December 10, 2021

To:
EPA CASAC Particulate Matter (PM) Panel
Peer Review of 2021 Draft Supplement to 2019 EPA PM Integrated Science Assessment
and 2021 Draft EPA PM Policy Assessment
U.S. Environmental Protection Agency
https://casac.epa.gov/ords/sab/f?p=105:19:15763176931927:::RP,19:P19_ID:962

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Comments on September 2021 Supplement to December 2019 EPA PM Integrated Science Assessment

The September 2021 EPA PM ISA Supplement must be entirely redone because it deliberately falsifies and exaggerates the adverse health effects of PM2.5 and incorrectly claims that PM2.5 *causes* premature deaths. The ISA focuses almost exclusively on the positive associations between PM2.5 and mortality that have been promoted by the Chinese-funded Harvard TH Chan School of Public Health (Harvard Chan) since the publication of Dockery 1993 and Pope 1995. This deliberate falsification of the research record has been documented by a word search of the ISA which counts the citations of first authors in the text and all authors in the references. Among Harvard Chan and Northeastern investigators, the top 8 (Bell, Dominici, Hart, Laden, Pope, Schwartz, Thurston, Zanobetti) are cited 171 times; 5 Chinese co-authors of Dominici are cited 84 times; 10 Canadian investigators are cited 218 times, although their Canadian evidence is not relevant to US evidence on PM2.5 and mortality; 4 legacy promoters of PM2.5 deaths (Dockery, Samet, Thun, Gapstur) are cited 8 times. Table 1 shows that these 27 (8+5+10+4) key promoters of PM2.5 deaths are cited a total of 481 times. Table 2 shows that all 30 Chinese co-authors of Dominici, including the 5 in Table 1, are cited 236 times. My understanding is that Chinese graduate students are used because they are extremely smart, they work extremely hard, they are eager to come to the US via Harvard Chan, and they prefer to focus on US air pollution rather than Chinese air pollution. Currently, the most aggressive promoters of PM2.5 deaths in the US are Schwartz, Dominici, and Pope. They are being helped by the Chinese, Canadians, and others in Tables 1, 2, and 4.

The falsification of the research record is made clear in Table 3. It shows that the ISA does not cite the published null findings and criticism of 61 investigators, including myself and prior CASAC Chairs Cox, McClellan, and Wolff. Only 4 of the 61 critics are cited at all and these 4 (Lipfert, Smith, Wyzga, Young) are cited just 12 times, with only Young 2017 showing null findings. Although there has been an ongoing 30-year controversy about claims that PM2.5 *causes* deaths based on "secret science" findings that are not transparent and reproducible, a word search reveals that the 303-page ISA does not contain the words controversy, transparency, reproducibility, and integrity. The ISA totally ignores Enstrom 2017, my independent CPS II reanalysis which found major flaws in Pope 1995, the 2000 HEI Reanalysis, and the 2009 HEI Follow-up (doi: 10.1177/1559325817693345a). If the ACS had allowed truly independent access to CPS II data, beyond the access allowed for the flawed 2000 HEI Reanalysis, my reanalysis could have been done during 1995-1997 and the 1997 PM2.5 NAAQS might never have been established.

A specific example of the falsification of the research record by EPA is the 2012 Fann *Risk Analysis* article "Estimating the national public health burden associated with exposure to ambient PM2.5 and ozone" (doi: 10.1111/j.1539-6924.2011.01630.x). This article claimed that 130,000 annual US deaths are *caused* by PM2.5 based on the CPS II results in HEI 2009. Cox disputed this EPA claim in his 2012 *Risk Analysis* letter "Miscommunicating risk, uncertainty, and causation: fine particulate air pollution and mortality risk as an example" (doi: 10.1111/j.1539-6924.2012.01806.x). The validity of the Cox letter is supported by Enstrom 2017, which found no significant relationship between PM2.5 and total mortality in the CPS II cohort. In addition, my detailed June 29, 2020 EPA Comment defending the existing PM2.5 NAAQS included strong evidence that PM2.5 *does not cause* deaths in the US (http://www.scientificintegrityinstitute.org/EPAPM25JEE062920.pdf). Below I have attached the Cox letter and key pages from my EPA Comment.

Most of the recent US evidence on PM2.5 deaths in the PM is based on very complex statistical analyses of the Medicare records of up to 69 million recipients, after indirectly imputing air pollution levels and lifestyle characteristics to recipients defined by their zip code. However, I have been unable to confirm that Dominici, Schwartz, Bell, Zigler, Shi, and others have proper authorization to use Medicare records for methodologically flawed ecological epidemiology. These well-known epidemiologic flaws, which date back to the famous 1988 AJE article "The Ecological Fallacy," are described in my detailed 31-page July 8, 2021 review of a now rejected ES&T manuscript by Shi and Schwartz and others (http://scientificintegrityinstitute.org/ESTJEEAdd070821.pdf).

Keep in mind that 69 million Americans, including myself, have NEVER granted permission for their private Medicare records to be used for ecological research that violates basic epidemiologic principles and produces weak associations that are claimed to be *causal* by activist authors and activist EPA staffers. I believe that this ecological research violates US HHS Human Research Protections 45 CFR 46 (https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html). In order to conduct a legitimate epidemiologic cohort study, each subject must understand the purpose and details of the study and then must give their informed consent to be enrolled in the study. For instance, every subject in the CPS II cohort that I analyzed in Enstrom 2017 was voluntarily enrolled in 1982 using the attached "CPS II Instructions for Researchers" and "CPS II Fact Sheet". I was an ACS Researcher who properly enrolled CPS II subjects as per these two documents.

Furthermore, unless strict confidentiality policies are continuously enforced, I believe that individual Medicare recipients can be identified from the detailed "de-identified" zip-code-level information used by Dominici, et al. Such identification would directly violate Americans' HIPAA privacy rights. Since June 2021, key Medicare investigators have refused to provide me with evidence that they have proper access to Medicare records (http://scientificintegrityinstitute.org/CurranJEE083021.pdf). Thus, I am now attempting to obtain this evidence from the Center for Medicare and Medicaid Services (CMS), specifically the appropriate Medicare Data Use Agreement and details on Medicare security procedures (https://www.hhs.gov/guidance/document/instructions-completing-data-use-agreement-dua-form-cms-r-0235).

In addition to systematic falsification of the published research record, the ISA totally ignores the many unpublished null PM2.5 findings that are posted on the Internet. These null findings have been rejected by the same prominent journals that publish positive PM2.5 findings. For instance, *SCIENCE* rejected without review my proposed March 2020 Policy Forum response to its aggressive and repeated opposition to the EPA Transparency Rule (http://scientificintegrityinstitute.org/EPATransJEE041720.pdf). *JAMA* rejected without review my proposed March 2020 Letter to the Editor pointing out that the February 2020 *JAMA* Fineberg-Allison

Viewpoint opposing the EPA Transparency Rule did not cite Enstrom 2017, which demonstrated the importance of transparency (http://scientificintegrityinstitute.org/EPATransJEE051820.pdf). *NEJM* rejected without review my proposed September 2020 Letter to the Editor countering the August 2020 *NEJM* Sounding Board "The Need for a Tighter Particulate-Matter Air-Quality Standard" by the Independent Particulate Matter Review Panel (IPMRP). *NEJM* rejected my letter in both published format and on-line format (http://scientificintegrityinstitute.org/NEJMJEE091020.pdf). Finally, a prominent epidemiology journal rejected the findings described in EPA SAB Member Richard Smith's November 17 public comment, which showed NO relationship between PM2.5 and total mortality below 12 μg/m³. Smith's important null findings are attached below and posted here (http://rls.sites.oasis.unc.edu/postscript/rs/Smith-Medicare-PM.pdf).

Please note that the 19 IPMRP authors of the *NEJM* Sounding Board include 9 PM Panel Members (CASAC Chair Sheppard, CASAC Member Chow, Adams, Allen, Balmes, Gordon, Kleinman, Sarnat, and Turpin). Thus, even before the 2021 PM ISA Supplement had been prepared, 9 of the 22 PM Panel Members stated that they are unequivocally in favor of tightening the PM2.5 NAAQS of 12 μg/m³. The August 2020 *NEJM* Sounding Board, my proposed *NEJM* letter, and the *NEJM* rejection are attached below. Table 4 provides evidence that all 22 PM Panel Members have a strong bias toward adverse PM2.5 health effects, based on their 348 PM2.5-related publications on PubMed.gov (http://scientificintegrityinstitute.org/PMPanelPubs121021.pdf).

The PM Panel members have rarely, if ever, cited the extensive null evidence of the 61 PM2.5 NAAQS critics in Table 3. None have ever cited my publications. In addition, the authorship of these 348 publications shows a strong interrelationship between PM Panel Members and the Pro-PM2.5 authors in Table 1 and elsewhere. Also, these publications indicate that essentially all PM Panel Members have received funding from EPA, NIEHS, and/or HEI. One half (11) of the PM Panel Members are from three states with aggressive air regulatory agencies (CA, MA, NY). There are NO PM Panel Members from 39 states. NO PM Panel Member has published criticism of the relationship between PM2.5 and mortality.

Comments on October 2021 EPA PM Policy Assessment

Along with the September 2021 PM ISA Supplement, the October 2021 PM PA must be entirely redone because it deliberately exaggerates the adverse health effects of PM2.5 and makes policy recommendations that are based on invalid claims that PM2.5 *causes* premature deaths. Like the ISA Supplement, the PA focuses almost exclusively on the positive associations between PM2.5 and mortality that have been promoted by the Chinese-funded Harvard TH Chan School of Public Health investigators. This deliberate falsification of the research record has been documented by a word search of the PA which counts the number of citations of first authors in the text and all authors in the references. Among Harvard Chan and Northeastern investigators, the top 8 (Bell, Dominici, Hart, Laden, Pope, Schwartz, Thurston, Zanobetti) are cited 315 times; 5 Chinese co-authors of Dominici are cited 226 times; 10 Canadian investigators are cited 410 times, although their Canadian evidence is not relevant to US evidence on PM2.5 and mortality; 4 legacy promoters of PM2.5 deaths (Dockery, Samet, Thun, Gapstur) are cited 35 times. Table 1 shows that these 27 (8+5+10+4) key promoters of PM2.5 deaths are cited a total of 986 times. Table 2 shows that all 30 Chinese co-authors of Dominici, including the 5 in Table 1, are cited 325 times.

As with the ISA Supplement, the falsification of the research record in the PA is made clear in Table 3. It shows that the PA does not cite the published null findings and criticism of 61 investigators, including myself and prior CASAC Chairs Cox, McClellan, and Wolff. Only 4 of the 61 critics are cited at all and

these 4 (Cox, Lipfert, Smith, Wyzga) are cited only 22 times, with only Cox's 2019 CASAC Letters describing null findings. Although there has been an ongoing 30-year controversy about claims that PM2.5 *causes* deaths based on "secret science" findings that are not transparent and reproducible, a word search reveals that the 649-page PA does not contain the words controversy, transparency, reproducibility, and integrity. Just like the ISA, the PA totally ignores Enstrom 2017, my independent CPS II reanalysis which found major flaws in Pope 1995, the 2000 HEI Reanalysis, and the 2009 HEI Follow-up (doi: 10.1177/1559325817693345a). If the ACS had not blocked independent access to CPS II data, my reanalysis could have been done during 1995-1997 and the 1997 PM2.5 NAAQS might never have been established. Rather than acknowledging my reanalysis and errors in PM2.5 death claims, HEI has increased funding of research associating low level PM2.5 with deaths. The ISA Supplement and PA focus on these implausible low-level PM2.5 death effects, based primarily on improper use of Medicare records, and they ignore valid criticism of these results as well as evidence of NO PM2.5 death effects.

