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OPTIMIZING EXPOSURE AND HEALTH EFFECTS RESEARCH TO INFORM THE NATIONAL AMBIENT AIR QUALITY STANDARDS (NAAQS)

April 30, 2024

Purpose of the session

- Explore how EPA uses science to inform NAAQS decisions
- Examine how scientific research informs different steps in the standard-setting process, ranging from the development of the Integrated Science Assessment to the evaluation of policy options in the Policy Assessment
- Highlight gaps in the types of data/information currently evaluated/reported in many studies that limit usefulness for standard-setting decisions and supporting analyses

Science is the Backbone of the NAAQS: Assessments for a NAAQS Review

Integrated Science Assessment: comprehensive evaluation and synthesis of policy-relevant science

- Characterization of the strengths and uncertainties of the evidence
- Conclusions on causality for health effects
- Characterization of evidence for potentially at-risk populations
- Assessment of evidence for dose/concentration-response relationships

Risk and Exposure Assessment: quantitative analyses of estimated population exposure and risk

- Assesses the nature and magnitude of exposures and associated health risks under various air quality conditions
- Informs our understanding of how exposures and risks may be experienced by at-risk populations

Policy Assessment: bridge between scientific & risk information and Administrator's judgments on NAAQS

- Focuses on strongest conclusions from the ISA and policy-relevant quantitative exposure and risk analyses
- Examines scientific studies with the greatest potential to inform the evaluation of policy options, including studies showing adverse health effects at ambient concentrations near the standards or in at-risk populations
- Addresses key policy-relevant questions related to the existing standards and alternative standards

Optimizing Research to Inform the NAAQS

How does research inform the standard setting process?

Integrated Science Assessments

Research informs key scientific conclusions:

- Causality Determinations (Hazard ID)
- At-Risk Populations
- Shape of the C-R/D-R Relationship

Policy Assessments

Evidence-Based Consideration

Risk and Exposure Analyses

- Nature, magnitude, and importance of risks associated with current/alternative standards
- Uncertainties in the risk estimates

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Current Primary NAAQS Standards: Defined by 4 Elements

Indicator Pollutant		Averaging Time	Level	Form
Carbon Monoxide		8-hour	9 ppm	Not to be exceeded more than once per year
		1-hour	35 ppm	
Lead		Rolling 3-month avg	0.15 µg/m^3	Not to be exceeded
Nitrogen Dioxide		1-hour	100 ppb	98th percentile of 1-hour daily maximum concentrations, averaged over 3 years
		Annual	53 ppb	Annual Mean
Ozone		8-hour	0.070 ppm	Annual fourth-highest daily maximum 8-hr concentration, averaged over 3 years
Particle Pollution	**$PM_{2.5}$**	Annual	9 µg/m^3	Annual mean, averaged over 3 years
		24-hour	35 µg/m^3	98th percentile, averaged over 3 years
	PM_{10}	24-hour	150 µg/m^3	Not to be exceeded more than once per year on average over 3 years
Sulfur Dioxide		1-hour	75 ppb	99th percentile of 1-hour daily maximum concentrations, averaged over 3 years

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Current NAAQS Primary Standards: Defined by 4 Elements Cont'd

Pollutant		Averaging Time	Level	Form
Particle Pollution	$PM_{2.5}$	Annual	9 µg/m^3	Annual mean, averaged over 3 years
		24-hour	35 µg/m^3	98th percentile, averaged over 3 years
Sulfur Dioxide		1-hour	75 ppb	99th percentile of 1-hour daily maximum concentrations, averaged over 3 years

- The four elements of the NAAQS (indicator, averaging time, level and form) are informed by scientific evidence and must be considered collectively in evaluating health protection afforded by current/alternative standards
  - Ideally, scientific studies will be designed and report comparable metrics
- SO_2: Controlled human exposures indicate short-term effects associated with exposure
  - Averaging time of 1-hour is designed to protect against short-term peak exposures above a level of 75 ppb
  - 99th percentile form provides protection against repeated peak exposures
- $PM_{2.5}$: Epidemiologic evidence indicates long-term exposures are associated with health effects (e.g. mortality)
  - Annual averaging time designed to protect against long-term exposures
  - Annual mean form with a level of 9 µg/m^3 ensures long-term ambient concentrations will be maintained below the mean observed in key epidemiologic studies
  - The long-term standard works in conjunction with the short-term standard to protect against peak exposures

