0	0	0
Martin	Hetzel	Represents 112 German Lung Specialists	GER	0	0	0	0
Thomas W	Hesterberg	Navistar International & CTEH	IL	0	0	0	0
Jon M	Heuss	Air Improvement Resource	MI	0	0	0	0
John L	Hoare	AIR, Inc	NZ	0	0	0	0
Walter W	Holland	St Thomas's Hospital Medical School, London	UK	0	0	0	0
Michael	Hunnicutt	Texas Commission on Environmental Quality	TX	0	0	0	0
Geoffrey C	Kabat	Einstein CoM Retired & geoffreykabat.com	NY	0	0	0	0
Matthias	Klingner	Represents 112 German Lung Specialists	GER	0	0	0	0
Thomas	Koch	Represents 112 German Lung Specialists	GER	0	0	0	0
Dieter	Köhler	Represents 112 German Lung Specialists--Leader	GER	0	0	0	0
Gary	Koop	U Leicester	UK	0	0	0	0
Goran	Krstic	Fraser Health	CN	0	0	0	0
Sabine S	Lange	Texas Commission on Environmental Quality	TX	0	0	0	0
Marlo	Lewis	Competitive Enterprise Institute	DC	0	0	0	0
Frederick W	Lipfert	Brookhaven Nat Lab Retired & Consultant	NY	1	8	0	0
Joseph L	Lyon	U Utah	UT	0	0	0	0
Roger O	McClellan	Toxicology Expert & Consultant	NM	0	0	0	0
Henry I	Miller	Hoover Institution & Pacific Research Inst	CA	0	0	0	0
Steven J	Milloy	JunkScience.com & 'Scare Pollution' Author	MD	0	0	0	0
A Alan	Moghissi	George Mason U & Institute Reg Sci	VA	0	0	0	0
Suresh	Moolgavkar	U Washington & Exponent	WA	0	0	0	0
Daniel L	Nebert	U Cinncinati Retired	OH	0	0	0	0
Mikko	Paunio	U Helsinki	FIN	0	0	0	0
Douglas A	Popken	Cox Associates & U Colorado Denver	CO	0	0	0	0
Robert F	Phalen	UC Irvine	CA	0	0	0	0
Anne E	Smith	National Economic Research Associates	DC	0	0	0	0
Richard L	Smith	U North Carolina	NC	0	0	0	0
Anthony V	Swan	Public Health Laboratory, London	UK	0	0	0	0
Lise	Tole	U Leicester	UK	0	0	0	0
Robert E	Waller	Department of Health, London	UK	0	0	0	0
George T	Wolff	Air Improvement Resource	MI	0	0	0	0
Ronald E	Wyzga	Electric Power Research Institute	CA	0	0	0	0
S Stanley	Young	NISS Retired & CGStat	NC	0	0	0	0
Grand Total Citations				10	8	0	0

Table 3. CASAC Member & Consultant Citations in 2011 & 2019 EPA PM Policy Assesment and 2011 & 2019 ALA State of the Air October 17, 2019

EPA CASAC Members and EPA CASAC Consultants Cited					**EPA PM PA**	**EPA PM PA**	**ALA SOTA**	**ALA SOTA**
First Name	Last Name		Institution	State	2019	2011	2019	2011
EPA CASAC Members 2019								
L Anthony	Cox	Chair	Cox Associates & U Colorado Denver *	CO	9	0	0	0
James	Boylan		Georgia Department of Natural Resources	GA	0	0	0	0
Mark W	Frampton		U Rochester Medical Center	NY	0	0	0	0
Ronald J	Kendall		Texas Tech University	TX	0	0	0	0
Sabine	Lange		Texas Commission on Environmental Quality	TX	0	0	0	0
Corey M	Masuca		Jefferson County Department of Health	AL	0	0	0	0
Steven C	Packham		Utah Department of Environmental Quality	UT	0	0	0	0
Total Citations					9	0	0	0

* All 9 citations refer to April 11, 2019 CASAC Review of the 2018 PM ISA submitted to EPA by Chair Tony Cox (Cox 2019)

EPA CASAC Consultants for PM Policy Assessment October 2019							
Constantin	Aliferis	U Minnesota	MN	0	0	0	0
Brent	Auverman	Texas A&M U	TX	0	0	0	0
Dan A	Jaffe	U Washington-Bothell	WA	6	1	0	0
John J	Jansen	Southern Company Services, Inc.	AL	0	0	0	0
Kristen	Johnson	Washington State U	WA	0	0	0	0
Frederick W	Lipfert	Brookhaven Lab & Enviro Consultant	NY	1	8	0	0
Joseph L	Lyon	U Utah	UT	0	0	0	0
D Warner	North	NorthWorks & Stanford U	CA	0	0	0	0
David D	Parrish	NOAA & Consultant	CO	0	0	0	0
Lorenz	Rhomberg	Gradient	MA	0	0	0	0
Sonja	Sax	Ramboll	MA	0	0	0	0
Duncan C	Thomas	U Southern California	CA	1	5	4	4
Total Citations				8	14	4	4

3. 2019 PM PA Authors Must Acknowledge and Address the PM2.5 Deaths Controversy

A very troubling aspect of the 2019 PM PA is the fact that the EPA Office of Air Quality Planning and Standards (OAQPS) authors refuse to acknowledge or address the intense scientific controversy that surrounded the establishment of the 1997 PM2.5 NAAQS and that continues unabated to this day. Since the specific authorship of the 2019 PM PA is not stated anywhere in the 457-page document, I requested the authorship information from the listed contact person, Dr. Scott Jenkins. Since he did not rapidly respond to my request, I looked up the 2011 PM PA ACKNOWLEDGMENTS, which state in part "This Policy Assessment is the product of the Office of Air Quality Planning and Standards (OAQPS). It has been developed as part of the Environmental Protection Agency's (EPA) ongoing review of the national ambient air quality standards (NAAQS) for particulate matter (PM). The PM NAAQS review team has been led by Ms. Beth Hassett-Sipple. Dr. Karen Martin has managed the project. For the chapter on health effects associated with fine particle exposures and the primary PM2.5 standards, the principal authors include Ms. Beth Hassett-Sipple, Dr. Pradeep Rajan, and Dr. Zach Pekar. . . ."