Before California regulations are nationalized by EPA, it is important to note the adverse consequences of FALSE PM2.5 death claims and excessive PM2.5 regulations. The October 19 California Business Roundtable letter to Governor Newsom describes ways to solve the Supply Chain Crisis at the Ports of Los Angeles and Long Beach (https://cbrt.org/wp-content/uploads/2021/10/Port-Crisis-Letter-FINAL.pdf). One way is to suspend the CARB regulations that prohibit older diesel trucks from entering the ports. Instead of suspending these regulations, CARB (particularly Balmes) voted on December 9 to implement new DMV smog check regulations on all trucks (https://ww2.arb.ca.gov/news/carb-passes-smog-check-regulation-heavy-duty-trucks-and-buses). These regulations are justified by the FALSE claim that they will "prevent 7,500 air-quality related deaths," when there is overwhelming evidence that there are NO PM2.5-related deaths in California from diesel engines or any other source, dating back to Enstrom 2005 (http://www.scientificintegrityinstitute.org/IT121505.pdf). On December 9 CARB (particularly Balmes) also voted to ban small gasoline-powered off-road engines, like leaf blowers and lawn mowers (https://ww2.arb.ca.gov/news/carb-approves-updated-regulations-requiring-most-new-small-road-engines-be-zero-emission-2024). These ruthless CARB regulatory actions directly hurt blue collar workers, like truck drivers and gardeners, and they inflate the cost of living for all Californians.

Evidence challenging the tightening of the PM2.5 NAAQS is powerfully summarized in the November 17 public comments to EPA CASAC PM Panel made by a courageous toxicology PhD candidate, Enstrom, and Milloy (https://www.youtube.com/watch?v=P6OhZaaexv8&ab_channel=SamuelDelk). This evidence includes the fact that there is no etiologic mechanism by which inhaling 100 μg of PM2.5 per day can cause death and the fact that the US already has a very low PM2.5 level of 7 $\mu g/m^3$, whereas our competitor China has the very high level of 48 $\mu g/m^3$. Nevertheless, on December 2, 20 of the 22 PM Panel Members recommended lowering the annual PM2.5 NAAQS of 12 $\mu g/m^3$ and the remaining 2 previously recommended lowering the NAAQS; 17 Members recommended a NAAQS of 8-10 $\mu g/m^3$.

The Biden EPA should not be focused on tightening the PM2.5 NAAQS while the Chinese are sending their PM2.5 across the Pacific Ocean to America and while dozens of Chinese researchers are improperly accessing and analyzing the confidential Medicare records of 69 million Americans. The December 2 recommendation of the PM Panel confirms the validity of the writings of renowned New York Times journalist John Tierney on "The Left's War on Science" (https://www.manhattan-institute.org/html/lefts-war-science-11161.html), renowned physicist Lawrence Krauss on "The Ideological Corruption of Science" (https://www.wsj.com/articles/the-ideological-corruption-of-science-11594572501), and Enstrom on Environmental Lysenkoism regarding PM2.5 science and regulations (http://scientificintegrityinstitute.org/NASJEEA020820.pdf). Thus, there is a current lawsuit against the Biden EPA CASAC and Science Advisory Board for violation of the Federal Advisory Committee Act (https://junkscience.com/2021/10/former-casac-chair-added-as-plaintiff-in-young-v-epa/).

Table 1. Key Pro PM2.5 Authors Cited in 2021 EPA PM ISA Supplement & 2021 PM PA James E Enstrom, PhD December 10, 2021

Authors Cited First Name	Last Name	Institution (connection to HTHCSPH)	State	PM ISA Supp Sep 2021	PM PA Oct 2021
Group 1) Key Harvard TH Chan School of Public Health & Other Northeast Investigators					
Michelle L	Bell	JHBSPH-->Yale U (2002 PhD Enviro Eng JHU)	MD-CT	6	25
Francesca	Dominici	JHBSPH-->HTHCSPH (1997 PhD Statistics U Padua IT)	IT-MD-MA	21	50
Jaime E	Hart	HTHCSPH (2008 ScD Env Health HTHCSPH)	MA	15	24
Francine	Laden	HTHCSPH (1998 ScD Epidemiology HTHCSPH)	MA	10	18
C Arden	Pope III	BYU (1981 PhD AgEcon ISU & 1993 IPH Env Health HTHCSPH)	UT-MA-UT	33	43
Joel D	Schwartz	US EPA-->HTHCSPH (1980 PhD Physics Brandeis)	MA	55	77
George D	Thurston	NYU (1983 ScD Env Health Sci HTHCSPH)	MA-NY	7	29
Annette	Zanobetti	HTHCSPH (1999 PhD Statistics U Florence IT)	IT-MA	24	49
Total Citations				171	315
Group 2) Key Chinese Co-Authors of Dominici (and/or Schwartz					
Roger D	Peng	JHBSPH (2003 PhD Statistics UCLA)	CA-MD	2	20
Qian	Di	Tsinghua U (2015 PhD Env Health HTHCSPH)	PRC-MA-PRC	31	118
Liuhua	Shi	Emory U (2016 ScD Env Health HTHCSPH)	PRC-MA-GA	7	31
Yan	Wang	HTHCSPH ScD Env Health & Biostat Candidate	PRC-MA		
Yun	Wang	HTHCSPH PhD Research Biostatistics Scientist	PRC-MA	44	57
Total Citations				84	226
Group 3) Key Canadian Investigators					
Jeffrey R	Brook	U Toronto DLSPH	CN	14	26
Richard T	Burnett	Health Canada, Ottawa	CN	29	73
Daniel L	Crouse	U New Brunswick, Fredericton	CN	45	38
Daniel	Krewski	U Ottawa	CN	3	20
Randall V	Martin	Dalhousie University, Halifax	CN	25	51
Lauren	Pinault	Statistics Canada, Ottawa	CN	48	24
Michelle L	Turner	U Ottawa	CN	4	37
Aaron	van Donkelaar	Dalhousie University, Halifax	CN	26	71
Scott	Weichenthal	Health Canada, Ottawa	CN	12	35
Michael	Jerrett	U Toronto-->USC-->UCB-->UCLA	CN-CA	12	35
Total Citations				218	410
Group 4) Key Legacy Investigators Who Have Promoted PM2.5 Deaths					
Douglas W	Dockery	HTHCSPH (1979 ScD Env Health at HTHCSPH)	MA	2	7
Jonathan M	Samet	JHBSPH->USC DPM->CO SPH (1977 MS Epi HTHCSPH)	MD-CA-CO	2	10
Michael J	Thun	ACS National Retired (1983 MS Epi HTHCSPH)	GA	1	4
Susan M	Gapstur	ACS National Retired	GA	3	14
Total Citations				8	35
Grand Total Citations				481	986

Table 2. Chinese Authors Cited in 2021 EPA PM ISA Supplement & 2021 PM PA James E Enstrom, PhD December 10, 2021

Authors Cited First Name	Last Name	Institution	State	PM ISA Supp Sep 2021	PM PA Oct 2021
Chinese PM2.5 Co-Authors of Dominici (and often Schwartz)					
Howard H	Chang	Emory	MD-GA	5	7
Chen	Chen	HTHCSPH	PRC-MA	0	5
Yeonseung	Chung	HTHCSPH	PRC-MA	0	0
Linouhen	Dai	HTHCSPH	PRC-MA	3	6
Qian	Di	HTHCSPH	PRC-MA	31	118
Yiking	Dou	HTHCSPH	PRC-MA	0	0
Seulkee	Heo	HTHCSPH	PRC-MA	0	0
Lifang	Hou	HTHCSPH	PRC-MA	0	0
Wan	Jiao	HTHCSPH	PRC-MA	0	0
Chanmin	Kim	HTHCSPH	PRC-MA	5	1
Honghyok	Kim	HTHCSPH	PRC-MA	0	4
Hyung Joo	Lee	HTHCSPH	PRC-MA	6	9
Kyu Ha	Lee	HTHCSPH	PRC-MA	4	7
Nanye	Lee	HTHCSPH	PRC-MA	5	11
Jia Coca	Liu	HTHCSPH	PRC-MA	12	10
Pengfeu	Liu	HTHCSPH	PRC-MA	14	10
Roger D	Peng	JHBSPH	CA-MD	2	20
Luu	Pham	HTHCSPH	PRC-MA	1	2
Changyu	Shen	HTHCSPH	PRC-MA	0	0
Liuhua	Shi	HTHCSPH	PRC-GA	7	31
Helen H	Shu	Tufts	MA	7	0
Ji-Young	Son	HTHCSPH	PRC-MA	6	4
Shengzhi	Sun	HTHCSPH	PRC-MA	3	5
Yan	Wang	HTHCSPH	PRC-MA		
Yun	Wang	HTHCSPH	PRC-MA	44	57
Yaguang	Wei	HTHCSPH	PRC-MA	35	6
Xiao	Wu	HTHCSPH	PRC-MA	29	12
Meihn	Yan	HTHCSPH	PRC-MA	17	0
Xu	Yue	HTHCSPH	PRC-MA	0	0
Jia	Zhao	HTHCSPH	PRC-MA	0	0
Total Citations				236	325

Table 3. Critical PM2.5 Authors Cited in 2021 EPA PM ISA Supplement & 2021 PM PA James E Enstrom, PhD December 10, 2021

Authors Cited First Name	Last Name	Institution (NONE Trained at HTHCSPH)	State	PM ISA Supp Sep 2021	PM PA Oct 2021	
Published Critics of the Claim that PM2.5 Causes Deaths						
Sarah R	Armstrong	Cambridge Environmental	MA	0	0	
Jerome C	Arnett	Pulmonology Expert & CEI Retired	WV	0	0	
Daren	Bakst	Heritage Foundation	DC	0	0	
Brent	Bennett	Texas Public Policy Foundation	TX	0	0	
Lester	Breslow	CA Dept Public Health & UCLA Former	CA	0	0	
W Matt	Briggs	wmbriggs.com & Cornell U retired	NY	0	0	
William B	Bunn	Navistar International & U So Carolina	SC	0	0	
Edward J	Calabrese	U Massachuetts Amherst	MA	0	0	
Alan	Carlin	EPA Retired	VA	0	0	
L Anthony	Cox	Cox Associates & U Colorado Denver	CO	0	9	CASAC Chair Letters 041119&121619
Edmund A C	Crouch	Cambridge Environmental	MA	0	0	
John D	Dunn	Darnall Army Medical Center	TX	0	0	
Myron	Ebell	Competitive Enterprise Institute	DC	0	0	
James E	Enstrom	UCLA Retired & Scientific Integrity Institute	CA	0	0	
Gordon J	Fulks	Gordon Fulks and Associates & CO2 Coalition	OR	0	0	
Michael	Fumento	AEI and Hudson Institute	DC	0	0	
John F	Gamble	Exxon Retired	NJ	0	0	
Lawrence	Garfinkel	ACS National Former	NY	0	0	
Julie E	Goodman	Gradient	MA	0	0	
John D	Graham	Harvard & Indiana U School Public Affairs	IN	0	0	
Laura C	Green	Cambridge Environmental	MA	0	0	
E Cuyler	Hammond	ACS National	NY	0	0	
Martin	Hetzel	Represents 112 German Lung Specialists	GER	0	0	
Thomas W	Hesterberg	Navistar International & CTEH	IL	0	0	
Jon M	Heuss	Air Improvement	MI	0	0	
John L	Hoare	AIR, Inc	NZ	0	0	
Walter W	Holland	St Thomas's Hospital Medical School, London	UK	0	0	
Michael	Hunnicutt	Texas Commission on Environmental Quality	TX	0	0	
Thomas W	Hesterberg	Navistar International	AR	0	0	
Warren	Kindzierski	U Alberta	CN	0	0	
Matthias	Klingner	Represents 112 German Lung Specialists	GER	0	0	
Thomas	Koch	Represents 112 German Lung Specialists	GER	0	0	
Dieter	Köhler	Represents 112 German Lung Specialists--Leader	GER	0	0	
Gary	Koop	U Leicester	UK	0	0	
Goran	Krstic	Fraser Health	CN	0	0	
Sabine S	Lange	Texas Commission on Environmental Quality	TX	0	0	
Timothy L	Lash	Emory U & Epidemiology Journal	GA	0	0	
Marlo	Lewis	Competitive Enterprise Institute	DC	0	0	
Frederick W	Lipfert	Brookhaven Nat Lab Retired & Consultant	NY	1	6	Lipfert 2006 & 2020, no null findings
Joseph L	Lyon	U Utah	NM	0	0	
Roger O	McClellan	Toxicology Expert & Consultant	NM	0	0	
Henry I	Miller	Hoover Institution & Pacific Research Inst	CA	0	0	
Steven J	Milloy	JunkScience.com & Author	MD	0	0	
A Alan	Moghissi	George Mason U & Inst Reg Science	VA	0	0	
Suresh	Moolgavkar	U Washington & Exponent	WA	0	0	
Daniel L	Nebert	U Cinncinati Retired	OH	0	0	
Dennis	Paustenbach	Paustenbach & Associates	WY	0	0	
Mikko	Paunio	U Helsinki	FIN	0	0	
Steven	Piantadosi	JHBSPH->Cedars Sinai->Brigham&Women's	MA	0	0	
Douglas A	Popken	Cox Associates & U Colorado Denver	CO	0	0	
Robert F	Phalen	UC Irvine	CA	0	0	
Anne E	Smith	National Economic Research Associates	DC	0	1	Smith on visibility, not PM2.5 deaths
Richard L	Smith	U North Carolina	NC	3	0	Young 2017
Anthony V	Swan	Public Health Laboratory, London	UK	0	0	
Lise	Tole	U Leicester	UK	0	0	
Peter A	Valberg	Gradient	MA	0	0	
Robert E	Waller	Department of Health, London	UK	0	0	
Kathleen H	White	Texas Public Policy Foundation	TX	0	0	
George T	Wolff	Air Improvement	MI	0	0	
Clint	Woods	Americans for Prosperity & AAPCA	VA	0	0	
Ronald E	Wyzga	Electric Power Research Institute	CA	5	6	Lipfert 2006 & 2020, no null findings
S Stanley	Young	NISS Retired & CSTAT	NC	3	0	Young 2017
Total Citations				12	22	

