Table 2. Countries of Origin for Research Article Funding Sources Included in US Preventive Services Task Force Systematic Reviews, 2014–2016[a]

Country	Articles, No. (%)[b]
United States	640 (39)
United Kingdom	177 (11)
Australia	67 (4)
Canada	66 (4)
The Netherlands	64 (4)
Denmark	62 (4)
Japan	50 (3)
Germany	47 (3)
Sweden	36 (2)
France	32 (2)
Finland	30 (2)
Switzerland	29 (2)
Italy	28 (2)

[a] Other countries that supported less than 2% of articles are not listed in the Table, including Norway, Spain, Belgium, New Zealand, China, South Korea, Ireland, Taiwan, India, Israel, Iran, Brazil, Greece, Greenland, Saudi Arabia, Singapore, Sri Lanka, Thailand, United Arab Emirates, Argentina, Austria, Mexico, Philippines, and Scotland.

[b] Percentages do not add to 100% because some articles reported more than 1 funding source.

identified for 79% of the research articles. Government agencies provided support for 931 articles (56%). The remaining support came from nonprofits or universities (530 articles, 32%) and industry (282 articles, 17%). The sources of funding varied by recommendation topic; for example, behavioral counseling for sexually transmitted infections had the highest proportion of government funding (91%), whereas screening for chlamydia and gonorrhea had the highest proportion of industry funding (75%). The sources of funding originated from 37 countries with 640 articles (39%) supported by US-based funders (**Table 2**). The National Institutes of Health (NIH) was the single largest contributor (420 articles, 25%). The next largest funders were the United Kingdom's Medical Research Council (48 articles, 3%), the US Centers for Disease Control and Prevention (39 articles, 2%), Australia's National Health and Medical Research Council (37 articles, 2%), the United Kingdom's National Health Service Research and Development Programme (36 articles, 2%), and the Netherlands Organisation for Health Research and Development (35 articles, 2%).

Discussion | The USPSTF considered scientific evidence supported by a broad range of funders in making recommendations for clinical preventive services. Government agencies worldwide provided funding for most of the research articles, with the NIH being the largest funder. This finding is important because physicians may view certain funders (ie, industry) as less credible than others (ie, NIH).[4]

Many of the research articles were supported by governments and organizations outside of the United States. Although the preventive services evidence base includes many high-quality studies conducted in the United States, there are well-designed clinical and epidemiologic studies carried out abroad that further enhance it.

Because this study identified funding sources from research articles as opposed to research studies, the results may overestimate the contributions of funders that supported large studies with results reported in more than 1 scientific article included in the systematic reviews. Another limitation is missing data: 21% of the articles reviewed did not identify any funding source, potentially lessening the precision of the estimates of funding support.

Future studies should investigate the sources of funding for the evidence base of other national clinical guidelines.

Jennifer Villani, PhD, MPH
Quyen Ngo-Metzger, MD, MPH
Isaah S. Vincent, PhD
Carrie N. Klabunde, PhD

Author Affiliations: Office of Disease Prevention, National Institutes of Health, Rockville, Maryland (Villani, Vincent, Klabunde); Agency for Healthcare Research and Quality, Rockville, Maryland (Ngo-Metzger).

Accepted for Publication: April 4, 2018.

Corresponding Author: Jennifer Villani, PhD, MPH, Office of Disease Prevention, National Institutes of Health, 6100 Executive Blvd, Ste 2B03, Rockville, MD 20892 (villani@nih.gov).

Author Contributions: Dr Villani had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: All authors.
Acquisition, analysis, or interpretation of data: Villani, Ngo-Metzger, Vincent.
Drafting of the manuscript: Villani, Ngo-Metzger.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Villani, Vincent.
Administrative, technical, or material support: Vincent.
Supervision: Villani, Klabunde.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. The Agency for Healthcare Research and Quality (AHRQ) supports the US Preventive Services Task Force. No other disclosures were reported.

Disclaimer: The views expressed in this article are solely the opinions of the authors and do not necessarily reflect the official policies of the US Department of Health and Human Services, the National Institutes of Health (NIH), or AHRQ; nor does mention of the department or agency imply endorsement by the US government.

Additional Contributions: We thank the AHRQ and the Evidence-based Practice Centers at Kaiser Permanente, RTI International—University of North Carolina, Pacific Northwest/Oregon Health and Science University, University of Alberta, and Vanderbilt for providing full citations of research articles; Elizabeth Neilson, PhD, MPH, MSN, Kathryn Koczot, and David Tilley, MPH, MS, CPH (all from NIH Office of Disease Prevention), for assistance with study design, data collection and cleaning, and analytic advice, respectively. Their assistance was provided as part of their official duties in the NIH Office of Disease Prevention.