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Active NAAQS Review Status

	PM[1]	Lead	Secondary (Ecological) NO_2, SO_2, PM[2]	Primary NO_2	Ozone
Last Review Completed	March 2024	Oct 2016	Mar 2012	April 2018	Dec 2020
Recent or Upcoming Major Milestone(s)	March 6, 2024 Final Rule (Reconsideration of 2020 Decision)	Jan 2024 Final Integrated Science Assessment Later in 2024 Draft Policy Assessment	April 3, 2024 Proposed Decision (consent decree) Dec. 10, 2024 Final Decision (consent decree)	Dec 2022 Call for Information March 2024 Integrated Review Plan Volumes1 & 2	May 2024 Science-Policy Workshop Fall 2024 Integrated Review Plan Volumes 1 & 2

Additional information regarding current and previous NAAQS reviews is available at: http://www.epa.gov/ttn/naaqs/

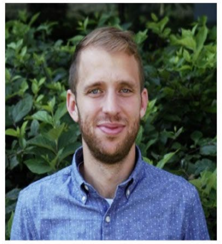
[1]Combined primary and secondary (non-ecological effects) review of PM

[2] Combined secondary (ecological effects only) review of NO_2, SO_2, and PM

Agenda: Optimizing Exposure and Health Effects Research to Inform the NAAQS


A deeper dive into current gaps in data in studies informing the NAAQS

Evan Coffman and Lars Perlmutt, U.S. EPA




Optimizing Exposure Assessment for Policy Decisions

Joshua Apte, University of California, Berkeley

Designing epidemiological studies to inform the NAAQS: Experiences studying air pollution, mortality, and inequalities using Medicare data

Rachel Nethery, Harvard T.H. Chan School of Public Health

The NAAQS: Substantial success and the challenges ahead

Armistead Russell, Georgia Institute of Technology

Panel discussion and Q&A

Featuring the speakers above, along with Howard Kipen, Rutgers School of Public Health

Optimizing Research to Inform the NAAQS:

An Overview of How Studies are Considered, Evaluated, and Synthesized in the ISAs

Evan Coffman

Center for Public Health and Environmental Assessment

Office Of Research and Development

U.S. Environmental Protection Agency

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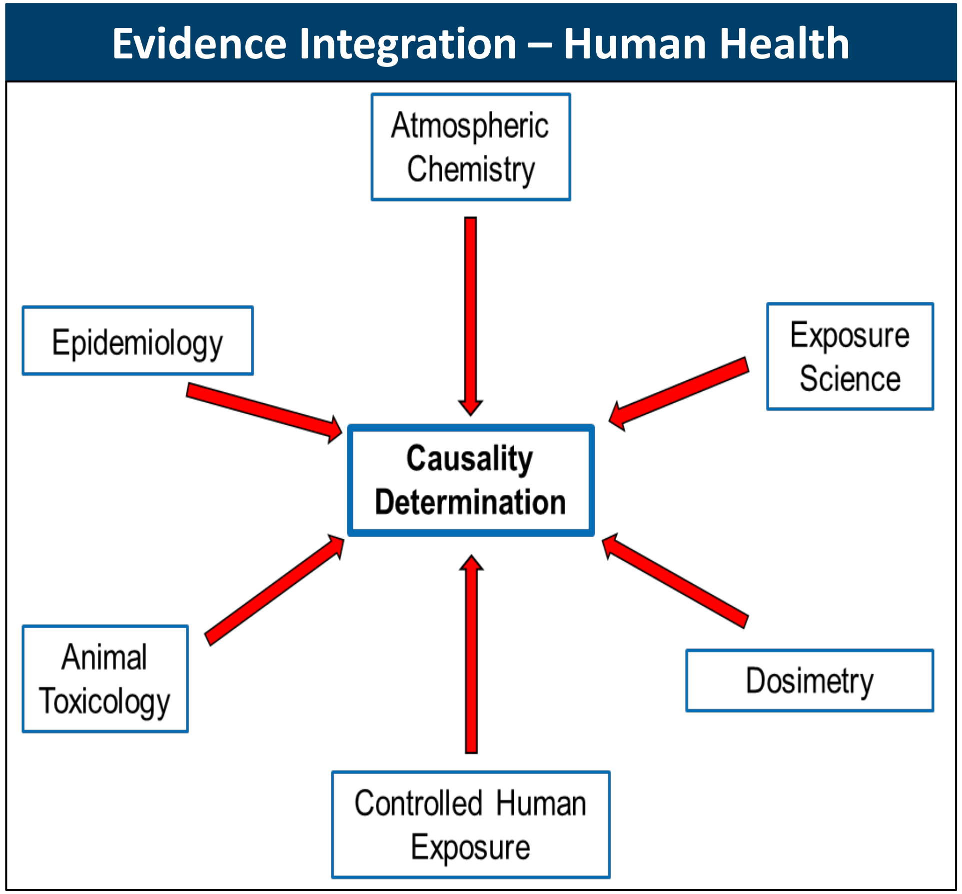
Outline of Presentation – Part One