Table 4. Information on EPA CASAC Particulate Matter Panel Members James E Enstrom, PhD December 10, 2021

Authors Cited First Name	Last Name	Primary Institution	Positions Promoting PM2.5 Deaths/Regs	State	Recommend New PM2.5	PM2.5-AP Pubs	Pro-PM2.5, EPA, NAS, or PM Panel Co-authors
CASAC Members on PM Panel							
Elizabeth A	Sheppard	U Washington	IPMRP, HEI Health	WA		35	Fann (EPA), Laden, Peel, Schwartz
Michelle L	Bell	Yale U	HEI Health Review	CT	8-10	41	Dominici, Peng, Rich, Schwartz, Zanobetti
James W	Boylan	Georgia Natural Res	CASAC 2020	GA	10-11	3	Russell (NAS NAAQS)
Judith C	Chow	Desert Research Inst	IPMRP	NV	8-10	55	Watson JG
Mark W	Frampton	U Rochester	CASAC 2020	NY	8-10	6	Rich, Hopke & Utell (former CASAC)
Christina H	Fuller	Georgia State U		GA	9-11	18	Sarnat
Alexandra G	Ponette-Gonzalez	U North Texas		TX	8-10	0	
Remaining PM Panel Members							
Peter J	Adams	Carnegie Mellon U	IPMRP	PA		5	Lave
George A	**Allen**	**NESCAUM**	**NESCAUM**, IPMRP	MA	8-10	5	Dockery, Speizer
John R	**Balmes**	UCSF & UCB	**CARB**, IPMRP	CA	8-10	13	Burnett, Gapstur, Jerrett, Pope, Turner
Jane E	Clougherty	Drexel U	HEI Health Review	PA	8-10	20	Dominici, Laden
Deborah A	Cory-Slechta	U Rochester		NY	8-10	19	Balmes
Terry	Gordon	New York U	IPMRP	NY	9-11	11	Thurston, Lippmann (former CASAC)
Michael T	**Kleinman**	UC Irvine	**CARB SRP**, IPMRP	CA	8-10	6	
Stephanie	Lovinsky-Desir	Columbia U		NY	8-10	12	
Jennifer L	Peel	Colorado State U	HEI Review Comm	CO	8-10	14	Sarnat, Sheppard
David Q	Rich	U Rochester		NY	8-10	19	Bell, Dockery, Frampton, Hopke & Utell
Jeremy A	Sarnat	Emory U	IPMRP	GA	8-10	23	Peel, Russell, Schwartz, Zanobetti
Neeta	Thakur	UCSF		CA	8-10	6	Balmes
Barbara J	Turpin	U North Carolina	IPMRP, HEI Health	NC	8-10	20	Hopke, Rich
Marc G	Weisskopf	HTHCSPH	HEI Health Review	MA	8-10	11	Dominici, Hart, Laden, Schwartz, Zanobetti
Corwin M	Zigler	U Texas Austin	HEI Health Review	TX	8-10	6	Dominici, Samet
			Total PM2.5-AP Publications by PM Panel			348	

June 29, 2020

To:
Docket ID No. **EPA–HQ–OAR–2015–0072**
FRL–10008–31–OAR
Review of the National Ambient Air Quality Standards for Particulate Matter
https://www.regulations.gov/comment?D=EPA-HQ-OAR-2015-0072-0069
U.S. Environmental Protection Agency
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This Comment strongly supports the EPA Administrator's proposed decision to retain the current **National Ambient Air Quality Standards for Particulate Matter**, as described in the April 30, 2020 Federal Register. The summary of this decision is "Based on the Environmental Protection Agency's (EPA's) review of the air quality criteria and the national ambient air quality standards (NAAQS) for particulate matter (PM), the Administrator has reached proposed decisions on the primary and secondary PM NAAQS. With regard to the primary standards meant to protect against fine particle exposures (*i.e.,* annual and 24-hour PM2.5 standards), the primary standard meant to protect against coarse particle exposures (*i.e.,* 24-hour PM10 standard), and the secondary PM2.5 and PM10 standards, the EPA proposes to retain the current standards, without revision." and "the Administrator proposes to conclude that the scientific evidence that has become available since the last review of the PM NAAQS, together with the analyses in the PA based on that evidence, does not call into question the public health protection provided by the current annual and 24-hour PM2.5 standards." Currently, the EPA has primary and secondary standards for PM2.5 (annual average standards with levels of 12.0 micrograms per cubic meter (µg/m³) and 15.0 µg/m³, respectively; 24-hour standards with 98th percentile forms and levels of 35 µg/m³; values are averaged over 3 years).

1. The first justification for retaining the current PM NAAQS is contained in the 257-page December 16, 2019 EPA Clean Air Scientific Advisory Committee (CASAC) PM Policy Assessment (PA) Report. The CASAC Chair LOUIS ANTHONY (TONY) COX, JR., PhD, is a distinguished scientist and a renowned expert in the health risks associated with PM2.5. His impressive background is summarized in his own Bio Sketch shown below.

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Tony Cox is a risk analyst and President of Cox Associates (www.cox-associates.com), a Denver-based applied operations research and analytics company specializing in data science and statistics applied to public and occupational health, safety, and environmental risk analysis; epidemiology; policy analytics; and customer behavior modeling. Since 1986, Cox Associates' analysts and scientists have applied epidemiological, risk analysis, and operations research models and advanced analytics to measurably improve health and environment risk assessment and decision-making for public and private sector clients. In 2006, Cox Associates was inducted into the Edelman Academy of the Institute for Operations Research and Management Science (INFORMS), recognizing outstanding real-world achievements in the practice of operations research and the management sciences. In 2012, Dr. Cox was inducted into the National Academy of Engineering (NAE), "For applications of operations research and risk analysis to significant national problems." He has served as a member of the National Academies' Board on Mathematical Sciences and their Applications (BMSA) (2012-2016) and currently chairs the Clean Air Scientific Advisory Committee (CASAC) for the United States Environmental Protection Agency (EPA).

Dr. Cox holds a Ph.D. in Risk Analysis and an S.M. in Operations Research, both from MIT; an AB from Harvard University; and is a graduate of the Stanford Executive Program. He has served as Honorary Full Professor of Mathematics at the University of Colorado, Denver, lecturing on applied statistics, data science, decision and risk analysis, biomathematics, health risk modeling, and causality; on the Faculties of the Center for Computational Mathematics and the Center for Computational Biology; and as Clinical Professor of Biostatistics and Informatics at the University of Colorado Health Sciences Center. He has served as an expert in risk analysis on many National Academies, World Health Organization, EPA, USDA, and other agency projects, committees, and advisory boards.

Dr. Cox is Editor-in-Chief of *Risk Analysis: An International Journal.* He is Area Editor for Real World Applications for the *Journal of Heuristics,* and is on the Editorial Boards of *Decision Analysis* and the *International Journal of Operations Research and Information Systems*. He is a Fellow and an Edelman Laureate of INFORMS, a member of the American Statistical Association (ASA), and a lifetime Fellow of the Society for Risk Analysis (SRA). In 2015 and 2018, his research applying machine learning to high-throughput screening data for endocrine disruptors and carcinogenicity won Best Published Papers Demonstrating an Application of Risk Assessment awards from the Society of Toxicology Risk Assessment Specialty Section. His previous research has won the Society of Toxicology's Outstanding Published Paper in Risk Assessment Award and the Society for Risk Analysis Outstanding Risk Practitioner Award. In 2008, his solution to a challenge on "Statistical Methods to Predict Clinical Response" won an Inno Centive Award.

Dr. Cox has taught many graduate and professional courses in risk analysis, decision analysis, and advanced analytics. He has authored and co-authored over 200 journal articles and book chapters on these fields. His most recent books are *Causal Analytics for Applied Risk Analysis*(Springer, 2018), *Breakthroughs in Decision Science and Risk Analysis* (Wiley, 2015), *Improving Risk Analysis* (Springer, 2013), *Risk Analysis of Complex and Uncertain Systems* (Springer, 2009) and the *Wiley Encyclopedia of Operations Research and Management Science* (Wiley, 2011), which Dr. Cox co-edited. He has over a dozen U.S. patents on applications of artificial intelligence, signal processing, statistics and operations research. His current research interests include computational statistical methods for causal inference in public and occupational health risk analysis, data-mining, and advanced decision analysis, optimization, and learning in uncertain and changing environments.

Key quotes from the December 16, 2019 CASAC PM PA Report, with key phrases in bold, are as follows:

Page 1: 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 a 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, **some 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 PM2.5 annual standard**.

Page 3: Future changes in public health risks that might be caused by reducing PM2.5 exposures are currently highly uncertain. The CASAC recommends that the PM PA better characterize this uncertainty using quantitative uncertainty analysis. Such an analysis should account for model uncertainty, exposure estimation errors, and both inference (internal validity) and generalization (external validity) uncertainties. As described above and in further detail in the consensus responses, the CASAC members did not come to consensus on whether the new scientific evidence and data reasonably call into question the public health protection afforded by the current 2012 PM2.5 annual standard. The CASAC recommends that the final PM PA provide quantitative uncertainty and sensitivity analyses to provide a clearer technical and scientific basis for data interpretation and policy making. **The CASAC agrees with the EPA and finds that the available evidence does not call into question the adequacy of public health protection afforded by the current 24-hour PM2.5 standard and concurs that it be retained.**

Page B-10: To "serve as a source of policy-relevant information that informs the Agency's review of the NAAQS for PM," the PA should use valid and empirically validated scientific methods to address the question of whether and how much changes in policy would affect public health risks. As just mentioned, the current draft PA is based largely on epidemiological evidence of positive associations between exposures and health effects in studies that do not fully test and control for confounding, coincident historical trends, and other non-causal sources of associations. These associations (such as the beta coefficients in Table C-1) are then used as if they were known to be valid causal predictors for simulating how changes in exposure would change health risks. This is not sound science. **The resulting conclusions and predictions are not scientifically valid and should not be used to guide policies that are to be based on sound science.**

Page B-19: The PA provides no valid scientific information about how changing PM air quality standards would change (or, in the recent past, has changed) public health risks. A scientifically sound analysis would require considering relevant real-world evidence that the PM has ignored ; clearly defining and then appropriately calculating beta values (or other formulas for quantifying causal effects on public health of changing PM2.5) while correcting for causally relevant covariates (e.g., month and high and low daily temperatures and other confounders), exposure estimation errors, and modeling errors and biases; and distinguishing between association and causation. **Since the PA does not do these things, it should not be used as if it provided valid scientific information about health risks.**