Then I asked Dr. Zackary Pekar to provide me with the overall authorship information and state his specific role in writing 2019 PM PA Chapter 3 REVIEW OF THE PRIMARY STANDARDS FOR PM2.5. Since Dr. Pekar has not responded to me, I assume that he played a major role in writing Chapter 3, as he did in the 2011 PM PA "chapter on health effects associated with fine particle exposures and the primary PM2.5 standards." It is important for CASAC members to know that Dr. Pekar was a lead EPA representative at the February 26, 2010 CARB Symposium "Estimating Premature Deaths from Long-term Exposure to PM2.5." During 2008 and 2009 I was instrumental in providing the scientific impetus for this CARB Symposium, which is still fully documented on the CARB website. The CARB Symposium weblink includes the Agenda, the Panel, the individual PowerPoint presentations, the entire nine-hour webcast, the entire transcript, and an August 31, 2010 HEI follow-up analysis of the California ACS CPS II cohort data. The supporters of CARB position on PM2.5 premature deaths were Drs. Michael Jerrett, Daniel Krewski, Michael Lipsett, Melanie Marty, Suzanne Paulson, Arden Pope, Jonathan Samet, and George Thurston, as well as Zachary Pekar and Mary Ross of US EPA, and Daniel S. Greenbaum and Aaron Cohen of the Health Effects Institute (HEI). The critics of the CARB position were Drs. Thomas Hesterberg, Frederick Lipfert, Roger McClellan, Suresh Moolgavkar, Robert Phalen, and me.

Thus, Dr. Pekar was a first-hand witness to the intense ongoing PM2.5 deaths controversy almost ten years ago and since then he has been a primary author of PM2.5 health effects for the 2011 PM PA and the 2019 PM PA. Both of these policy assessments seriously misrepresent the research record and grossly exaggerate the adverse health effects of PM2.5 in the US. The misrepresentation is worse now because the 2019 PM PA does not even acknowledge the existence of or the importance of the proposed April 30, 2018 EPA Transparency Rule "Strengthening Transparency in Regulatory Science." Dr. Pekar and the other PM PA authors uncritically accept the validity of the 'positive author' findings and ignore the 'null author' findings. They do not demonstrate understanding of the scientific method and the importance of transparency and reproducibility in scientific assessment of PM2.5 health effects. The CASAC members and the CASAC consultants must assess whether the evidence I have presented above represents falsification by OAQPS of the research record on PM2.5 deaths in the US.

4. Enstrom Analyses of Data for Four Key US Cohorts Support the Need for EPA Transparency Rule

I provide strong support for use of the EPA Transparency Rule in finalizing the 2019 PM PA. I summarize below the four major cohorts for which I possess underlying data that is relevant to the PM2.5 NAAQS and the current Policy Assessment. The data that I possess has been kept strictly confidential and the identity of all subjects has been protected. My analyses of all four cohorts show NO relationship between PM2.5 and total mortality. NONE of the findings that I have published on three of these cohorts is cited in the 2019 PM PA.

A. 118,000 California Subjects in 1959 ACS CPS I (CA CPS I) Cohort with 1960-2002 Deaths

Since 1991 I have possessed the fully identified data for the 118,000 California subjects in the 1959 ACS Cancer Prevention Study (CA CPS I) cohort. With ACS approval, I have actively and passively followed these subjects from 1960 to 2002. My December 15, 2005 *Inhalation Toxicology* article "Fine particulate air pollution and total mortality among elderly Californians, 1973-2002" found NO relationship between PM2.5 and total mortality in the CA CPS I cohort from 1973 to 2002. A February 18, 2004 unpublished analysis "Particulate Air Pollution and Mortality in 118,000 Californians, 1960-98" by Dr. Frederick Lipfert and me found NO relationship between PM2.5 and total mortality in the CA CPS I cohort from 1960 to 1998. For instance, Table 3 shows the 10 variable-adjusted RR (95% CI) = 0.985 (0.962-1.009) among 85,978 CA CPS I subjects classified by 1979-1983 IPN PM2.5 level and followed for 1960-1972 mortality. The value shown refers to the relative risk (RR and 95% CI) of total mortality associated with an increase of 10 $\mu g/m^3$ in PM2.5. Table 6 shows the 10 variable-adjusted RR (95% CI) = 0.989 (0.946-1.034) among 105,724 CA CPS I subjects classified by 1961 self-described 'heavy air pollution' exposure (yes versus no) and followed for 1962-1972 mortality.

These null mortality findings in CA CPS I are consistent with the null 1960-1965 lung cancer mortality findings in the March 1980 *Preventive Medicine* article "General Air Pollution and Cancer in the United States" by Dr. E. Cuyler Hammond and Lawrence Garfinkel. Comparing subjects by level of total suspended particulates (TSP) among those not occupationally exposed: 8 cities with High TSP 130-180 $\mu g/m^3$ versus 14 cities with low TSP 35-99 $\mu g/m^3$ found RR ~ 0.89/1.10 = 0.81 for lung cancer deaths during 1960-1965. Also, the observed lung cancer deaths were not increased in the high pollution California counties of Los Angeles, Orange, and Riverside. Since high air pollution levels during the 1960s were not related to mortality, it is implausible that the current low levels of air pollution are related to mortality.

B. 1,200,000 US subjects in 1982 ACS CPS II Cohort with 1982-1988 Deaths

Since 2016 I have possessed the original de-identified version of the underlying data for the 1,200,000 US subjects in the 1982 ACS Cancer Prevention Study (CPS II) cohort, which ACS followed for mortality from 1982 to 1988. The positive relationship between PM2.5 and total mortality in the CPS II cohort (Pope 1995) provided the primary epidemiologic evidence that was used to establish the 1997 PM2.5 NAAQS. My reanalysis presented in Enstrom 2017 and Enstrom 2018 provides unrefuted evidence that the positive relationship in Pope 1995 is not robust. Specifically, Table 3 of Enstrom 2018 shows substantial variation in the 1982-1988 relative risk (RR and 95% CI) of total mortality associated with PM2.5 defined in two different ways. For CPS II subjects residing in 47 US counties, RR = 1.081 (1.036-1.128) based on the 1979-1983 HEI PM2.5 values used in Pope 1995, but RR = 1.021 (0.984-1.058) based on the 1979-1983 IPN PM2.5 values used in Enstrom 2017 and Enstrom 2018. My reanalysis challenges the validity of the PM2.5 NAAQS and demonstrates the urgent need for the EPA Transparency Rule.