Additional Information: NIH staff led the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

1. US Preventive Services Task Force. About the USPSTF. https://www.uspreventiveservicestaskforce.org/Page/Name/about-the-uspstf. Accessed February 16, 2018.

2. Krist AH, Wolff TA, Jonas DE, et al. Update on the methods of the US Preventive Services Task Force: methods for understanding certainty and net benefit when making recommendations. *Am J Prev Med*. 2018;54(1S1):S11-S18.

3. US Preventive Services Task Force. Published recommendations. https://www.uspreventiveservicestaskforce.org/BrowseRec/Index. Accessed February 16, 2018.

4. Kesselheim AS, Robertson CT, Myers JA, et al. A randomized study of how physicians interpret research funding disclosures. *N Engl J Med*. 2012;367(12):1119-1127.

COMMENT & RESPONSE

Air Pollution and Mortality in the Medicare Population

To the Editor Mr Di and colleagues[1] found that short-term exposures to ambient fine particulate matter ($PM_{2.5}$) and

ozone were associated with increased mortality in older adults using statistical analyses of a large database. However, they used incomplete exposure data and an inappropriate outcome measure, and they neglected regional variability.

The 1952 London fog established the lethality of air pollution.[2] The measure of risk used to investigate that event was the sum over lag days, but Di and colleagues relied on significance testing of individual lags of 0 or 1 day. Summing over lags from 0 to 4 days would increase the estimated risk.

Exposures were limited to outdoor air, although most individuals spend 85% of their time indoors, where $PM_{2.5}$ can be augmented by indoor sources[3] and ozone is adsorbed onto interior surfaces.

$PM_{2.5}$ is not a pollutant per se but a regulatory construct largely based on facility of monitoring. It comprises a mixture of various particle sizes and composition, only some of which may be toxic, elemental carbon being more important than sulfate.[4] When $PM_{2.5}$ composition and toxicity vary, a counterintuitive dose-response function, as shown in Figure 5 in the article,[1] may result. Subgroup analyses of regions having typically different $PM_{2.5}$ compositions would have been useful.

Persons most at risk and physiological mechanisms remain largely unknown. Di and colleagues found risks sharply increasing with age but posited that a random individual could succumb to a small perturbation in outdoor air quality. Another mortality model considered prior frailty and acute excursions of pollution and temperature combined.[5] This model estimated that deaths among older persons in Chicago were limited to a small subset of frail individuals for which PM_{10}, ozone, nitrogen dioxide, sulfur dioxide, or carbon monoxide contributed losses of fewer than 2 days. It found an increased mortality risk for this frail population over 15 days of 0.83% with each increase of 10 $\mu g/m^3$ of PM_{10}, similar to the results of the current study. In this alternative model, thresholds could occur with decreases in either individual frailty or pollution, but the former is unlikely because a day without frailty would be rare.

Frederick W. Lipfert, PhD

Author Affiliation: Greenport, New York.

Corresponding Author: Frederick W. Lipfert, PhD, 1500 Brecknock Rd, Apt 155, Greenport, NY 11944 (fred.lipfert@gmail.com).

Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

1. Di Q, Dai L, Wang Y, et al. Association of short-term exposure to air pollution with mortality in older adults. *JAMA*. 2017;318(24):2446-2456.

2. Lipfert FW. *Air Pollution and Community Health: A Critical Review and Data Sourcebook*. New York, NY: Wiley; 1994.

3. Lipfert FW. An assessment of air pollution exposure information for health studies. *Atmosphere*. 2015;6(11):1736-1752. doi:10.3390/atmos6111736

4. Lipfert FW, Wyzga RE, Baty JD, Miller JP. Air pollution and survival within the Washington University-EPRI veterans cohort: risks based on modeled estimates of ambient levels of hazardous and criteria air pollutants. *J Air Waste Manag Assoc*. 2009;59(4):473-489.

5. Murray CJ, Lipfert FW. Inferring frail life expectancies in Chicago from daily fluctuations in elderly mortality. *Inhal Toxicol*. 2013;25(8):461-479.

To the Editor In a case-crossover study, the authors noted that "In the US Medicare population from 2000 to 2012, short-term exposures to $PM_{2.5}$ and warm-season ozone were significantly associated with increased risk of mortality. This risk occurred at levels below current national air quality standards, suggesting that these standards may need to be reevaluated."[1] Such studies of association fail to address the key causal question: How would public health effects change if exposure concentrations were reduced? Instead, they addressed an easier, noncausal question: What are the estimated ratios (or slope factors or regression coefficients) of health effects to past pollution levels in selected models and data sets? Answers to the second question are inadequate substitutes for answers to the first question for several reasons.