Page B-21: "The PA states (p. 3-21) that "The draft ISA concludes that, 'collectively, this body of evidence is sufficient to conclude that a causal relationship exists between long-term PM2.5 exposure and total mortality'." However, since "this body of evidence" consists primarily of associations in studies that did not fully control for causally relevant covariates (such as month and daily high and low temperatures) and that were not designed or analyzed to permit valid causal inferences, **the conclusion that "this body of evidence is sufficient to conclude that a causal relationship exists between long-term PM2.5 exposure and total mortality" is unwarranted. It is not implied by, or consistent with, the principles of sound science previously discussed.**

2. The second justification for retaining the current PM NAAQS is my extensive epidemiologic evidence that there is NO relationship between PM2.5 and total mortality in the US. This weak epidemiologic relationship drives the claim that PM2.5 *causes* premature deaths and the cost-benefit justification for many EPA Regulations. The evidence that there is NO relationship negates the primary public health justification for the PM2.5 NAAQS. There are six primary reasons that PM2.5 does not *cause* premature deaths:

a) No Etiologic Mechanism: This is no experimental proof that 1-5 lifetime grams (<µg/day) of PM2.5 causes death $PM_{2.5}\mu g/m^3$

b) Weak Epidemiologic Risk: Tiny positive relative risks (RR<1.10) do not prove that PM2.5 causes death and reductions of in PM2.5 levels have not clearly reduced the supposed mortality risks

c) Ecological Fallacy: PM2.5 monitors of ambient air provide inaccurate measurements of individual human exposure and there are NO PM2.5 measurements of individual exposure

d) Uncontrolled Confounding Variables: Co-pollutants, temperature, geography, and other factors can reduce or eliminate an apparent relationship

e) Access to Underlying Data: Enstrom independent analysis of American Cancer Society data (CA CPS I and CPS I) demonstrates the importance of access to underlying epidemiologic data (see next section)

f) Totality of US Cohort Studies Shows NO Relationship: Objective meta-analysis shows NO statistically significant relationship between long-term PM2.5 exposure and total mortality in nine US and six California prospective epidemiologic cohorts

My detailed October 17, 2019 Comment on the 2019 Draft EPA PM PA contains strong evidence that there is NO causal relationship between PM2.5 and total mortality in the US and it demonstrates the importance of access to underlying data as per the proposed EPA Transparency Rule. 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. 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 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 (MCAPS) 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. First, I document that there is NO relationship between PM2.5 and total mortality in California.

II Table B7: Intrepid Insight Computation of Fixed and Random Effects Meta-Analysis

Six CA 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

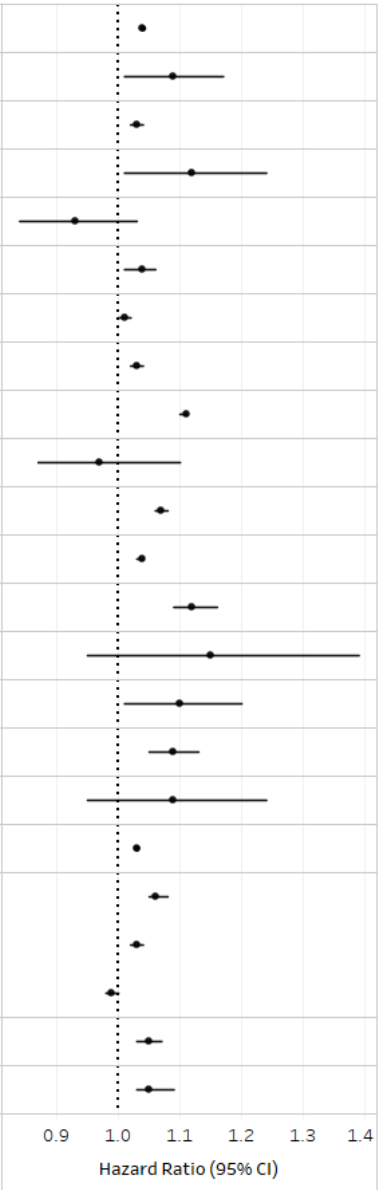
California Cohort Studies	Author Year	RR Table	F-U Years	RR	95%CI(L)	95%CI(U)
Adventist Health Study (AHSMOG)	McDonnell 2000	T3+	1977-1992	1.000	0.950	1.050
CA ACS Cancer Prevention (CA CPS I)	Enstrom 2005	T7	1983-2002	0.997	0.978	1.016
Medicare (MCAPS) Western US	Zeger 2008	T3	2000-2005	0.989	0.970	1.008
CA ACS Cancer Prevention (CA CPS II)	Krewski 2010	T2	1982-2000	0.968	0.916	1.022
California Teachers Study	Ostro 2015	Appx	2001-2007	1.010	0.980	1.050
CA NIH-AAPR Diet and Health Study	Thurston 2016	T2 F3	2000-2009	1.017	0.990	1.040
Intrepid Insight Fixed Effects Meta-Analysis		Summary RR		0.999	0.988	1.009
Intrepid Insight Random Effects Meta-Analysis		Summary RR		0.999	0.988	1.009

Q Test Statistic = 4.7683 I^2 -4.86%
Cochrane's Q Test for Homogeneity of Studies (Null Hypothesis: Studies are Homogenous)
P-Value = 0.4448 → Since Studies satisfy Test for Homogeneity, Fixed and Random Effects Meta-Analysis Yield Summary RR = 0.999 (0.988-1.009), which is statistically consistent with 1.000 (NO relationship)

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 Professionals	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)



3. The third justification for retaining the current PM NAAQS is the strong evidence that I provided in my March 18, 2020 Comment and my April 17, 2020 Comment in support of the March 18, 2020 Supplemental Proposed EPA Rule supplemental rule "Strengthening Transparency in Regulatory Science." in the Federal Register "This supplemental notice of proposed rulemaking (SNPRM) includes clarifications, modifications and additions to certain provisions in the Strengthening Transparency in Regulatory Science Proposed Rulemaking." On April 30, 2018, the EPA published its proposed rule in the Federal Register "This document proposes a regulation intended to strengthen the transparency of EPA regulatory science. The proposed regulation provides that when EPA develops regulations, including regulations for which the public is likely to bear the cost of compliance, with regard to those scientific studies that are pivotal to the action being taken, EPA should ensure that the data underlying those are publicly available in a manner sufficient for independent validation." My independent access to underlying ACS data (CA CPS I and CPS II) made possible the NULL evidence that I have published shown NO relationship between PM2.5 and total mortality, as shown in II Table B3 and II Table B7 above.

The request for data underlying EPA regulations dates back to the May 16, 1994 CASAC Chair George T. Wolff, MD letter to EPA regarding the then forthcoming Particulate Matter Review: "As scientists affiliated with CASAC, we are concerned that the appropriate analyses be conducted prior to our review. In that spirit, we request that the Agency take steps to assure that crucial data sets linking exposure to particulate matter and health responses are available for analysis by multiple analytical teams, thereby assuring the validity of the results before they are used in making regulatory decisions on the National Ambient Air Quality Standards for Particulate Material." The full 1994 letter is shown below.

The June 13, 1996 CASAC Chair George T. Wolff, MD letter to EPA illustrates the weaknesses of the evidence regarding the establishment of the 1997 PM2.5 NAAQS. Of the eight PM experts in the three most relevant disciplines (epidemiology, toxicology, and statistics), four (Drs. Larntz, Mauderly, Sly, and Stolwijk) recommended an annual PM2.5 standard that varied from 15 to 30 $\mu g/m^3$ and averaged 23.1 $\mu g/m^3$, and four (Drs. McClellan, Menzel, Samet, and Speizer) recommended NO annual PM2.5 standard. The annual 1997 PM2.5 standard as set at 15 $\mu g/m^3$, the low end of all these recommendations. A key quote from the letter states the uncertainties that still exist "The diversity of opinion also reflects the many unanswered questions and uncertainties associated with establishing causality of the association between PM2.5 and mortality. The Panel members who recommended the most stringent PM2.5 NAAQS, similar to the lower part of the ranges recommended by the Staff, did so because they concluded that the consistency and coherence of the epidemiology studies made a compelling case for causality of this association. However, the remaining Panel members were influenced, to varying degrees by the many unanswered questions and uncertainties regarding the issue of causality. The concerns include: exposure misclassification, measurement error, the influence of confounders, the shape of the dose-response function, the use of a national PM2.5 / PM10 ratio to estimate local PM concentrations, the fraction of the daily mortality that is 2.5 advanced by a few days because of pollution, the lack of an understanding of toxicological mechanisms, and the existence of possible alternative explanations." The full 1996 letter is shown below.

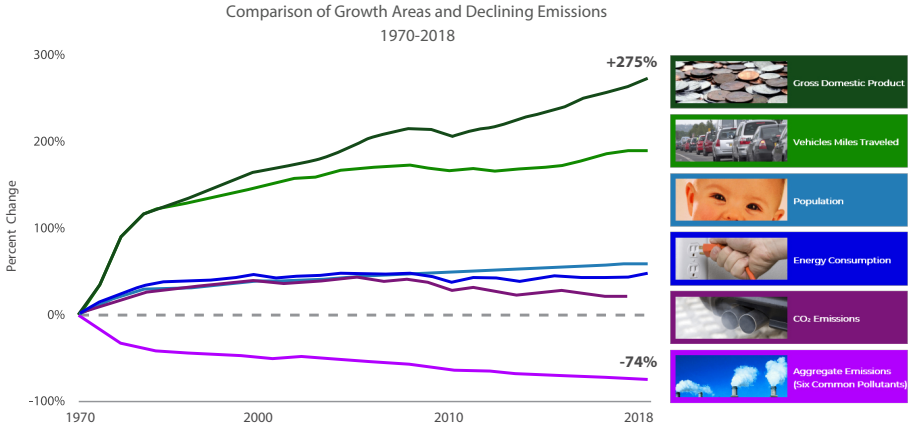
Our Nation's Air

Air Quality Improves as America Grows

https://gispub.epa.gov/air/trendsreport/2019

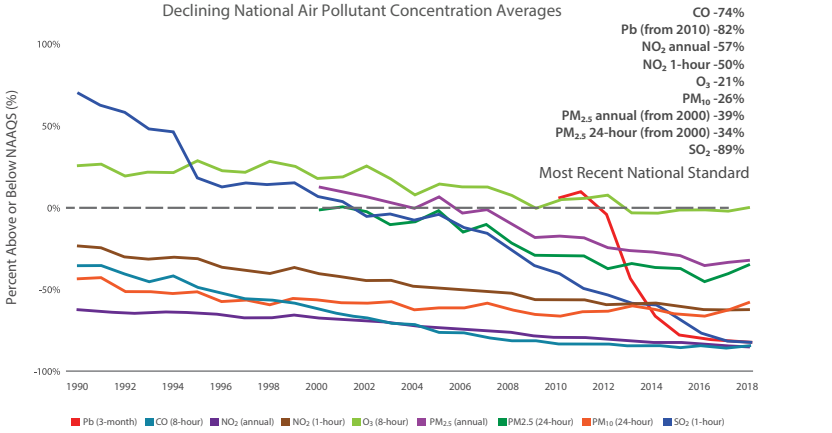
Economic Growth with Cleaner Air

Between 1970 and 2018, the combined emissions of the six common pollutants ($PM_{2.5}$ and PM_{10}, SO_2, NO_X, VOCs, CO and Pb) dropped by 74 percent. This progress occurred while the U.S. economy continued to grow, Americans drove more miles and population and energy use increased.