C. 160,000 California Subjects in 1995 NIH-AARP Diet and Health Study Cohort with 2000-2009 Deaths

Since 2012 I have possessed the de-identified public use file for the 160,000 California subjects in the NIH-AARP Diet and Health Study cohort, including 1995-2010 total mortality follow-up data. In 2011 I applied for full NIH-AARP database, but I was only able to obtain the California subjects because Dr. George Thurston applied for and received the full database in 2009. Dr. Thurston demonstrates the variation in PM2.5 mortality risk based on his own analyses of this cohort. His August 7-11, 2011 IEA World Congress of Epidemiology Abstract P1-355 LONG-TERM PM2.5 AIR POLLUTION EXPOSURE AND MORTALITY AMONG CALIFORNIA RESIDENTS IN THE NIH-AARP COHORT shows a strongly positive RR = 1.09 (1.05-1.12) for total mortality in California. However, his 2016 EHP article shows the null RR = 1.02 (0.99-1.04) in Table 3 and the null RR = 1.017 (0.990-1.040) in Figure 3. The null 2016 RRs are in good agreement with my null RR = 1.001 (0.949-1.055) for total mortality in California, as shown in Enstrom 2017 Table B1. The NIH-AARP Diet and Health Study is a great example of how to facilitate independent analysis of epidemiologic cohort data without violating subject confidentiality. This is further evidence in support of the EPA Transparency Rule.

D. 8,096 Subjects in the Harvard Six Cities Study with 1989-2009 Deaths

Following the August 1, 2013 House Science Committee Subpoena, I received a fully de-identified version of the 1974 Harvard Six Cities Study (H6CS) cohort data for the subpoenaed July 2012 EHP article by Lepeule, Laden, Dockery, and Schwartz (Lepeule 2012). This is a SAS data file in the Anderson-Gill format named "**Lepeule2012_data_0713.sas7bdat**." Six key variables for ten sample records are:

cityc	rstrata	ptime	ypm2_5 y	pm2_5b	deadt
The first five records are:					
STL	4	1	25.2	25.2	0
STU	4	1	39.5	39.5	0
STL	17	1	25.2	25.2	0
STU	17	1	39.5	39.5	0
STL	20	1	25.2	25.2	0
Last five records are:					
TOP	25615	1	9.8	12.3	0
TOP	25620	0.058864	11.2	11.7	1
TOP	25620	1	11.2	11.7	0
TOP	25632	1	10	11.6	0
TOP	25643	0.640657	8.7	12.1	0

The October 11, 2013 Enstrom Tang Analysis of **Lepeule2012_data_0713.sas7bdat** was able to exactly reproduce several tables in Lepeule 2012. However, since 1974-1988 death information was omitted from the SAS file, the tables involving deaths could not be fully reproduced. Also, it was not possible to reproduce the findings in the seminal article Dockery 1993. In any case, this de-identified data demonstrates that NO subject confidentiality has been violated, contrary to unjustified claims by opponents of the EPA Transparency Rule. CASAC members should request this H6CS data from the Lepeule 2012 authors and/or EPA in order to confirm the 2013 Enstrom Tang Analysis and to confirm that NO subject confidentiality has been violated in the entire file. This would provide further support for the EPA Transparency Rule. Finally, it is important to realize that the weak relationship between PM2.5 and mortality in the tiny H6CS cohort does not justify the PM2.5 NAAQS. Indeed, Laden 2006 Table 2 and Lepeule 2012 Table 2 show NO relationship between PM2.5 and total deaths since 1990.

5. 2019 PM PA Must be Revised as per CASAC Review and Criticism by Enstrom and Others

In summary, the 2019 PM PA provides no evidence that supports changing the PM2.5 NAAQS. To the contrary, the evidence I have presented in the four sections above support the need to reassess the entire scientific basis for the PM2.5 NAAQS. Since the 2011 PM PA went through three drafts in September 2009, March 2010, and June 2010 before being finalized in April 2011, CASAC should recommend that a similar process be followed for the 2019 PM PA. All criticism of the September 2019 PM PA by the CASAC members and the CASAC consultants, as well as the criticism by me and others, must be addressed in the second draft of the 2019 PM PA.

Despite over 25 years of claims about the adverse health effects of PM2.5, there is still NO established etiologic/biologic mechanism for PM2.5 to cause premature death. The average amount of PM2.5 inhaled by each person in the US is infinitesimal: about 50 micrograms (µg) per day, about 0.02 grams per year, and about 1.5 grams during an 80-year lifespan. All the PM2.5 epidemiologic cohort study results are subject to the ecological fallacy because there are NO direct measurements of actual PM2.5 exposure among the cohort subjects. Also, the cohort study results are subject to uncontrolled confounding variables, such as, co-pollutants. The small positive relative risks ($0<RR\leq1.15$) reported in the US cohort studies do not satisfy the established Hill criteria that are used to establish a causal epidemiologic relationship. Indeed, based on the null evidence I have described above for the CA CPS I, CPS II, NIH AARP, and H6CS cohorts, I believe that all of the results for the US studies, if transparently and objectively analyzed, are consistent with NO relationship between PM2.5 and total mortality. In any case, the objective meta-analysis of the published results for nine major US cohorts in II Table B3 above found a summary RR that is consistent with NO relationship between PM2.5 and total mortality.

To reinforce the above points, please examine three major critiques of the claim that PM2.5 causes premature deaths: the 2016 Steven J. Milloy book "Scare Pollution: Why and How to Fix the EPA," my July 20, 2019 DDP lecture "The PM2.5 Deaths Controversy: Combating Pseudoscientists," and the September 18, 2019 William Matt Briggs video "The Epidemiologist Fallacy Exposed."