- Background and Framing
- NASEM Report on the ISA Causality Framework
- Advances in ISA Scoping and Study Quality Evaluation
  - Researcher Reporting Checklist
- Causality Determinations and other Key Scientific Conclusions
  - Designing Informative Studies

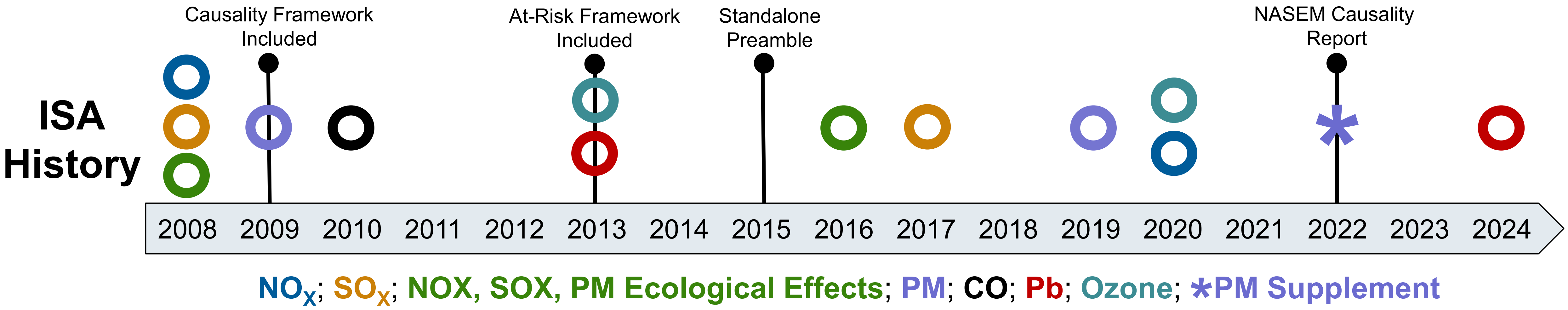
ISA Purpose and Key Conclusions

- **Purpose:** ISAs assess the evidence for the "criteria pollutants" and provide the scientific foundation for reviewing the NAAQS
- ISA conclusions inform exposure and risk assessments, evaluation of policy options, and proposed and final decisions
  - **Causality determinations** reflect the strength of evidence for causal relationships – they rely on integrating evidence across disciplines and applying an established causality framework
  - Conclusions on **populations that may be at increased risk** are also informed by applying integrated evidence to an established framework
- Some ISA conclusions vary by assessment depending on available data – these often include:
  - Concentration-, exposure-, or dose-response relationships
  - Strengths/limitations of various study designs, exposure metrics
  - Impact of potential confounding factors
  - Timing of effects



Framing: Evolution of the ISA Development Process

- In 2015, the process for ISA development was formalized in a standalone ***Preamble to the ISAs***.
- Since 2015, individual ISAs have incorporated incremental advances that build on the approach described in the Preamble.
- In October 2022, the National Academies (NASEM) released a report detailing recommendations on the Preamble's ISA causality framework.
- We are using the Integrated Review Plan (IRP) for the NO_2 primary NAAQS to begin this process, with a focus on health; subsequent review(s) will broaden the updates to include welfare, ultimately providing a foundation for **revising the 2015 Preamble**.