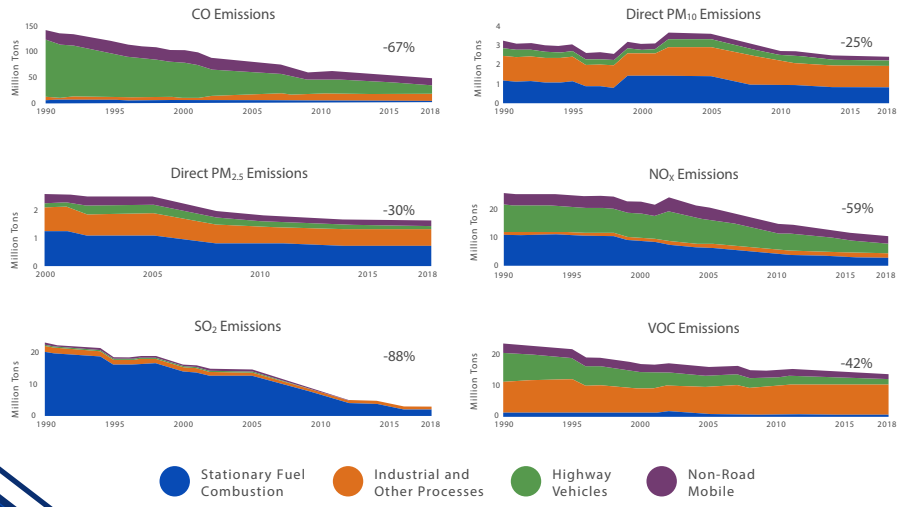
Air Quality Trends Show Clean Air Progress

While some pollutants continue to pose serious air quality problems in areas of the U.S., nationally, criteria air pollutant concentrations have dropped significantly since 1990 improving quality of life for many Americans. Air quality improves as America grows.



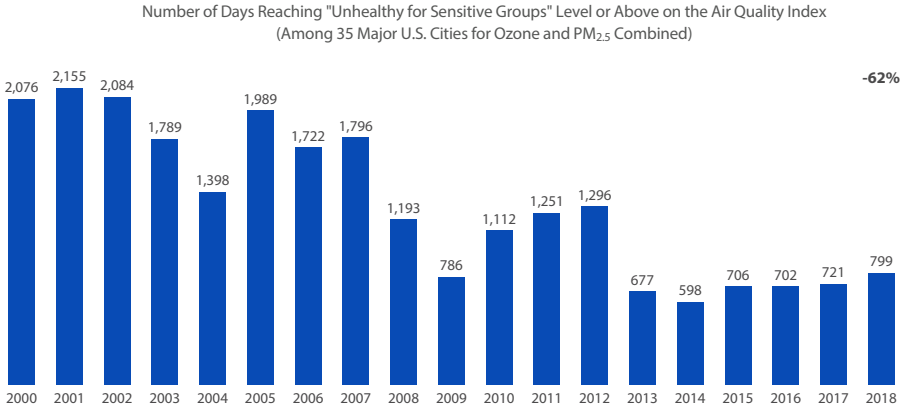
Air Pollutant Emissions Decreasing

Emissions of key air pollutants continue to decline from 1990 levels. These reductions are driven by federal and state implementation of stationary and mobile source regulations.



Unhealthy Air Days Show Long-Term Improvement

The Air Quality Index (AQI) is a color-coded index EPA uses to communicate daily air pollution for ozone, particle pollution, NO_2, CO, and SO_2. A value in the unhealthy range, above national air quality standard for any pollutant, is of concern first for sensitive groups, then for everyone as the AQI value increases. Fewer unhealthy air quality days means better health, longevity, and quality of life for all of us.



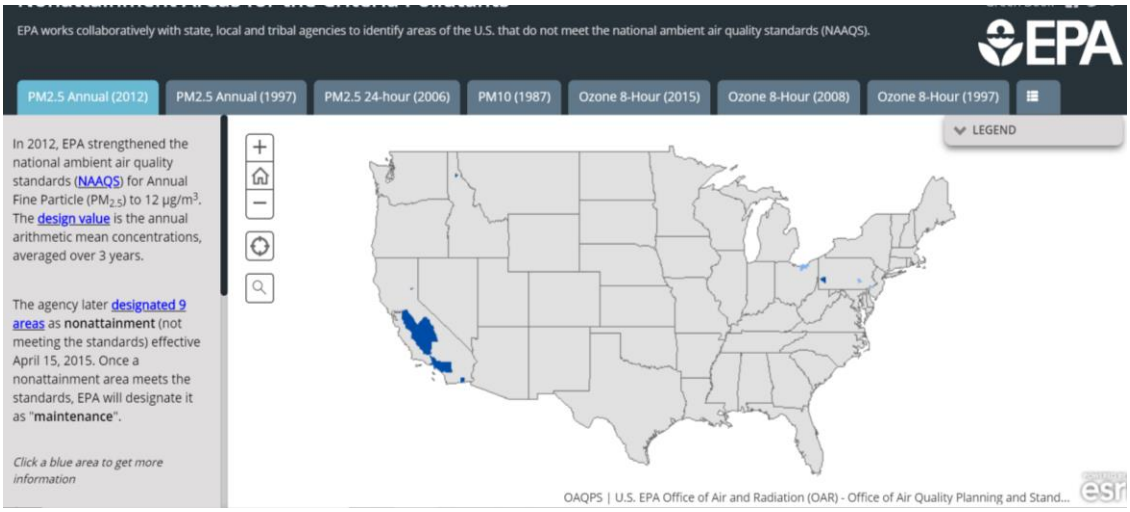
Unhealthy air quality days vary year to year, influenced not only by pollution emissions but also by natural events, such as dust storms and wildfires, and variations in weather.

Status and Trends Through 2018

4. The fourth justification for retaining the current PM NAAQS is contained in Our Nation's Air Summary Chart of "Air Quality Improves as America Grows" shown above and in the points below

a. Recent trends in air quality, including innovation-driven progress across emissions, concentrations, and U.S. competitiveness, demonstrate that a more stringent particulate matter NAAQS is not necessary.

b. In the entire U.S., only 9 full counties and 7 partial counties (out of more than 3,000) fail to meet the most recent national standards for fine particulate matter, which were set by the Obama Administration at a level designed to protect public health with an adequate margin of safety for susceptible populations. 14 of these counties are located in California:



c. In recent years, the U.S. has had far lower fine particulate matter levels than nearly any country on earth. At present, U.S. concentrations are less than one-sixth the global average, seven times below China, and roughly half of particulate matter levels in continental Europe.

d. EPA's June 2020 Our Nation's Air report demonstrates dramatic recent progress for particulate matter. Across the U.S., fine particulate matter concentrations have dropped by roughly 43 percent between 2000 and 2019. Over that same period, direct emissions of fine particulate matter also fell by 43 percent, and anthropogenic emissions of pollutants that can be a precursor to PM2.5 followed a similar trend, including sulfur dioxide (down 88 percent), oxides of nitrogen (down 61 percent), and volatile organic compounds (down 28 percent).

e. Between 1970 and 2019, the combined emissions of the six common pollutants (PM2.5 and PM10, SO2, NOx, VOCs, CO and Pb) dropped by 77 percent. This progress occurred while the U.S. economy continued to grow, Americans drove more miles, and population and energy use increased.

Risk Analysis, Vol. 32, No. 5, 2012 DOI: 10.1111/j.1539-6924.2012.01806.x

Letter to the Editor

Miscommunicating Risk, Uncertainty, and Causation: Fine Particulate Air Pollution and Mortality Risk as an Example

Louis Anthony (Tony) Cox*

A recent paper in this journal (Fann *et al*., 2012) estimated that "about 80,000 premature mortalities would be avoided by lowering $PM_{2.5}$ levels to 5 $\mu g/m^3$ nationwide" and that 2005 levels of $PM_{2.5}$ cause about 130,000 premature mortalities per year among people over age 29, with a 95% confidence interval of 51,000 to 200,000 premature mortalities per year.(1) These conclusions depend entirely on misinterpreting statistical coefficients describing the association between $PM_{2.5}$ and mortality rates in selected studies and models as if they were known to be valid causal coefficients. But they are not, and both the expert opinions of EPA researchers and analysis of data suggest that a true value of zero for the $PM_{2.5}$ mortality causal coefficient is not excluded by available data. Presenting continuous confidence intervals that exclude the discrete possibility of zero misrepresents what is currently known (and not known) about the hypothesized causal relation between changes in $PM_{2.5}$ levels and changes in mortality rates, suggesting greater certainty about projected health benefits than is justified.

KEY WORDS: Air pollution; causality; Granger causality; mortality; $PM_{2.5}$

The belief that one can prolong large numbers of lives through well-understood preventive actions is surely exciting and gratifying. In advocating regulations intended to protect public or occupational health, such beliefs are commonly expressed in vivid, easily remembered forms that link recommended actions to desired consequences, such as, "For every unit of reduction in exposure to hazard X, mortality rate will be reduced by Y%," or "Each unit of reduction in exposure to hazard X corresponds to a Y% reduction in mortality rate." The first of these is a causal assertion, predicting that reducing exposure will reduce mortality rate; the second describes a statistical association (that plotting or regressing mortality rate against exposure level shows a positive slope between them), meaning that higher mortality rates tend to co-occur with higher exposures. It is important not to conflate these two distinct concepts. For example, they may have opposite signs in the same data set (i.e., two variables X and Y may be statistically positively correlated, even if increasing X would reduce Y, as when X = daily aspirin consumption and Y = heart attack risk); and a misspecified statistical model may produce an apparently statistically significant association even where no causal relation exists (as when "significantly positive" values of k are obtained in the regression model $Y = kX$, even if X and Y are statistically independent positive random variables). In referring to the slope of a statistical relation, the ratio of risk reduction to exposure reduction goes by various names; in air pollution epidemiology and health effects research, it is often called the "concentration-response" (C-R) coefficient.

Recently, EPA researchers published mortality risk reductions that they project would be caused by hypothetical (simulated) future reductions in fine particulate ($PM_{2.5}$) levels, using C-R

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coefficients drawn from previously published studies of $PM_{2.5}$ mortality associations in U.S. cities.[1] They "estimate that about 23,000 $PM_{2.5}$-related mortalities would be avoided as a result of lowering 2005 annual mean $PM_{2.5}$ levels down to 10 $\mu g/m^3$ nationwide . . . [and] estimate about 80,000 premature mortalities would be avoided by lowering $PM_{2.5}$ levels to 5 $\mu g/m^3$ nationwide." They also display an annual impact estimate (relative to nonanthropogenic background) of 130,000 premature mortalities per year due to 2005 levels of $PM_{2.5}$ exposures among people over age 29, with a 95% confidence interval, which excludes zero, of 51,000–200,000 premature mortalities per year. They conclude that "[d]espite significant improvements in air quality in recent decades, recent levels of $PM_{2.5}$ and ozone still pose a nontrivial risk to public health."

These explicitly causal conclusions depend on interpreting statistical C-R coefficients as if they were causal coefficients. However, no such interpretation is justified. The two underlying data sources (the American Cancer Society cohort study and the National Mortality and Morbidity Air Pollution Study (NMMAPS)) were designed to allow statistical associations to be quantified, not to provide valid estimates of the causal impacts on future mortality rates of future reductions in exposure levels. C-R coefficients based on them express statistical associations, and causal projections based on them have no known validity.

The main scientific uncertainty about the $PM_{2.5}$ mortality causal relation for present and future ambient exposures is discrete: Does a nonzero causal relation exist? The answer is not illuminated by presenting a continuous range of positive values (e.g., 51,000–200,000 premature deaths per year as a 95% confidence interval, based on simulation assumptions), as such a continuous range says nothing about the (discrete) probability that the true value is zero. If the statistical association between levels of pollutants such as $PM_{2.5}$ and mortality rates is not causal (e.g., if it arises solely from residual confounding by days with spatiotemporally correlated cold winter temperatures, causing both high death rates[2] and high $PM_{2.5}$ levels, only incompletely controlled for in statistical models, e.g., using moderately flexible smoothing splines[3]), then the projected number of premature deaths caused by exposure should be zero. If only some fraction of the statistical association is causal, then that fraction should be included in calculating prevented premature mortalities and increases in life expectancy.

Uncertainty about causation is important enough so that it should be (and sometimes has been) quantified and clearly communicated. For example, seven experts who provided judgments to EPA on $PM_{2.5}$ C-R estimates (including Schwartz, Pope, Dockery, and Krewski, who did much of original work) gave elicited probabilities of a causal C-R relation for $PM_{2.5}$ and mortality at 7 $\mu g/m^3$ that ranged from 35% to 99%, with a mean of 81%.[4] Studies that attempt to account more objectively for model uncertainty (via Bayesian model averaging) have reduced previously published C-R estimates and suggested that the probability of a nonzero statistical C-R coefficient relation could be much lower.[5] Thus, projecting annual premature mortalities based on a causal interpretation of previously estimated statistical C-R coefficients, without quantifying the fraction of the association that is causal, may substantially overestimate the life-saving benefits of lower pollutant levels. Similarly, presenting a continuous uncertainty interval without a discrete probability for the possibility of a zero slope for the causal relation does not communicate this key uncertainty.