The EPA OAQPS authors have a special obligation to increase the transparency, objectivity, and scientific integrity of the 2019 PM PA, especially regarding Chapter 3. They must properly cite the results and criticisms of the 'null authors' and they must not uncritically accept and cite the findings of the 'positive authors.' They must show support for the EPA Transparency Rule by releasing the August 1, 2013 House Science Committee Subpoena H6CS data that they must possess. The CASAC members and CASAC consultants need to examine this H6CS data in order to independently assess the H6CS findings and confirm that this de-identified data does not violate subject confidentiality. If the EPA OAQPS authors will not release this H6CS data, I will release the H6CS data that I possess to the CASAC members. Also, the EPA OAQPS must encourage the ACS investigators to release a de-identified version of the CPS II data that has been used as the basis for the CPS II findings cited in the 2019 PM PA. If the ACS investigators continue to refuse to release this data, then I will work with the CASAC members in a full analysis of the original CPS II data that I used in Enstrom 2017 and Enstrom 2018.

The evidence and criticism above provide a very strong basis for reexamining the entire PM2.5 NAAQS and I strongly encourage the CASAC members and CASAC consultants to undertake this reexamination.

Additional Criticism of EPA-452/P-19-001 September 2019 Policy Assessment for the Review of the National Ambient Air Quality Standards for Particulate Matter, External Review Draft

James E. Enstrom, PhD, MPH, FFACE
UCLA and Scientific Integrity Institute
http://www.scientificintegrityinstitute.org/
http://scientificintegrityinstitute.org/biography.html
jenstrom@ucla.edu

December 11, 2019

This Comment adds additional criticism of the 2018 Draft EPA PM ISA (PM ISA) and the 2019 Draft EPA PM PA (PM PA) to the criticism contained in my detailed October 17, 2019 Comment (https://yosemite.epa.gov/sab/sabproduct.nsf/F729E7D8E248A2C5852584970009565A/$File/Enstrom+Comment+to+CASAC+re+090519+EPA+PM+PA+101719.pdf) or (http://scientificintegrityinstitute.org/JEEPMPA102219.pdf). My October 17 Comment presented strong evidence that 1) there is NO causal relationship between PM2.5 and total mortality in the US, 2) the PM PA cites 'positive authors' and omits 'null authors' and their criticism, 3) the PM PA does not address the PM2.5 deaths controversy, 4) my analyses of underlying data for four key US cohorts, including H6CS and ACS CPS II, support the need for the proposed EPA Transparency Rule, and 5) the PM PA must be revised to incorporate the CASAC Review and the criticisms by me and others.

My criticism of the PM PA is now supported by the 297-page November 13, 2019 Draft CASAC Review of the PM PA, which contains this summary statement: "Overall, the CASAC finds that the Draft PM PA depends on a Draft Particulate Matter (PM) Integrated Science Assessment (ISA) that, as noted in the April 11, 2019, CASAC Report on the Draft PM ISA, does not provide a sufficiently comprehensive, systematic assessment of the available science relevant to understanding the health impacts of exposure to PM, due largely to lack of a comprehensive, systematic review of relevant scientific literature; inadequate evidence and rationale for altered causal determinations; and a need for clearer discussion of causality and causal biological mechanisms and pathways. Given these limitations in the underlying science basis for policy recommendations, and diverse opinions about what quantitative uncertainty analysis and further analysis of all relevant data using the best available scientific methods would show, most CASAC members conclude that the Draft PM PA does not establish that new scientific evidence and data reasonably call into question the public health protection afforded by the current 2012 $PM_{2.5}$ annual standard." (https://yosemite.epa.gov/sab/sabproduct.nsf/ea5d9a9b55cc319285256cbd005a472e/0a46bdbe59c86531852584b10077b0f6!OpenDocument) or (https://junkscience.com/2019/11/winning-epa-science-advisers-reject-epa-staff-particulate-matter-claims/).

On November 18, 2019 I sent an email message to those October 22, 2019 public speakers who have criticized and/or do not support the 2019 EPA CASAC Reviews of the PM ISA and PM PA. I asked these speakers to send me their assessment of my criticism of the PM ISA and PM PA or indicate a willingness

to discuss my criticism (http://www.scientificintegrityinstitute.org/CASACCritics111819.pdf). Not one of the speakers who received my message has responded to my offer. This nonresponse indicates that it is virtually impossible to have a dialog with PM2.5 investigators who do not agree with me scientifically. No one wants to discuss any of the issues in my October 17 Comment, particularly the fact that my independent reanalysis of CPS II data has revealed severe flaws in the primary study underlying the PM2.5 NAAQS. Five individuals and two organizations who received my November 18 email message made comments to EPA CASAC on December 3 and none of them addressed the points in my October 17 Comment.

Therefore I am so appreciative of the excellent work of the current CASAC, which has produced a Draft Review that identifies serious flaws in the PM ISA and PM PA, consistent with the findings in my October 17 Comment. Rather than specific comments about the details the CASAC Draft Review, I describe three clear examples of serious corruption in the assessment of PM2.5 health effects that are not known to CASAC and that are highly relevant to the PM2.5 NAAQS. These examples illustrate the five types of bias that have led to exaggerated PM2.5 health effects: investigator bias, journal editor bias, journal reviewer bias, EPA funding bias, and EPA assessment staff bias. Given these serious biases and flaws, an entire reassessment of the PM2.5 NAAQS is justified.

1) 2018 Draft EPA PM ISA and 2019 Draft EPA PM PA Violate EPA Principles of Scientific Integrity

On June 12, 2019 I submitted a formal complaint to EPA Scientific Integrity Official (SIO) Francesca T. Grifo, PhD, against Assessment Lead Jason D. Sacks, MPH, regarding the 2018 Draft EPA PM ISA (http://www.scientificintegrityinstitute.org/SOIGrifo061219.pdf). I presented strong evidence that Mr. Sacks violated the basic rule for ethical behavior by EPA employees regarding "Interpreting and presenting results" as defined in the EPA Principles of Scientific Integrity. I stated that three sentences in Section 11.2.7 'Summary and Causality Determination' are utterly false regarding US evidence: 'Recent extended analyses and reanalysis of these cohorts continues to support this relationship, demonstrating consistent positive associations for total (nonaccidental mortality),' 'Overall, recent epidemiologic studies build upon and further reaffirm the conclusions of the 2009 PM ISA for total mortality,' and 'Collectively, this body of evidence is sufficient to conclude that a causal relationship exists between long-term PM2.5 exposure and total mortality.'