First, published associations are often assumption and model dependent. Exposure may have a positive association with mortality in some regression models and a negative association in others; which is reported depends on the model selected.[2] Second, omitted confounders can create spurious exposure-response associations. Mr Di and colleagues[1] omitted lagged temperatures for days 2 to 7. Yet, in publicly available data,[3] lagged temperatures were associated with both $PM_{2.5}$ and mortality. $PM_{2.5}$ predicts mortality only if lagged temperatures are omitted.

Third, model specification errors create spurious associations. In data from Los Angeles, $PM_{2.5}$ predicted mortality using Poisson regression by reducing specification error; in nonparametric analyses, it was not a predictor.[3] Fourth, ignored measurement errors can create spurious low-dose associations.[4] The model used by Di and colleagues[1] omitted exposure measurement error. This can make even threshold exposure-response relations look linear at low doses,[4] consistent with the finding in the study that responses "were almost linear, with no indication of a mortality risk threshold at very low concentrations."[1]

Evaluating adequacy of air quality standards requires addressing the first causal question. Causal analytics methods and software can help. Doing so will give regulators the scientific information they most need.

Louis Anthony Cox Jr, PhD

Author Affiliation: Cox Associates, Denver, Colorado.

Corresponding Author: Louis Anthony Cox Jr, PhD, Cox Associates, 503 N Franklin St, Denver, CO 80218 (tcoxdenver@aol.com).

Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported receiving personal fees from the US Environmental Protection Agency (EPA), Society for Epidemiological Research, Society for Benefit Cost Analysis, and American Industrial Hygiene Council; fees to his company from the American Chemistry Council (ACC), American Petroleum Institute (API), and their members; salary for teaching from the University of Colorado; serving as the chair of the US EPA Clean Air Science Advisory Committee and a board member of EPA's Science Advisory Board; and being editor in chief of *Risk Analysis: An International Journal*.

Disclaimer: The contents of this letter are solely the views of the author and do not necessarily represent any view or opinion on behalf of EPA, its Clean Air Science Advisory Committee, API, ACC, *Risk Analysis*, or the Society for Risk Analysis.

1. Di Q, Dai L, Wang Y, et al. Association of short-term exposure to air pollution with mortality in older adults. *JAMA*. 2017;318(24):2446-2456.

2. Dominici F, Greenstone M, Sunstein CR. Science and regulation: particulate matter matters. *Science*. 2014;344(6181):257-259.

3. Cox LAT Jr. Do causal concentration-response functions exist? a critical review of associational and causal relations between fine particulate matter and mortality. *Crit Rev Toxicol*. 2017;47(7):603-631.

4. Rhomberg LR, Chandalia JK, Long CM, Goodman JE. Measurement error in environmental epidemiology and the shape of exposure-response curves. *Crit Rev Toxicol*. 2011;41(8):651-671.

To the Editor There are many aspects of the study by Mr Di and colleagues[1] that call into question their finding that air quality was associated with increased deaths: size of the effects, modeling bias, and flexibility of analysis. These methodological aspects are especially concerning given that recent large studies found no association between air quality and mortality.[2,3]

The size of the effects in the study by Di and colleagues were small, 1% or less. Any small bias or model misspecification could produce such a small effect,[4] as could aspects of the analysis, such as multiple testing and multiple modeling.[5] For example, the baseline factors in Table 1 in the article[1] could produce 80 subgroup analyses. Consider the treatment of temperature and time lags. Each could exert an effect on the day in question or either of the previous 2 days, for 3 × 3 = 9 combinations. Modeling of exposure data could produce 720 possible analyses. Although the authors cited no negative studies, one offers a possible explanation for the positive results of the current analysis: confounding variables that differ across locations.[3] Di and colleagues did not do a within- and across-location analysis.

When results are dependent on statistical analyses, it is the obligation of the authors to provide strong evidence, address conflicting studies, and make their data set and analysis code available. Considering the number of analysis options available, the results of this study could have been the result of the analysis choices made.

S. Stanley Young, PhD

Author Affiliation: CGStat, Raleigh, North Carolina.

Corresponding Author: S. Stanley Young, PhD, CGStat, 3401 Caldwell Dr, Raleigh, NC 27607 (genetree@bellsouth.net).

Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

1. Di Q, Dai L, Wang Y, et al. Association of short-term exposure to air pollution with mortality in older adults. *JAMA*. 2017;318(24):2446-2456.