Although the literature on PM mortality associations expresses many opinions, speculations, and assumptions about causation (including implicit causal assumptions such as those of Fann *et al.*), it contains remarkably little formal statistical testing of causal hypotheses. Fortunately, the NMMAPS data set is freely available (www.ihapss.jhsph.edu/). It can be combined with census data to estimate daily mortality rates in over 100 U.S. cities for which estimated daily $PM_{2.5}$ estimates and meteorological measurements (such as temperature extremes and humidity) are also available. In this data set, statistical regression models can easily be developed that exhibit statistically significant positive associations between daily mortality rates and concurrent (and lagged) estimated $PM_{2.5}$ values. Other models can be as easily developed in which there is no such significant association (e.g., by conditioning on daily minimum temperature, which acts as a strong confounder in this data set: both $PM_{2.5}$ levels and daily mortality rates are highest on cold winter days in many cities). To test more rigorously for a possible causal C-R relation between $PM_{2.5}$ and mortality rates, one may apply the R library *granger.test* (http://rss.acs.unt.edu/Rdoc/library/MSBVAR/html/granger.test.html) to paired time series of estimated daily $PM_{2.5}$ exposure concentrations and daily mortality rates. Its documentation explains that *granger.test*:

> Estimates all possible bivariate Granger causality tests for m variables. Bivariate Granger causality tests for two variables X and Y evaluate whether the past values of X are useful for predicting Y once Y's history has been modeled. The null hypothesis is that the past p values of X do not help in predicting the value of Y. The test is implemented by regressing Y on p past values of Y and p past values of X. An F-test is then used to determine whether the coefficients of the past values of X are jointly zero. This produces a matrix with $m^*(m-1)$ rows that are all of the possible bivariate Granger causal relations. The results include F-statistics and p-values for each test. Tests are estimated using single equation OLS models.

Applying this test to each of 190 city-specific data sequences in the NMMAPS data set that have estimated $PM_{2.5}$ and mortality rates for at least 50 consecutive days showed that fewer than 4% of them exhibit a significant positive $PM_{2.5}$ mortality association (for all-cause mortality and also for cardiovascular disease and respiratory mortalities), consistent (at $p < 0.05$) with no positive causal relation between $PM_{2.5}$ exposures and any mortality rate. These results do not warrant a causal interpretation for statistical C-R associations in the NMMAPS data set.

In summary, Fann *et al*. have estimated substantial numbers of premature deaths avoided and life-years added by reducing $PM_{2.5}$, with confidence intervals that do not include zero. This miscommunicates current knowledge and uncertainty by interpreting statistical C-R coefficients as if they were known to represent causal relations. The causal interpretation is unwarranted: the study designs, data, and analyses used do not provide valid causal coefficients. Thus, the exciting prediction that further reductions in $PM_{2.5}$ would cause further extensions of life expectancy is not justified: it remains plausible that further (and recent) reductions in $PM_{2.5}$ may cause no incremental human health benefits—a possibility whose probability is not quantified by Fann *et al*., but that appears to be substantial based on expert opinions and studies of model uncertainty.

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Public Comment for CASAC

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1 Introduction

I am a professor of Statistics and Biostatistics, University of North Carolina, Chapel Hill (UNC). I am a member of EPA's Science Advisory Board (SAB) and a member of a National Academies Committee on *Assessing Causality from a Multidisciplinary Evidence Base for National Ambient Air Quality Standards*. The study I report below was partially financed by an industry sponsor. The views I express here are entirely my own views and do not reflect the opinions of UNC, the SAB, the National Academies or the industry sponsor.

First, I would like to thank the EPA and CASAC for organizing this public comment session. As a member of the SAB, I have often found the public comments to be very helpful in orienting the discussion. I hope you find today's comments similarly helpful.

2 My Study

This study [2] concerned analyzed short-term mortality associations with $PM_{2.5}$ above and below 12 $\mu g/m^3$ (the current long-term standard). Specific details include:

- Medicare data: ≈16 million deaths, 1999–2013;
- $PM_{2.5}$ data from EPA data product (the Remote Sensing information Gateway), and monitors;
- Temperature and dewpoint data from NOAA (the Global Summary of Data dataset);
- Analysis by case-crossover method with 28-day comparison window;
- Concentration-response functions: linear, non-linear or "broken stick" model (two straight lines joined at 12 $\mu g/m^3$), applied to $PM_{2.5}$, mean of day 0 and day 1 lags;
- Meteorological adjustment: nonlinear functions of temperature and dewpoint both current day and average of 3 lagged days.

The results may be summarized as follows:

- Positive (statistically significant) dependence between mortality and $PM_{2.5}$ when linear C-R function is fitted to full range or broken stick model above 12 $\mu g/m^3$;

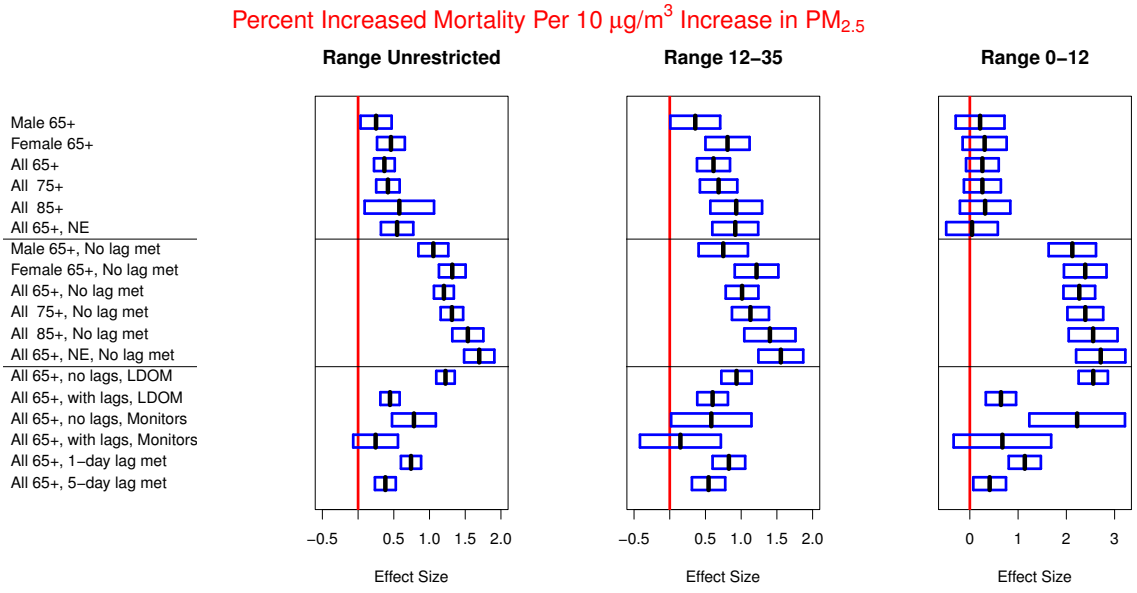

Figure 1: Estimated percent change in mortality and 95% confidence intervals associated with 10 μg/m^3 rise in $PM_{2.5}$ for various subpopulations and statistical models. Left group of plots: linear concentration-response function fitted to full range of $PM_{2.5}$. Middle and right groups: "broken stick" model fitted to ranges 12–35 and 0–12 μg/m^3. Top to bottom: models that include lagged meteorology; models that exclude lagged meteorology; various sensitivity analyses.

- No significant effect below 12 μg/m^3;
- But if lagged meteorology is omitted, the effects are larger across the board, and statistically significant in all ranges;
- These results are robust across various sensitivity analyses;
- Non-linear C-R curves confirm a similar discrepancy between the results that do or do not include lagged meteorology.

These results are illustrated in Figures 1 and 2.

3 Relevance to the ISA

There is another study that included many of the same variables. This study was highly cited in the ISA (and the PA) [1]. This study:

- Used Medicare data from almost the same time period;
- Different constructions of $PM_{2.5}$ and meteorology;
- Similar but not identical statistical and computational methodology;

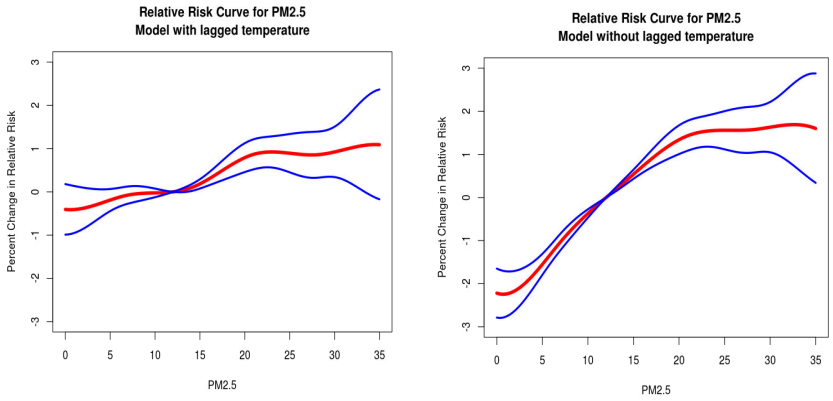

Figure 2: Nonlinear risk curves: percent change in mortality compared with a reference level of 12 μg/m^3 $PM_{2.5}$, with pointwise 95% confidence limits

- Included nonlinear meteorology effects for day of death, but *not* for lagged days;
- This study found highly statistically significant effects for $PM_{2.5}$ both above and below 12 μg/m^3.

I believe this study was deficient. If they had investigated the confounding effect of lagged meteorology, they would have found the same thing as I did.

4 Discussion

This is *not* about discrediting that particular group of researchers. They are a very well known group who have made many creative contributions to air pollution epidemiology.

Rather, I believe this highlights the generic problem with all observational studies: the results can sometimes be highly sensitive to seemingly minor changes in the statistical methodology.

For the remainder of this presentation, I want to focus on two broader issues.

4.1 Publication Bias

This paper was submitted to one of the major epidemiology journals. The referees found no technical fault with the paper. Nevertheless, the editor rejected it. After extensive correspondence with the editor, I felt I had no choice but to withdraw the paper. The paper is now (about to be) resubmitted to another journal.

I do not dispute the right of journal editors to select papers for publication as they see fit, but I believe this creates a distinct bias in the EPA assessment process.

4.2 Transparency and Reproducibility

The previous Administrator of EPA introduced a "Transparency Rule", ostensibly to insure that data from air pollution studies would be available for reanalysis. Numerous scientific commentators, *including his own Science Advisory Board*, objected that the rule was unworkable. The rule was reversed by the current Administrator.

Despite these developments, there has been no progress towards insuring greater reproducibility (or replicability) in EPA studies

5 Recommendations

- EPA should establish a public database of air pollution studies that have been approved by an IRB or equivalent body, much as exists for clinical trials.
  - The results of these studies should be retained in the database, regardless of their outcome;
  - If this system had been in place, the results of my study would have been available two years ago, and there would be no argument about their eligibility for the ISA.
- EPA should set aside funds for reanalysis of air pollution studies when appropriate, preferably through open competition among academic researchers.
- CASAC should include "replicability" as an explicit criterion for weighting air pollution studies. For some of the papers in the ISA, it's very hard for me to see how they could ever be replicated.

In conclusion, I thank you for your attention.