In his September 4, 2019 response to my June 12, 2019 complaint, Deputy SIO Vincent Congliano, PhD, did not address my specific evidence that Mr. Sacks violated the basic rule for ethical behavior by EPA employees regarding "Interpreting and presenting results." Instead he stated "peer review by a federal advisory committee with the accompanying public comment satisfies the requirements of EPA's Scientific Integrity Policy" (http://www.scientificintegrityinstitute.org/SOIGrifo090419.pdf). His response indicates that the EPA SIO does not require that EPA staff, specifically Assessment Lead Sacks, prepare "a comprehensive, systematic review of relevant scientific literature" in the PM ISA and the PM PA. Instead, the EPA SIO expects "peer review by a federal advisory committee [CASAC] with the accompanying public comment [like mine]" to force EPA staff to hopefully produce "a comprehensive, systematic review of relevant scientific literature." In my opinion, current key EPA senior staff like Mr. Sacks have indeed violated the EPA Principles of Scientific Integrity regarding "Interpreting and presenting results" and should no longer be involved in preparing the PM ISA and the PM PA.

2) Deliberate Falsification of Research Record re Enstrom Reanalysis of ACS CPS II Cohort Data

Since 2016 I have possessed the original de-identified version of the underlying data for the 1,200,000 US subjects in the 1982 ACS Cancer Prevention Study (CPS II) cohort, which ACS followed for mortality from 1982 to 1988. The positive relationship between PM2.5 and total mortality in the CPS II cohort (Pope 1995) provided the primary epidemiologic evidence that was used to establish the 1997 PM2.5 NAAQS. The reanalysis presented in Enstrom 2017 (https://doi.org/10.1177/1559325817693345) and Enstrom 2018 (https://doi.org/10.1177/1559325818769728) provides unrefuted evidence that the positive relationship in Pope 1995 is not robust. Specifically, Table 3 of Enstrom 2018 shows substantial variation in the 1982-1988 relative risk (RR and 95% CI) of total mortality associated with PM2.5 defined in two different ways. For CPS II subjects residing in 47 US counties, RR = 1.081 (1.036-1.128) based on the 1979-1983 HEI PM2.5 values used in Pope 1995, but RR = 1.021 (0.984-1.058) based on the 1979-1983 IPN PM2.5 values used in Enstrom 2017 and Enstrom 2018. My reanalysis challenges the validity of the PM2.5 NAAQS and demonstrates the urgent need for the proposed EPA Transparency Rule.

Instead of acknowledging my reanalysis, the Pope 1995 authors and other PM2.5 investigators have simply refused to cite it and are now falsifying the research record regarding the 25-year PM2.5 deaths controversy. ACS Officials Gapstur and Brawley still have not acknowledged that I possess the CPS II data and they have refused to respond to my 2019 emails. In 2017 they implied that Enstrom 2017 was not based on CPS II data, but Enstrom 2018 proves conclusively that Enstrom 2017 is based on CPS II data. Pope has published three recent articles on the relationship between PM2.5 and total mortality using US National Health Interview Survey cohort data: April 1, 2018 *Air Quality, Atmosphere & Health* article (https://doi.org/10.1007/s11869-017-0535-3), July 24, 2019 *EHP* article (https://doi.org/10.1289/EHP4438), and November 21, 2019 *Environmental Health* article (https://doi.org/10.1186/s12940-019-0544-9). All three articles omit reference to Pope 1995, HEI 2000, HEI 2009, Enstrom 2017, and Enstrom 2018, thereby falsifying the research record regarding my peer reviewed evidence challenging the validity of Pope 1995 and related PM2.5 death claims.

The May 3, 2018 *PLoS Medicine* Editorial by Ioannidis "All science should inform policy and regulation" (https://doi.org/10.1371/journal.pmed.1002576) praises HEI 2000 with regard to Pope 1995: "importantly, detailed re-analysis of results and assessment of their robustness by entirely independent investigators." Although Enstrom 2017 found that the Pope 1995 results were not robust, Ioannidis omitted reference to Enstrom 2017. The August 20, 2019 *PLoS Biology* Primer by Ioannidis "Air pollution as cause of mental disease: Appraisal of the evidence" (https://doi.org/10.1371/journal.pbio.3000370) omitted reference to Enstrom 2017 and Enstrom 2018 and stated regarding the Pope 1995 findings that the HEI 2000 "reanalyses reached mostly similar conclusions, although there are still some dissenters."

The December 1, 2019 *AnnalsATS* Focused Review by Schraufnagel and Balmes "Health Benefits of Air Pollution Reduction" (https://doi.org/10.1513/AnnalsATS.201907-538CME) claims that total mortality can be reduced by reduction of PM2.5 but does not acknowledge the 2018 Intrepid Insight evidence in my October 17 Comment that there is NO *causal* relationship between PM2.5 and total mortality in nine US cohort studies. This review also omits reference to Enstrom 2017 and Enstrom 2018. Enstrom 2018 contains Figure 3 based on Jerrett 2007 (http://scientificintegrityinstitute.org/jerrett051707.pdf), which shows no reduction in PM2.5-related mortality relative risk from 1982 to 2000 in the CPS II cohort.

3) *Science* and AAAS Continue to Aggressively Oppose the Proposed EPA Transparency Rule

On November 26, 2019, Herbert Holden Thorp, Editor-in-Chief of the *Science* family of journals (https://www.sciencemag.org/news/2019/08/aaas-names-chemist-holden-thorp-editor-chief-science), along with the editors of *Nature, PLoS, PNAS, Cell Press*, and *Lancet*, issued a "Joint statement on EPA proposed rule and public availability of data (2019)," which was published as a Letter in December 6, 2019 *Science* (https://doi.org/10.1126/science.aba3197). Also, *Science* published a December 6 news item about this letter (https://www.sciencemag.org/news/2019/11/major-journal-editors-blast-epa-s-secret-science-rule-again). Two key sentences in the letter are "As leaders of peer-reviewed journals, we support open sharing of research data, but we also recognize the validity of scientific studies that, for confidentiality reasons, cannot indiscriminately share absolutely all data" and "We are also concerned about how the agency plans to consider options related to existing regulations." These sentences are very deceptive because the proposed EPA Transparency Rule does not require that investigators whose research is used as the basis for EPA regulations to "indiscriminately share absolutely all data." There just needs to be enough access to underlying data to independently assess the validity of implausible and widely disputed environmental claims, such as, the claim that PM2.5 causes premature deaths. Absolute confidentiality can be maintained if the investigators involved in the data sharing are ethical and the data involved are de-identified to the degree necessary to protect subject confidentiality.

