Public Comments for Chartered CASAC's Peer Review of EPA's Integrated Science Assessment for Particulate Matter (External Review Draft - October 2018)

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My name is Kevin Cromar, PhD, and I am the Director of the Air Quality Program at the Marron Institute of Urban Management, an associate professor of environmental medicine and population health at NYU School of Medicine, and a member of the Utah Air Quality Board. I am speaking today in my role as the vice-chair of the Environmental Health Policy Committee of the American Thoracic Society.

The purpose of these comments is to publically recognize the quality and rigor of the PM ISA that has been prepared for external review.[i] In reviewing the document, we find that the ISA has appropriately focused on findings across multiple disciplines using a variety of study designs and draws upon the results of relevant studies of sufficient quality. The document is a good representation of the scientific evidence concerning health effects of particle pollution and the scientific conclusions and causal determinations are supported by a well-constructed framework.[ii] It is our opinion that the authors of the ISA have used sound scientific judgment in evaluating the variety of study designs, results, and analyses and have carefully avoided erroneous inferences about estimated effects and causal relationships.

Scientists have long debated how to best infer causality in empirical research.[iii] There has been sufficient confusion and recent interest in causality to merit a brief discussion of the topic. Causal inference techniques, as utilized in observational studies, are designed to eliminate confounding bias from estimates of causal effects[iv] or in other cases to assess the sensitivity of causal conclusions with respect to unmeasured confounding.[v] What is critical to note is that while statistical models can permit valid inferences about causal mechanisms under specific assumptions, these assumptions are rarely, if ever, fully satisfied.[vi] This is why scientific judgment is always necessary, regardless of the statistical approach used in a research study, in order to assess the plausibility of potential causal relationships. The true value of causal inference tools (whether it be structural equation models, causal diagrams, mediation analysis, sensitivity analysis, etc.) is not to provide absolute claims of causality but rather to help "clarify important relationships and pathways [that] contribute to the development of mechanism-based explanations."[vii]

We have a high level of confidence that the causal conclusions reported in the ISA cannot be explained away by unmeasured confounders or other unidentified biases. This confidence is based, in part, on the ISA's consideration of multiple studies for each health endpoint conducted in various settings using different subjects, pollution exposures, and assessed using a variety of statistical approaches. For this reason we strongly disagree with the notion that associations of the health impacts of particle pollution cannot help inform causal determinations in the ISA unless specific statistical approaches were used. While there are many different statistical

methods available to detect and control for potential confounding and to address potential bias, none of these individual methods by themselves is completely satisfactory. Therefore, it is not advisable to seek for a uniform statistical approach to addressing issues of causality in air pollution research; rather scientists should continue to conduct studies using a wide-range of reasonable statistical approaches to provide the strongest evidence to help in the scientific evaluation of causal relationships.

Finally, if there are genuine concerns regarding the ability of observational studies to contribute to our understanding of causality in the ISA, it is not sufficient to simply appeal to the possibility of misspecification or omission of confounders based solely on study design. Rather, such concerns regarding unaccounted confounding must be substantiated explicitly before a study is dismissed from providing information relevant to assessing causal relationships between particle pollution and relevant health outcomes.

Signed,

Kevin Cromar, PhD

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[i] U.S. EPA. Integrated Science Assessment (ISA) for Particulate Matter (External Review Draft). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-18/179, 2018.

[ii] U.S. EPA. Preamble to the Integrated Science Assessments (ISA). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-15/067, 2015.

[iii] Pearl J. "Causal diagrams for empirical research (with discussions)." Biometrika (1995), 82, 4, p669-710. Available (as of 12/5/2018) at: http://bayes.cs.ucla.edu/R218-B.pdf

[iv] Pearl, J. (2009). Causal inference in statistics: An overview. Statistical Surveys, vol. 3, p 96-146.

[v] Ding, Peng; VanderWeele, Tyler J. "Sensitivity Analysis Without Assumptions." Epidemiology: (2016) 27, 3, p368–377. doi: 10.1097/EDE.0000000000000457

[vi] Rubin, D. (2009). Author's reply: Should observational studies be designed to allow lack of balance in covariate distributions across treatment groups? Statistics in Medicine, 28, 1420-1423.

[vii] Pratschke J, Haase T, Comber H, Sharp L, Cancela M, and H Johnson. "Mechanisms and mediation in survival analysis: toward an integrated analytical framework." BMC Med Res Methodol. (2016) 16:27. doi: 10.1186/s12874-016-0130-6