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The Need for a Tighter Particulate-Matter Air-Quality Standard

Independent Particulate Matter Review Panel

The Environmental Protection Agency (EPA) proposes to retain the current National Ambient Air Quality Standards (NAAQS) for fine particulate matter (particles with a diameter of ≤2.5 μm [$PM_{2.5}$]) — that is, levels not exceeding an annual average of 12 μg per cubic meter and a 24-hour average of 35 μg per cubic meter.[1] The current NAAQS were set in 2012 on the basis of a scientific review that was largely completed in 2010.[2] At that time, available epidemiologic evidence, supported by toxicologic evidence and a risk assessment conducted by EPA staff, indicated that annual exposure to $PM_{2.5}$ caused premature death at ambient concentrations as low as 11 μg per cubic meter. However, on the basis of more recent evidence, as described below, exposure to ambient $PM_{2.5}$ at the levels of the current standards is estimated by the EPA to be responsible for tens of thousands of premature deaths in the United States each year.[3]

The Clean Air Act requires air-quality standards that are "requisite to protect the public health" with an "adequate margin of safety." Such standards "shall accurately reflect the latest scientific knowledge" regarding "the kind and extent of all identifiable effects on public health." According to requirements of the Clean Air Act, the EPA administrator "shall appoint an independent scientific review committee," known as the Clean Air Scientific Advisory Committee, to periodically "review" the standards.

We were members of the EPA Clean Air Scientific Advisory Committee Particulate Matter (PM) Review Panel that was formed in 2015. By law, the Clean Air Scientific Advisory Committee, which we augmented, has seven members, including at least one physician. However, seven members are not enough to provide breadth, depth, and diversity of expertise, experience, and perspective in the multiple scientific disciplines necessary for these reviews. That is why, for four decades, the Clean Air Scientific Advisory Committee has been augmented with panels of additional experts for the periodic review of each regulated air pollutant. It has been common to have multiple experts in epidemiology, toxicology, and controlled human exposure studies on these panels, as well as experts in the measurement and modeling of air pollution, exposure and risk assessment, uncertainty analysis, and other areas.

In 2016, we advised the EPA administrator about the Integrated Review Plan for subsequent science and policy assessments. Our PM Review Panel was dismissed by press release on October 10, 2018, just before the draft science assessment was released. Shortly thereafter, we formed the nongovernmental Independent Particulate Matter Review Panel. Our volunteer panel continued to review the science and develop advice for the EPA administrator and the public. We reconvened, with support from the Union of Concerned Scientists and former EPA staff. During a 2-day meeting of our nongovernmental panel, conducted under the ground rules for an official EPA federal advisory committee, we deliberated on the strengths and limitations of available scientific evidence.[4]

In the past two decades, over multiple review cycles, the EPA has used evidence- and risk-based approaches to assess the NAAQS. The evidence-based approach takes into account empirical research on the health hazard posed by an air pollutant, as well as the ambient concentrations at which adverse effects are observed, and is based on a thoughtful and comprehensive synthesis of epidemiologic studies, controlled human exposure studies, and toxicologic studies in animals.[3,4] The risk-based approach uses concentration–response relationships inferred from key epidemiologic studies to estimate the population risk under current and potential alternative standards. Given uncertainties, the risk-based ap-

proach used by EPA staff provides useful qualitative insights regarding the magnitude of the risk and risk reduction. Our panel gave more weight to the evidence-based approach, with the risk-based approach providing supporting information.

We delivered our findings in a report submitted to the administrator and the EPA docket on October 22, 2019.[4] We concluded that the current $PM_{2.5}$ standards are insufficient to protect public health, on the basis of a review of the scientific evidence from epidemiologic studies, toxicologic studies in animals, and controlled human exposure studies; this evidence is consistent within each discipline and coherent among the multiple disciplines in supporting a causal, biologically plausible relationship between ambient concentrations well below the current $PM_{2.5}$ standards and adverse health effects, including premature death.[3] The epidemiologic evidence is consistent across studies with diverse designs, populations, pollutant mixtures, locations, and statistical approaches. For example, new epidemiologic studies consider large populations and report effects below the current annual standard, either by restricting the cohort analyzed to persons living in areas with lower levels of ambient exposure or because the average cohort exposures are well below the annual standard.[5-7] The populations in these studies are more than an order of magnitude larger than those in studies available for previous reviews, which has been made possible by scientific developments in quantification of spatial variability in ambient concentrations with the use of new modeling tools. We found no evidence for an ambient concentration threshold for health effects at the lowest observed levels, either for annual or for 24-hour exposure periods.

Populations with preexisting health conditions (e.g., cardiovascular disease, respiratory disease, diabetes, and obesity) or increased exposures (e.g., disadvantaged populations) represent a substantial portion of the U.S. population. These populations are at increased risk for harm from particulate air pollution, owing to their location near emission sources or to demographic or clinical characteristics (e.g., age or disease status) that increase their susceptibility.

The results of the evidence-based review clearly call into question the adequacy of the existing standards. Furthermore, the risk assessment conducted by the EPA shows that, in a sample of people 30 years of age or older living in 47 urban study areas, a large number of premature deaths are attributable to $PM_{2.5}$ exposure under the current standard.[3] The estimated all-cause mortality from long-term exposure to $PM_{2.5}$, calculated on the basis of the 2015 air quality adjusted to just meet the existing standards, ranges from 13,500 to 52,100 deaths annually. The actual air quality in the selected study areas is typically somewhat above the current standards and is adjusted downward, with the use of air-quality models, to enable quantification of what the risk would be if the current standards were met. In addition, the estimated all-cause mortality from short-term exposure to $PM_{2.5}$ ranges from 1200 to 3870 deaths annually. For locations in which ambient $PM_{2.5}$ concentrations would meet the annual standard but not the daily standard, the EPA estimates relative risk reductions of 21 to 27% by changing the standard from 12 μg per cubic meter to 9 μg per cubic meter. Although there is uncertainty around the estimates, the risk assessment supports the conclusions based on the scientific evidence that at the levels of the current fine-particle standards, the risk of premature death is unacceptably high.

The EPA risk assessment focused on all-cause mortality, mortality due to ischemic heart disease, and mortality due to lung cancer. Exposure to current levels of $PM_{2.5}$ is also causally linked to numerous other adverse health outcomes, including long- and short-term cardiovascular events, respiratory illnesses, death from cancers other than lung cancer, and nervous system diseases (e.g., cognitive decrements and dementia). Additional health concerns, such as adverse pregnancy and birth outcomes, are associated with particulate air pollution, although the evidence of causality is weaker.

We unequivocally and unanimously concluded that the current $PM_{2.5}$ standards do not adequately protect public health. An annual standard between 10 μg per cubic meter and 8 μg per cubic meter would protect the general public and at-risk groups. However, even at the lower end of the range, risk is not reduced to zero. The margin of safety increases as the level of the standard is lowered within this range. The choice of standard within this range is a policy judgment reserved for the EPA administrator. In the interest of environmental justice, we advised the administrator that disparities in health risk borne

by minority communities need to be taken into consideration in choosing a margin of safety.

In contrast to the recommendation of the EPA staff that the 24-hour $PM_{2.5}$ standard also be retained, the current 24-hour standard does not provide an adequate level of public health protection in locations for which the 24-hour standard, and not the annual standard, would be violated. On the basis of the scientific evidence, and with the acknowledgment that there is a continuum of adverse effects that decrease as the level of the standard decreases, the panel recommends that the 24-hour standard be set between 30 μg per cubic meter and 25 μg per cubic meter.

Between 2017 and 2018, all Clean Air Scientific Advisory Committee members were replaced. The seven-member committee newly appointed by the EPA largely reached a different conclusion than we did.[8] The lone physician–scientist on the committee found that the weight of evidence, including recent epidemiologic studies, reasonably calls into question the adequacy of the current long-term standard. However, the committee chair, an industry consultant, and some other members of the committee concluded that there is no evidence that calls into question the adequacy of the current standards. Nonetheless, the committee noted the "exceptional nature" of the current review, including the dismissal of our panel, the accelerated timeline, and the production of a policy assessment before the science assessment was completed. Although some committee members acknowledged our report, the Clean Air Scientific Advisory Committee largely disregarded the advice from our panel.

There is no doubt that on promulgating a final rule, the EPA will be sued. Federal courts have in the past given considerable deference to the Clean Air Scientific Advisory Committee regarding its scientific advice. Will the courts defer to a committee that has been arbitrarily and capriciously deprived of a particulate matter–specific expert panel? Or will the courts look elsewhere, such as to public comments from experts and input from the dismissed panel?

The dismissal of our review panel is just one of numerous recent ad hoc changes to scientific review of the NAAQS since 2017 that undermine the quality, credibility, and integrity of the review process and its outcome. Other changes include imposing nonscientific criteria for appointing the Clean Air Scientific Advisory Committee members related to geographic diversity and affiliation with governments, replacing the entire membership of the chartered committee over a period of 1 year, banning nongovernmental recipients of EPA scientific research grants from committee membership while allowing membership for persons affiliated with regulated industries, ignoring statutory requirements for the need for a thorough and accurate scientific review of the NAAQS in setting a review schedule, disregarding key elements of the committee-approved Integrated Review Plan, reducing the number of drafts of a document for committee review irrespective of whether substantial revision of scientific content is needed, commingling science and policy issues, and creating an ad hoc "pool" of consultants that fails to address the deficiencies caused by dismissing the Clean Air Scientific Advisory Committee PM Review Panel. The courts are already grappling with the ban on academic recipients of research grants.

Although our panel did not specifically assess other current EPA initiatives, there are at least two that are closely related to $PM_{2.5}$. One is the so-called Transparency in Regulatory Science proposed rule and supplement. This rule could exclude from regulatory consideration studies for which data are not publicly available, irrespective of their scientific rigor.[9] Such an exclusion could apply to studies based on data from human participants, including epidemiologic studies such as the seminal Harvard Six Cities and American Cancer Society studies, which were important in previous NAAQS reviews. The other initiative is a change to the EPA benefit–cost assessment to exclude "cobenefits." As an example, the Mercury and Air Toxics Standard for power plants reduces mercury emissions but has the cobenefit of also reducing $PM_{2.5}$ emissions.[10] For this and other rules, $PM_{2.5}$ cobenefits can be much larger than the direct benefits of reducing the pollutant specifically targeted by the rule. The multiple EPA initiatives aimed at undermining the appropriate role of scientific and economic assessment of adverse effects from $PM_{2.5}$ directly threaten health.

The 60-day public comment period for the proposed rule, which ends on June 29, 2020, is the last remaining opportunity for experts and stakeholders to provide input on a flawed rulemaking that ignores science and that will lead to avoidable premature deaths.

October 2019 meetings of the Independent Particulate Matter Review Panel were hosted by the Union of Concerned Scientists (UCS). Some panelists received travel reimbursement from UCS. Panelists did not accept honoraria or other compensation. This article reflects exclusively the deliberations of the panel.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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September 2, 2020

Letter to the Editor
New England Journal of Medicine
Retain the Current Particulate-Matter Air-Quality Standard

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The August 13 Sounding Board by the Independent Particulate Matter Review Panel (IPMRP)[1] incorrectly claims that fine particulate matter ($PM_{2.5}$) *causes* premature deaths in the United States and inappropriately criticizes the latest EPA CASAC assessment of $PM_{2.5}$ health effects.[2] There is no established etiologic means by which $PM_{2.5}$ *causes* deaths. Furthermore, objective meta-analysis of key results from the nine primary US cohorts finds NO relationship between $PM_{2.5}$ and total mortality (Table).[3] The original positive relationships used for establishing the 1997 $PM_{2.5}$ NAAQS have been invalidated by my independent reanalysis of the American Cancer Society Cancer Prevention Study[4] and the Harvard Six Cities Study.[3] The null findings of my reanalysis demonstrate the need for study data assess as per the proposed EPA rule "Transparency in Regulatory Science." This rule is opposed by the IPMRP, the *NEJM* Editor-in-Chief, eight Harvard professors who promote $PM_{2.5}$ deaths, and 86 other Harvard professors.[5] Extensive null epidemiological and toxicological evidence supports retaining the current $PM_{2.5}$ NAAQS. In fairness, the *NEJM* needs to publish a Sounding Board with this null evidence.

I report no potential conflict of interest relevant to this letter.

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Table: Random Effects Meta-Analysis of Nine US Cohorts That Analyzed Fine Particulate Matter (PM2.5) and Total (All-cause) Mortality[3]

Relative Risk (RR and 95% CI) of Total Mortality Associated with Increase of 10 $\mu g/m^3$ in $PM_{2.5}$

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)

From: **Letter** <letter@nejm.org>
Date: Thu, Sep 10, 2020 at 7:24 AM
Subject: RE: New England Journal of Medicine 20-28968
To: jenstrom@ucla.edu <jenstrom@ucla.edu>

Dear Dr. Enstrom,

I am sorry to say that the decision to decline your letter applied to both print and online publication.