In addition, on December 6, 2019, Marie Lynn Miranda, Professor of Statistics and Immediate Past Provost of Rice University, authored a lead *Science* Editorial "Getting the EPA back on track" (https://doi.org/10.1126/science.aba3769). This editorial contains inaccurate statements like "The EPA's proposed transparency rule does not ensure research rigor or improve transparency" and "Work by the Health Effects Institute, in which an industry-government–funded partnership reanalyzed data from the Harvard Six Cities Study and the American Cancer Society Study on the link between particulate matter pollution and mortality, represents an excellent model for evaluating the validity of research pivotal to environmental health regulations without compromising confidentiality or excluding studies." My independent reanalysis of ACS CPS II data, as described in Enstrom 2017 and Enstrom 2018, clearly demonstrates that data access does improve research rigor and transparency. Furthermore, my reanalysis reveals serious flaws in HEI 2000, the HEI Reanalysis of Pope 1995, and challenges the validity of the PM2.5 NAAQS. Either Miranda was and is not aware of my reanalysis or she deliberately ignored it. In any case, I have strong evidence supporting the value of the proposed EPA Transparency Rule. I have submitted a Letter to *Science* that addresses the inaccuracies in the Joint Statement and the Miranda Editorial (http://scientificintegrityinstitute.org/Science121119.pdf).

A major problem is the fact that *Science* and the other cited journals do not publish null findings that challenge the validity of existing EPA NAAQS and EPA regulations. For example, my 2017 reanalysis of the ACS CPS II data identified major flaws in the seminal Pope 1995 article, which provided the primary evidence used to establish the 1997 EPA PM2.5 NAAQS. The way *Science* dismissed my strong evidence that PM2.5 does not cause premature deaths is consistent with their repeated editorial opposition to data transparency and objective assessment of PM2.5 death claims (http://www.scientificintegrityinstitute.org/CPSIIRej122716.pdf).

On July 5, 2016 I submitted to *Science* for peer review my Manuscript No. aah4744 "Fine Particulate Matter and Mortality in Cancer Prevention Study Reanalysis." The Abstract clearly stated the importance of the data access necessary for my reanalysis: "Background. The EPA National Ambient Air Quality Standard (NAAQS) was established in 1997 for fine particulate matter (PM2.5), largely because

of its positive relationship to mortality in the 1982 American Cancer Society (ACS) Cancer Prevention Study (CPS II) cohort. This implausible and contested relationship has been used to justify many costly EPA regulations, most recently the Clean Power Plan. This paper presents the first truly independent examination of the CPS II data. . . . Conclusions. No significant relationship between PM2.5 and total mortality in the CPS II cohort was found when the best available PM2.5 data was properly included. The 1995 analysis and 2000 reanalysis misrepresented and exaggerated this relationship by selective use of CPS II and PM2.5 data. These findings demonstrate the importance of independent analysis of underlying data and raise serious doubts about the epidemiologic evidence supporting the PM2.5 NAAQS." On July 8, 2016 my manuscript was rejected after initial screening and NO in-depth review. This immediate rejection occurred in spite of the fact that my Reference 2 was the July 25, 1997 "Showdown over clean air science" article in *Science*, which described the PM2.5 deaths controversy. After I appealed the rejection, I was informed on July 11, 2016 that *Science* would not consider ANY resubmission of the manuscript. On July 13, 2016 I submitted to *Science Advances* for peer review the same manuscript, Manuscript No. ScienceAdvances-D-16-01615. On July 30, 2016 the manuscript was rejected after initial screening and NO in-depth review. The manuscript was eventually published on March 28, 2017 in *Dose-Response*, after being rejected by seven major journals. My independent reanalysis was possible because I was able to legally obtain an original version of the 1982-1988 CPS ACS II cohort data and documentation. Although, my reanalysis strongly challenges the validity of Pope 1995 and the epidemiologic justification for the 1997 PM2.5 NAAQS, it has been totally ignored by *Science*.

Science's repeated opposition to PM2.5 data transparency is further reflected in its extensive collaboration with the Union of Concerned Scientists (UCS), which has NO relevant expertise in PM2.5 science. In Summer 2015 nine accomplished scientists, including myself, responded to the May 29, 2015 *Science* Perspective "Congress's attacks on science-based rules" written by nine leaders of UCS and six others. *Science* immediately rejected without peer review three versions of our response to the UCS's misrepresentations regarding the need transparency and reproducibility in order to properly justify EPA regulations. This entire saga is described in the December 15, 2015 National Association of Scholars Blog "Concerns about National Academy of Sciences and Scientific Dissent" by Peter Wood, which describes examples of *Science's* suppression of minority views on the linear no threshold (LNT) hypothesis, man-made global warming (AGW), and PM2.5 deaths by then *Science* Editor-in-Chief Marcia McNutt (https://www.nas.org/blogs/dicta/nas_letter). The bottom line is that *Science* refuses to publish evidence that supports the need for transparency and reproducibility in the research findings used to justify EPA regulations.

4) *BMJ* Rejects Enstrom CPS II Reanalysis and Deletes Enstrom Review of Harvard PM2.5 Paper

On January 25, 2019 I was asked by Dr. Sophie Cook, *BMJ* UK Research Editor, to review Manuscript BMJ-2018-048424 by Yan Wang and Yaguang Wei, et al. "Air pollution and cause specific risks and costs of hospital admissions." In a series of thirteen more emails with Dr. Cook and Dr. Elisabeth Loder, *BMJ* Head of Research, up to April 1, 2019, I made several attempts to upload my nine-page January 24, 2019 Review in both PDF and Word format, but I was unsuccessful. My review recommended "Unequivocal Rejection of this Manuscript" and provided extensive details to back up my recommendation. On April 18, 2019, Dr. Loder made the surprising statement "Recently, I asked you to review Manuscript ID BMJ-2018-048424, entitled "Air pollution and cause-specific risks and costs of hospital admissions." It has since become apparent that I will not need you to review at this time." On May 6, 2019 I replied in part

"I want to make clear that my review is to remain in your review system and is to be used as part of the final decision on this manuscript." (http://scientificintegrityinstitute.org/BMJ050619.pdf). The *BMJ* editors had no further communication with me and I was never able to confirm that my review was actually entered into the *BMJ* Manuscript website." Then on November 27, 2019 the Research Article "Short term exposure to fine particulate matter and hospital admission risks and costs in the Medicare population: time stratified, case crossover study" by Yaguang Wei and Yan Wang, et al. was published as a 13-page *BMJ* Research Paper (*BMJ* 2019;367:l6258 http://dx.doi.org/10.1136/bmj.l6258).