2. Young SS, Smith RL, Lopiano KK. Air quality and acute deaths in California, 2000-2012. *Regul Toxicol Pharmacol*. 2017;88:173-184.

3. Greven S, Dominici F, Zeger S. An approach to the estimation of chronic air pollution effects using spatio-temporal information. *J Am Stat Assoc*. 2011;106(494):396-406.

4. Young SS. Statistical Analyses and Interpretation of Complex Studies. Medscape. 2008. https://www.medscape.org/viewarticle/571523. Accessed January 4, 2018.

5. Simonsohn U, Nelson LD, Simmons JP. P-curve: a key to the file-drawer. *J Exp Psychol Gen*. 2014;143(2):534-547.

In Reply Dr Lipfert criticizes our study for not including indoor-generated particles in our exposure. Indoor particles are a potential confounder, not an omitted part of outdoor particles. Differences in indoor exposure across persons cannot confound the results of our case-crossover study; the exposure contrast was within person, between case and control days. To confound, daily variation in particles from cooking, smoking, etc, must be correlated with daily variation in outdoor $PM_{2.5}$ of the same person. The Medicare Beneficiary Survey showed that 86% of beneficiaries were nonsmokers. It seems implausible that smokers consistently smoked more or that people fried more food on higher pollution days.

We believe total early deaths is an appropriate and policy-relevant outcome. We agree that frailty is an issue and examined modification by sex, race/ethnicity, poverty, and age; in other studies, medical conditions were examined as predisposing.[1] We disagree that only frail people die from air pollution; multicity studies have shown that this is not the case.[2] It would be useful to examine regional variations to learn about particle composition, but that does not imply that our national estimate is biased as a national average estimate. Such examination requires defining region by pollution mix and not census categories, a substantial effort we will consider in the future. In addition, many studies have found that for all-cause mortality, lags 0 and 1 are the most relevant averaging period.

Dr Cox questions our finding of effects below the US Environmental Protection Agency's current standard because with a wide range of exposure and considerable exposure error, nonlinear relationships may look linear. However, this is not relevant to our analysis restricted to observations when $PM_{2.5}$ was below 25 $\mu g/m^3$, well below the current standard of 35 $\mu g/m^3$. Because the root mean squared error of our exposure model was 2.7 $\mu g/m^3$, a significant association in the restricted analysis cannot be due to exposure error. Cox also cites a report that the association between $PM_{2.5}$ and daily deaths disappeared after control for more lags of temperature. Other studies have differed. In a 14-city case-crossover study,[3] a larger effect size for particles controlling for temperature lags 0 through 4 was found than with lags 0 and 1. Cox argues that causal modeling methods would be useful in air pollution epidemiology. We agree, and several causal modeling analyses of this question have been published, with more planned.[4,5] They all support the association we reported in this study.

Dr Young argues that our effect size estimate was small and that there are many possible choices that could affect our result, including subgroups analyzed, how covariates are modeled, and that the study could have been confounded by variables in Table 1 of our article that differed across locations. Because our primary analysis was all beneficiaries, the implication that choices of subgroups could affect the outcome is not correct. Variables that differ across locations cannot be confounders in a case-crossover analysis because the analysis was within person. Exposure contrasts were within participants, on a case day and nearby

control days at the same location. Moreover, because the analysis controls for all slowly varying individual covariates by matching, no question of different functional forms arises for those covariates. As for the effect size, our effect size is close to those of other large national studies, as well as recent meta-analyses.[6] The studies in the meta-analysis used multiple different modeling techniques and arrive at similar results to ours, indicating the robustness of the results, despite the outlier study he cites.

Joel D. Schwartz, PhD

Author Affiliation: Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, Massachusetts.

Corresponding Author: Joel D. Schwartz, PhD, Department of Environmental Health, Harvard T.H. Chan School of Public Health, Landmark Center W 404H, Boston, MA 02215 (jschwrtz@hsph.harvard.edu).

Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported receiving grants from the National Institutes of Health and the US Environmental Protection Agency and having been an expert consultant for the US Department of Justice regarding health impacts of Clean Air Act violations.

1. Bateson TF, Schwartz J. Who is sensitive to the effects of particulate air pollution on mortality? a case-crossover analysis of effect modifiers. *Epidemiology*. 2004;15(2):143-149.

2. Zanobetti A, Schwartz J, Samoli E, et al. The temporal pattern of mortality responses to air pollution: a multicity assessment of mortality displacement. *Epidemiology*. 2002;13(1):87-93.