Thank you for the opportunity to consider it.

Sincerely,

Caren Solomon, M.D., M.P.H.
Deputy Editor
New England Journal of Medicine

From: JAMES ENSTROM <jenstrom@ucla.edu>
Date: Tuesday, September 8, 2020 at 6:32 PM
To: "Solomon, Caren, M.D." <csolomon@nejm.org>
Subject: Fwd: New England Journal of Medicine 20-28968

September 8, 2020

Dear Deputy Editor Solomon,

I understand from the NEJM Author Center that "Letters accepted for publication will appear in print, on the *Journal's* website at NEJM.org, or both." Thus, please let me know if my letter to the editor was given consideration for publication ***only*** on the NEJM.org website, where there is no lack of space. In the interest of objectivity, NEJM should find a way to publish the strong evidence contained in my letter.

Thank you very much for your clarification regarding my letter.

Sincerely yours,

James E. Enstrom, PhD, MPH
jenstrom@ucla.edu
(310) 472-4274

AMERICAN CANCER SOCIETY
CANCER PREVENTION STUDY II

INSTRUCTIONS FOR RESEARCHERS

GENERAL INSTRUCTIONS:

Enroll about ten families; by families we mean households in which one or more persons live as a family unit. Each family must have **at least one person over the age of 45.** Please make a special effort to include families with people in their 50's and 60's. Enroll only those families you are reasonably certain will remain in the area for the next six years. If you can enroll more than ten families, please do so.

To help explain the purpose and plan of the study, leave a "Cancer Prevention Study II – Fact Sheet" with each family you enroll.

In each of the enrolled families, request that every member **over the age of 30** fill out a questionnaire, place it in the "Confidential Envelope," seal it and return it to you. Because of the size of the study, it is necessary to identify every questionnaire by a series of numbers. This is explained in item 3 below. Please follow the instructions carefully.

After collecting the questionnaires, fill out the four-page "List of Families and Persons Enrolled" folder. Include on this the name and address of a person who knows most of the enrolled families and who can act as a **substitute** for you during the next six years, if necessary. When this is completed, wrap the "Confidential Envelopes" (containing the completed questionnaires) in the "List of Families and Persons Enrolled" folder, secure with a rubber band and place in the large envelope. Deliver all completed materials according to the instructions you have been given.

DETAILED INSTRUCTIONS:

1. Check this packet to be sure that it contains:
   a) a supply of questionnaires for men (printed on blue paper);
   b) a supply of questionnaires for women (printed on white paper);
   c) a supply of "Confidential Envelopes;"
   d) a four-page "List of Families and Persons Enrolled" folder; and
   e) a supply of "Fact Sheets."
2. On the back of this instruction sheet, list the families (households) you know in which there is at least one person over the age of 45. The term "household" includes people living together as a family unit and also includes single persons living alone.

   Visit each family on your list and enroll only those you feel will be in the area during the next six years. Request that every member **over the age of 30** fill out a questionnaire. Do not exclude a family if one or two members refuse or fail to fill out a questionnaire after others have done so.
3. For purposes of identification, you have been assigned a Division No., Unit No., Group No., and Researcher No. Copy these numbers onto all questionnaires and confidential envelopes you use. In addition, be sure to enter all these identifying numbers, your name and address, and the name and address of a substitute who knows most of the families you have enrolled, on the top of the "List of Families and Persons Enrolled" folder.

Assign a Family No. to each family you enroll, the first being Family No. 1, the second being Family No. 2, etc. Also assign a Person No. to each person you enroll in **each** family, one member of a family being Person No. 1, another being Person No. 2, etc.

For example, your first family (Family No. 1) may consist of Mr. and Mrs. Doe; their 35-year-old son, Paul Doe; the wife's mother, Mrs. Smith; and a friend, Mr. Johnson. Thus, for Family No. 1, Mr. Doe is Person No. 1, Mrs. Doe is Person No. 2, Paul Doe is Person No. 3, Mrs. Smith is Person No. 4, and Mr. Johnson is Person No. 5. Next, Mr. and Mrs. Brown may be Family No. 2; Mr. Brown being Person No. 1; Mrs. Brown, Person No. 2, etc. in the family.

4. When a person agrees to fill out a questionnaire, write his or her name and all of the identifying numbers (including Family No. and Person No.) at the top of a questionnaire. Also write his or her name and **address** and all the identifying numbers on a "Confidential Envelope."

   Give the questionnaire and the "Confidential Envelope" to the participant. The questionnaire is designed to be filled out by the person **and the answers are confidential.** Ask that the participant fill out the questionnaire and then put it in the envelope and seal it. You are responsible for collecting the sealed envelopes. You may either wait while the participant completes the questionnaire or, if you prefer, you may leave the questionnaire and return some time later to pick it up.

5. Try to enroll all your families and collect the filled-out questionnaires within two weeks.

6. After you have collected completed questionnaires from all the people you have enrolled, fill out the "List of Families and Persons Enrolled," according to the instructions printed on this blue folder.

7. After this is completed, wrap the "Confidential Envelopes" in the "List of Families and Persons Enrolled" folder, secure with a rubber band and place in the large envelope and return it according to the instructions you have been given.

PURPOSE AND PLAN OF THIS STUDY

The first American Cancer Society Prevention Study was conducted over a 13-year period, from 1959-1972, and helped us identify a number of factors related to the development of cancer. In fact, most of what we know today about the causes of cancer has come from such epidemiologic studies. Cancer Prevention Study I, for instance, established cigarette smoking as a cause of lung cancer and implicated tobacco use in the development of other cancers, and heart and respiratory diseases. Other epidemiologic studies have linked skin cancer to a heavy exposure to X-rays, arsenic or certain types of tars and oils, bladder cancer to workers exposed to certain chemicals, and lung cancer to a long-term exposure to asbestos fibers. These are some of the environmental factors which can cause cancer. It is only by following a large number of people for a long period of time, as we plan to do in Cancer Prevention Study II, that we can uncover many other factors and determine which are hazardous to health and which ones are not.

In Cancer Prevention Study II, we are going to turn our attention to the changes that have occurred since our first study in the way we live, the products we use, and in our home and workplace environments. Recently, there has been widespread concern about the safety of saccharin, hair dyes, oral contraceptives, tranquilizers, and other drugs and medications. The effects of long-term exposure to X-rays, air and water pollutants, and carcinogens in the workplace have also been questioned. The

public and the scientific community want to find out the reason for the increased rates of cancer in black populations and pinpoint the special cancer risks among other minorities.

The plan of the American Cancer Society's new Cancer Prevention Study is to enroll more than 1,000,000 persons and to follow them for six years, and perhaps longer. As a volunteer researcher, you will be instrumental in helping to assemble vital research data. By keeping track of the persons you enroll, and reporting on them every other year, you will provide our health statisticians with information on how life-styles affect health and what factors either increase or decrease chances of getting cancer and other diseases.

Such an endeavor will add to our knowledge of cancer and enable us to identify those factors which cause cancer and can be controlled, as well as those which do not appear to increase risk of developing cancer. The final goal, of course, is to prevent cancer and save thousands of lives.

SOME QUESTIONS YOU MAY BE ASKED BY PEOPLE YOU ENROLL

Q. Why was I selected for this study?

A. We need to enroll a large sample of the American public: people of different ages, geographic areas, races, religions, habits, exposures, and life-styles. This way we'll find out which groups have higher cancer risks and which have lower ones.

Q. Are you interested mainly in people with cancer?

A. No, we are interested in all people, those who are in good health, as well as those who have or have had cancer.

Q. My 25-year-old son lives with me. Why don't you want him to answer the questionnaire?

A. We are excluding people below 30 because they have not been exposed to the factors under study as long as older people have. Also, the frequency of cancer generally increases with age and there would not be enough data to study if we enrolled people under 30.

Q. We already know that cigarette smoking causes cancer. Why do we need another study?

A. The cigarettes now smoked by more than fifty million people are considerably different from the ones smoked at the time of our first study. We need to determine whether low tar and low nicotine cigarettes have substantially affected health risks. We are also investigating the effects of cigarette smoking in the workplace environment and the possible health effects of "second-hand" smoke, that is, smoke inhaled by non-smokers.

Q. Why did you ask for my Social Security Number? Isn't that illegal?

A. Giving us your Social Security Number is strictly voluntary. By doing so, you will save us much time, effort and money in verifying our records later on (especially for people with the same names). Incidentally, it is not illegal to ask for your number; it is illegal to **require** it.

Q. Will the information on the questionnaire be kept confidential?

A. Yes. It will be used only for research purposes. We will **never** release information about any particular person and will not release addresses to any agency for any purpose, whatsoever.

AMERICAN CANCER SOCIETY
CANCER PREVENTION STUDY II
FACT SHEET

Thank you for agreeing to participate in the American Cancer Society's Cancer Prevention Study II. By completing the questionnaire, you will join one million other Americans who are helping us advance our knowledge of the causes and prevention of cancer. Such knowledge will enable us to work toward the goal of preventing cancer and saving thousands of lives.

THE FIRST STUDY: 1959-72

Data for the first Cancer Prevention Study were gathered over a 13-year period, from 1959-72, and helped us identify many factors related to cancer development. Information from study participants on personal habits and lifestyles, family and medical history, physical condition, and workplace exposures provided invaluable information about the risks of cancer. The study was instrumental in clarifying the link between smoking and cancer and in showing obesity is related to certain cancers. Information from the study also furnished data on risks for heart disease, stroke and other diseases. The landmark Surgeon General's Report on Smoking and Health was based in part on data from this American Cancer Society Study.

So far, about 65 scientific papers have been published from data in the study. These include a recent report that cigarettes lower in tar and nicotine reduce, but do not eliminate, the risk of lung cancer.

WHY A SECOND STUDY?

Since the first Cancer Prevention Study, many changes have taken place in the way we live, the foods we eat, the products we use, and in our home and workplace environments. In 1959 few people questioned the health effects of high fat or high cholesterol diets or the safety of many consumer products, such as artificial sweeteners, coffee, or hair dyes. Birth control pills and certain other drugs and medications were only starting to be widely used.

Since 1959, we have grown more aware of pollutants in our air and water, and carcinogens in the workplace. There is also increasing concern over the rising rates of cancer among blacks and the special health problems of minorities. A large study like this is the most effective way to find out which environmental factors increase cancer risk and need most control, and which carry little or no risk.

YOUR PART

Please answer every question. Be assured that the information you supply will be kept *confidential* and will be used *only* for research purposes. Your personal data will never be released to anyone for any reason. Later you may be given a short supplementary questionnaire. If you have any questions about your participation in this study, please contact your local American Cancer Society office.

Again we'd like to thank you for volunteering information that can help the American Cancer Society intensify its efforts in preventing cancer.

QUESTIONS YOU MAY HAVE ABOUT THIS STUDY

Q. Why was I selected for this study?
A. We need to enroll a cross-section of Americans: people of different ages, geographic areas, races, religions, occupations, exposures, and lifestyles. In this way we'll find out which groups have higher or lower risks.

Q. Are you interested mainly in people with cancer?
A. No, we are interested in all people now in good health, including those who have had cancer.

Q. My 25-year-old son lives with me. Why don't you want him to answer the questionnaire?
A. We are excluding people under 30 because the frequency of cancer generally increases with age and there would not be enough data to study younger persons.

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A. The cigarettes now being smoked are considerably different from the ones smoked at the time of our first study. We need to determine whether low tar and nicotine cigarettes have substantially affected health risks.
We are also studying the effects of cigarette smoking in workplace environments and the possible risks of "secondhand" smoke, smoke inhaled by nonsmokers.

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A. Giving us your Social Security Number is strictly voluntary. By doing so, you will save us time, effort and money in later verifying our records (especially for people with the same last names).

Q. Will my information be kept confidential?
A. Yes. We will use it only for research purposes and will not release addresses to any agency for any purpose.