BMJ "Peer Review" (https://www.bmj.com/content/367/bmj.l6258/peer-review) states "For research papers *The BMJ* has fully open peer review. This means that accepted research papers submitted from September 2014 onwards usually have their prepublication history posted alongside them on thebmj.com." The April 18, 2019 "First decision" by Dr. Loder stated "We sent it for external peer review and discussed it at our manuscript committee meeting. We hope very much that you will be willing and able to revise your paper as explained below in the report from the manuscript meeting. We are looking forward to reading the revised version and reaching a final decision." (https://www.bmj.com/sites/default/files/attachments/bmj-article/pre-pub-history/first_decision_18.4.19_1.pdf). This nine-page document includes reviews by Reviewer 1 "Dr Suzanne Bartington, Clinical Research Fellow, University of Birmingham"; Reviewer 2 "Ka Hung Chan, Research Fellow, University of Oxford"; Reviewer 3 "Cesaroni Giulia, Senior Researcher, Epidemiology Dept. of Lazio Regional Health Service, ASL RM1". There is NO mention of my January 24, 2019 Review. The August 26, 2019 "Second Decision" by Dr. Loder cites the above three reviewers, but makes NO mention of me (https://www.bmj.com/sites/default/files/attachments/bmj-article/pre-pub-history/second_decision_26.8.19_0.pdf). This Research Paper was finally accepted for publication on October 16, 2019 based on the reviews of three Europeans. In summary, the research was conducted at the Harvard TH Chan School of Public Health using several US funding sources and the large US Medicare data base and the lead authors are two Chinese doctoral students, Yaguang Wei and Yan Wang.

Compare the *BMJ* editorial treatment of this Harvard publication with the treatment that I received regarding my manuscript on the only independent reanalysis of the ACS CPS II cohort data identifying major flaws in Pope 1995 (http://www.scientificintegrityinstitute.org/CPSIIRej122716.pdf). On August 11, 2016 *BMJ* accepted for review my Manuscript ID BMJ.2016.035002 "Fine Particulate Matter and Mortality in Cancer Prevention Study Cohort Reanalysis." On August 14, 2016 Dr. Elisabeth Loder, *BMJ* Acting Head of Research, emailed me a rejection that read in part "Thank you for sending us your paper. We read it with interest but I am sorry to say that we do not think it is right for the *BMJ*. In comparison with the many other papers we have to consider, this one is a lower priority for us." On August 22, 2016 *BMJ Open* accepted for review my Manuscript ID bmjopen-2016-013986, which was identical to my *BMJ* manuscript. On September 2, 2016 *BMJ Open* Assistant Editor Emma Gray emailed me a rejection that read in part "I am writing to you in regard to manuscript # bmjopen-2016-013986, "Fine Particulate Matter and Mortality in Cancer Prevention Study Cohort Reanalysis", which you submitted to BMJ Open. Your manuscript has been evaluated and has been declined for publication in BMJ Open."

Thus, within less than a month, my manuscript showing no relationship between PM2.5 and total mortality was rejected without peer review by both *BMJ* and *BMJ Open*. However, after receiving my strongly negative January 24, 2019 peer review, *BMJ* spent ten months working with three reviewers with no experience in US PM2.5 epidemiology. On November 27, 2019 *BMJ* published a manuscript showing a positive relationship between PM2.5 and hospital admissions. The published "Peer Review" does not even acknowledge that existence of my review. This *BMJ* review process provides direct recent evidence of strong editorial bias by a major medical journal on highly controversial PM2.5 health effects.

January 24, 2019

Peer Review of Manuscript BMJ-2018-048424 by James E. Enstrom, PhD, MPH, FFACE

"Air pollution and cause-specific risks and costs of hospital admissions"
By Yan Wang, ScD; Yaguang Wei, MS; Qian Di, ScD; Christine Choirat, PhD; Yun Wang, PhD; Petros Koutrakis, PhD; Antonella Zanobetti, PhD; Francesca Dominici, PhD (Dominici); and Joel D. Schwartz, PhD (Schwartz) from Harvard T.H. Chan School of Public Health, Boston, MA, USA with Dominici and Schwartz as Senior Authors

Key Sentences from Abstract and Text:

"**Introduction:** Short-term exposure to particulate matter with an aerodynamic diameter of <2.5 μm (PM2.5) is associated with increased risks of deaths and hospital admissions.[1-8] The World Health Organization (WHO) set the air quality guideline for 24-hour average exposure to PM2.5 at 25 μg·m-3 in 2005.[9] The WHO air quality guidelines are currently being reviewed with the date of expected publication in 2020, and scientific evidence supporting the update of the guidelines is subject to an unprecedented level of scrutiny.[10]"
"**Results:** We discovered statistically significant positive associations between short-term $PM_{2.5}$ and hospitalizations for several prevalent but rarely studied diseases, including septicemia, fluid and electrolyte disorders, and acute and unspecified renal failure. We also found statistically significant positive associations for hospitalizations due to cardiovascular and respiratory diseases, Parkinson's disease, diabetes mellitus with complications, phlebitis, thrombophlebitis, and thromboembolism, confirming previous results."
"**Conclusions:** This study discovered new diseases and confirmed known diseases associated with short-term $PM_{2.5}$ exposure, demonstrating substantial health benefits linked to a small reduction in short-term $PM_{2.5}$."

Peer Review – Justification for Unequivocal Rejection of this Manuscript

• Originality - This work DOES NOT add enough to what is already in the published literature (references 1-8 by these same Senior Authors). This manuscript is latest addition to the massive effort by Schwartz and Dominici to promote the implausible and unproven hypothesis that many human health conditions, including premature death, are *caused* by short-term exposure to trace amounts of particulate matter, particularly fine particulate matter (PM2.5). This effort dates back to at least the 1992 Am J Epi article by Schwartz "Particulate Air Pollution and Daily Mortality in Steubenville, Ohio" (http://www.scientificintegrityinstitute.org/AJESchwartz1992.pdf)."