3. Schwartz J. The effects of particulate air pollution on daily deaths: a multi-city case crossover analysis. *Occup Environ Med*. 2004;61(12):956-961.

4. Schwartz J, Bind MA, Koutrakis P. Estimating causal effects of local air pollution on daily deaths: effect of low levels. *Environ Health Perspect*. 2017;125(1):23-29.

5. Wang Y, Lee M, Liu P, et al. Doubly robust additive hazards models to estimate effects of a continuous exposure on survival. *Epidemiology*. 2017;28(6):771-779.

6. Atkinson RW, Kang S, Anderson HR, Mills IC, Walton HA. Epidemiological time series studies of PM2.5 and daily mortality and hospital admissions: a systematic review and meta-analysis. *Thorax*. 2014;69(7):660-665.

Surgical Procedures for Patients With Severe Obesity

To the Editor The Editorial by Drs Arterburn and Gupta summarized the results of 2 randomized clinical trials comparing sleeve gastrectomy and Roux-en-Y gastric bypass.[1] Based on the 5-year results of these trials,[2,3] the authors concluded that the procedures "are overall quite similar in terms of their effects on weight and comorbid conditions," with a 1-unit difference in body mass index (BMI) between them at 5 years. We have a few concerns about this conclusion.

The equivalence in weight loss is not clear. The Sleeve vs Bypass (SLEEVEPASS) study[3] did not find the groups to be equivalent at a predefined margin of −9% to +9%. As mentioned in both studies, since the time of their design, excess weight loss has been replaced by total body weight loss as the standard outcome reporting measure in bariatric surgery.[4] Using that metric, both studies demonstrated significantly higher weight loss with gastric bypass than sleeve gastrectomy (28.1% vs 24.9% [P = .001][3] and 28.6% vs 25.0% [P = .02][2]). Excess weight-based measurements fail to adequately account for initial BMI.[4] The 3% to 4% total weight loss difference is similar to the weight loss observed with pharmacotherapy for obesity.[5] The clinical significance of this difference is unknown.

As mentioned in the Editorial, the reoperation rates were similar but of variable etiologies for the procedures. In the 2 studies, 5.8% to 9.0% of patients undergoing sleeve gastrectomy required conversion to Roux-en-Y gastric bypass for gastroesophageal reflux, and 8.7% to 14.3% of patients undergoing Roux-en-Y gastric bypass required reoperation for internal hernia.[2,3] A crucial differentiator is that an established strategy to decrease internal herniation after Roux-en-Y gastric bypass is available (closure of the mesenteric defects); however, this procedure was not routinely performed in either of the trials. There is no established modality to successfully prevent the development of severe reflux after sleeve gastrectomy. Closure of hiatal hernia at the time of sleeve gastrectomy is likely to decrease the development of gastroesophageal reflux disease symptoms, but the effect size and durability of this intervention is unknown.

Modification of Roux-en-Y gastric bypass technique to decrease the incidence of internal herniation may result in a bariatric intervention with higher weight loss and lower reoperation rate, favoring its performance over sleeve gastrectomy for the majority of patients. We agree with the Editorial that procedure selection for each patient is a complex process requiring patients to consider multiple factors, supported by their physicians in patient-centered shared decision making.

Tyler Cohn, MD
Aurora Pryor, MD
Konstantinos Spaniolas, MD

Author Affiliations: Stony Brook University, Stony Brook, New York.

Corresponding Author: Tyler Cohn, MD, Stony Brook University, Health Sciences Tower, Ste T18-040, Stony Brook, NY 11794-8191 (tyler.cohn@stonybrookmedicine.edu).

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Pryor reported receiving personal fees from Merck, Medtronic, Gore, Ethicon, and Stryker, and grants from Baronova and Obalon. No other disclosures were reported.

1. Arterburn D, Gupta A. Comparing the outcomes of sleeve gastrectomy and Roux-en-Y gastric bypass for severe obesity. *JAMA*. 2018;319(3):235-237.

2. Peterli R, Wölnerhanssen BK, Peters T, et al. Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass on weight loss in patients with morbid obesity: the SM-BOSS randomized clinical trial. *JAMA*. 2018;319(3):255-265.

3. Salminen P, Helmiö M, Ovaska J, et al. Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass on weight loss at 5 years among patients with morbid obesity: the SLEEVEPASS randomized clinical trial. *JAMA*. 2018;319(3):241-254.

4. Brethauer SA, Kim J, el Chaar M, et al; ASMBS Clinical Issues Committee. Standardized outcomes reporting in metabolic and bariatric surgery. *Surg Obes Relat Dis*. 2015;11(3):489-506.