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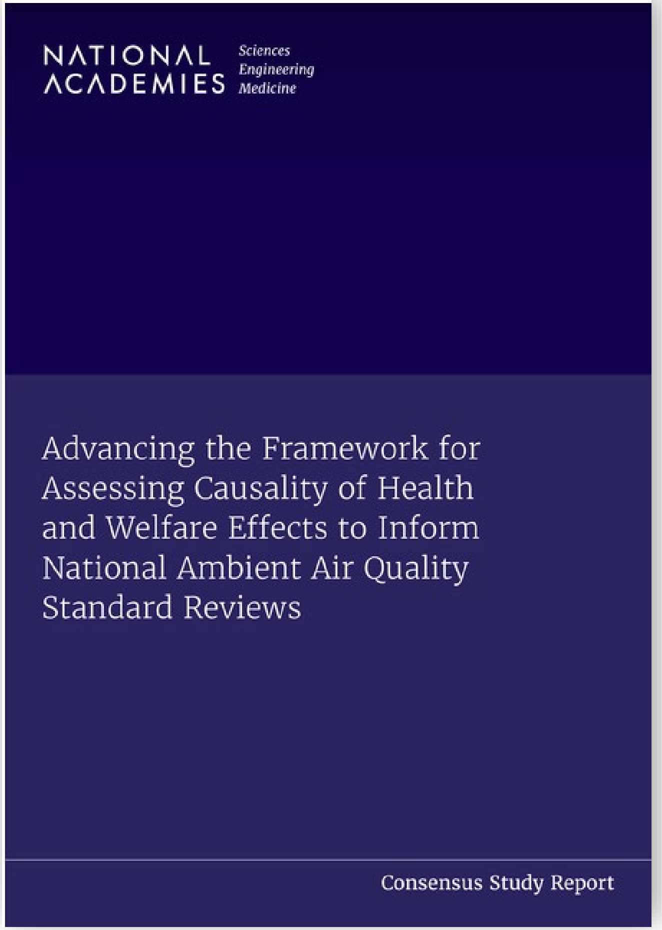
NASEM Report

NASEM Review of the ISA Causality Framework

The committee reached **7 conclusions,** 3 of which endorse core aspects of the current framework.

Additional conclusions were coupled with recommendations for the causality framework emphasizing the importance of **improving clarity and transparency**:

- **Clarifying the ISA's approaches to study evaluation, study selection, determining study relevance and influence, assessing confounder control**
- **Describing how heterogeneity in exposure responses is considered in causality determinations**
- Developing guidance for assessing study documentation and clarifying consideration of study reproducibility and replicability
- Articulating a process for incorporating necessary expertise for ISA development
- Monitoring the scientific literature to determine if emerging assessment approaches might be adapted to ISAs