• Importance of work to general readers – This work is NOT valuable to clinicians, patients, teachers, or policymakers because it is NOT scientifically transparent or valid for many reasons, as explained below. In addition, a general medical journal like BMJ is NOT the right place for a work that uses complex and non-transparent statistical analysis. This work is not written for the benefit of general readers. It is intended to influence the WHO and US EPA PM2.5 assessment and regulations.

• Scientific reliability – This research is not scientifically reliable because it is NOT transparent and NOT verifiable. Indeed, both Schwartz and Dominici co-signed a 60-page August 7, 2018 Harvard University anti-transparency letter by environmental lawyer Wendy B. Jacobs. This letter strongly opposes the currently proposed EPA rule "Strengthening Transparency in Regulatory Science" (http://www.scientificintegrityinstitute.org/HELEPATrans080718.pdf)

• Research Question – The research question is NOT appropriate and is NOT appropriately answered. The four lead Chinese co-authors, Wang, Wei, Di, and Wang, know that air pollution is a serious problem in China but not in the US. I filed a formal January 31, 2018 research misconduct complaint against the Duke/Chinese statistician Junfang Zhang, PhD, who wrote a deliberately incorrect editorial supporting the December 26, 2017 JAMA Di-Dominici-Schwartz study "Association of Short-term Exposure to Air Pollution With Mortality in Older Adults" (http://www.scientificintegrityinstitute.org/Zhang013118.pdf).

Zhang did not acknowledge that the Di-Dominic-Schwartz evidence on PM2.5 premature deaths in the Medicare population (as published in the June 29, 2017 NEJM and December 26, 2017 JAMA articles by Di et al) is severely flawed, as explained by Steve Milloy, JD, in his requests for retraction dated July 5, 2017 to the NEJM Editor (https://junkscience.com/2017/07/retraction-request-made-fornejm-air-pollution-kills-study/) and dated January 4, 2018 to the JAMA Editor (https://junkscience.com/2018/01/junkscience-com-requests-jama-retract-new-harvard-pm2-5study-on-basis-of-scientific-misconduct/). In addition, research misconduct complaints against Di et al have been filed with the US Office of Research Integrity by Mr. Milloy on September 5, 2017 (https://junkscience.com/2017/09/junkscience-requests-federal-research-misconductinvestigation-for-air-pollution-study/) and by John D. Dunn, MD, JD, on January 30, 2018.

• Overall design of study – The overall design of the study is NOT appropriate.

• Participants studied – The participants had 95 million Medicare inpatient hospital claims in the US during 2000–2012. I believe the participants include several of my relatives and friends without their knowledge or consent.

• Methods – The methods are described but it is impossible to use this description to independently replicate these findings. The manuscript contains this statement: "**Ethical approval:** This study was approved by the institutional review board at the Harvard T.H. Chan School of Public Health and was exempt from informed consent requirements as a study of previously collected administrative data."

I content that the study does NOT have "Ethical approval". I believe that the authors have obtained inappropriate access to 95 million Medicare hospitalization records during 2000-2012 for millions of Americans. Based on the authors' description, the records of several of my relatives and friends are presumably included in this study without their knowledge or consent. The persons I know NEVER gave Medicare administrators approval to release their hospitalization records for epidemiological research of the scientifically questionable type done by Dominici and Schwartz.

I plan to submit a complaint to Medicare officials to stop the release of Medicare hospitalization records for epidemiologic research unless specific approval is given by the subjects. My formal complaint will go to US DHHS Centralized Case Management Operations, citing HIPAA regulations (https://www.hhs.gov/hipaa/for-professionals/privacy/laws-regulations/index.html). Steve Milloy, JD, has already filed complaints requesting withdrawal of the 2017 NEJM and JAMA articles by Dominici and Schwartz, as well as complaints to the US DHH Office of Research Integrity, as cited above.

• Results – The results are NOT credible given all the objections described above. In any case, the relationships reported are too weak to qualify as a valid epidemiologic relationships.

• Interpretation and conclusions – The interpretation and conclusions are NOT based on an objective assessment of the data and its severe limitations. Instead, they are biased toward the authors' predetermined conclusion that they are "demonstrating substantial health benefits linked to a small reduction in short-term $PM_{2.5}$."

• References – The authors have selected only those references that support their research findings and there are glaring omissions. Following their prior pattern, Dominici and Schwartz have not addressed or cited the severe criticism of their 2017 NEJM and JAMA publications based on Medicare data. For example, the five omitted references shown below are all relevant to the validity of the findings presented in their current manuscript:
1) October 12, 2017 NEJM letter by this reviewer, James E, Enstrom, PhD, MPH;
2) May 22/29, 2018 JAMA letters by Air Pollution Expert Frederick Lipfert, PhD; EPA CASAC Chair Louis Anthony Cox Jr, PhD; and EPA Science Advisory Board Member S. Stanley Young, PhD;
3) June 1, 2011 JASA article by Sonja Greven, Francesca Dominici, and Scott Zeger, **"An Approach to the Estimation of Chronic Air Pollution Effects Using Spatio-Temporal Information",** with sentence "In either event, observational studies like these are subject to confounding by unmeasured variables.";
4) March 1, 2006 Am J Epi article by Roger D. Peng, Francesca Dominici, and Scott L. Zeger, "**Reproducible Epidemiologic Research",** with sentences "Scientific evidence is strengthened when important findings are replicated by multiple independent investigators using independent data, analytical methods, laboratories, and instruments. Replication, as described here, has long been the standard in the biologic and physical sciences and is of critical importance in epidemiologic studies, particularly when they can impact broad policy or regulatory decisions."
5) April 11, 2015 Lancet Editorial by Richard Horton "**Offline: What is medicine's 5 sigma?",** with sentences "The apparent endemicity of bad research behaviour is alarming. In their quest for telling a compelling story, scientists too often sculpt data to fit their preferred theory of the world."

• Abstract/summary/key messages/What this paper adds – These four items are severely flawed based on the reasons and evidence presented above.