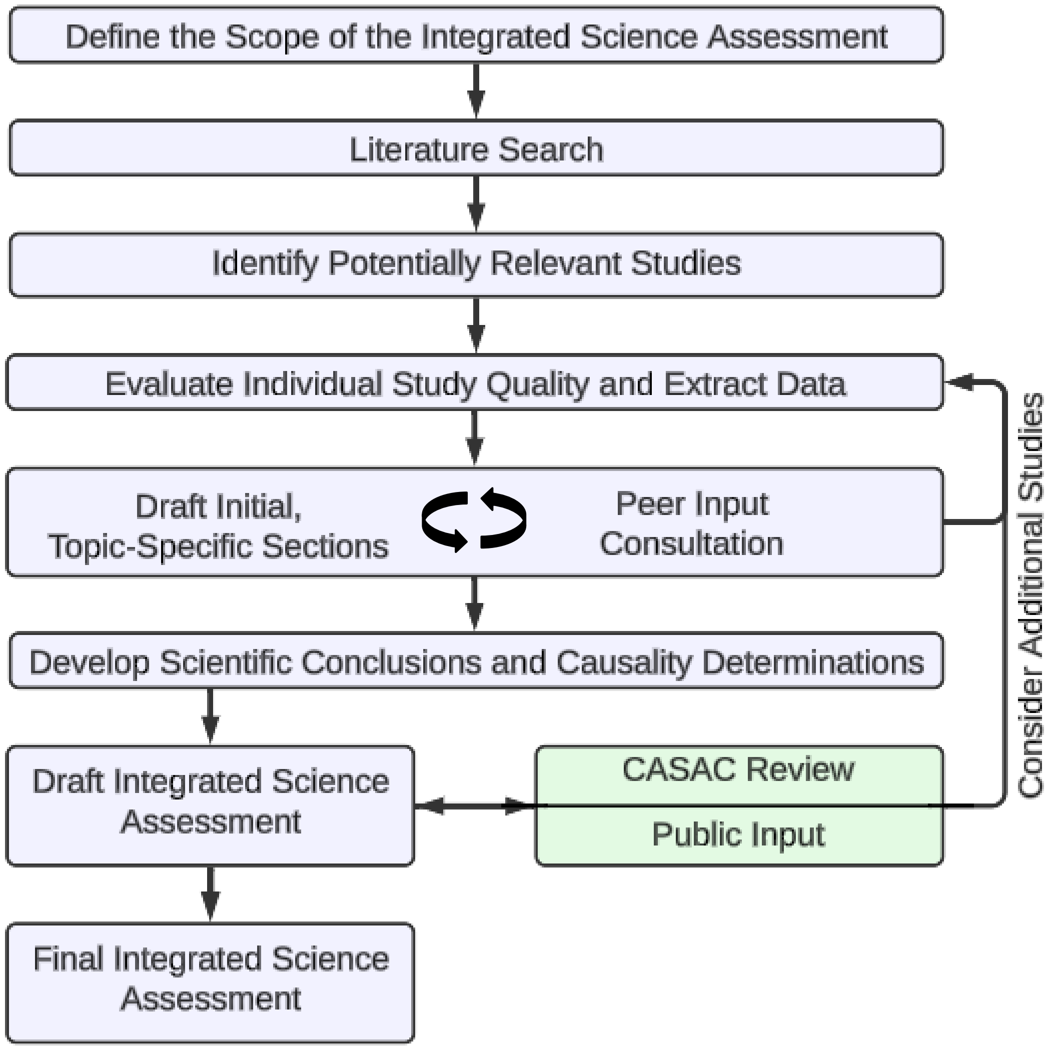


https://nap.nationalacademies.org/catalog/26612/advancing-the-framework-for-assessing-causality-of-health-and-welfare-effects-to-inform-national-ambient-air-quality-standard-reviews

Advances in ISA Development: Scoping and Study Quality Evaluation

Advances in ISA Development: Focus on Improving Clarity and Transparency

- Discipline-specific scoping criteria
- Systematic review tools used in literature search and screening
- Expanded approach to study quality evaluation, including discipline-specific criteria
- Use of evidence maps to inform planning
- Search results and screening decisions documented in Health and Environmental Research Online (HERO) database
- Expanded discussion of other issues highlighted in the NASEM report, including the connection between at-risk conclusions and causality, the broad expertise required for ISA development, the importance of study transparency, etc.



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Advances: Defining the ISA Scope

Scoping statements are developed for each topic area and used to guide:

- Literature search strategy
- Criteria for study inclusion/exclusion
- Type of data extracted
- Evidence integration
- Synthesis of results

Health Effects		Atmospheric and Exposure Science	
P	Population	S	Sources
E	Exposure	T	Transport and Transformation
C	Comparator	E	Exposure/Extent
O	Outcome	M	Measurement and Modeling
S	Study Design		

These scoping statements are **informed by** the body of evidence from previous ISAs and expert knowledge of the scientific literature.

Included studies must:

- Have undergone scientific peer review
- Present new information and/or analyses

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Advances: Evaluation of Individual Study Quality

- Consider the strengths and limitations of individual studies that may affect study interpretation and the strength of inference that can be drawn from study results
- Study attributes considered include:

Health Studies	Atmospheric and Exposure Science
▪ Study Design	▪ Applicability and Utility
▪ Study Population/Test Model	▪ Soundness
▪ Pollutant	▪ Clarity and Completeness
▪ Exposure Estimation or Assignment	▪ Uncertainty and Variability
▪ Outcome Assessment and Evaluation	
▪ Potential Confounding	
▪ Effect Modification (epidemiology only)	
▪ Statistical Methodology	

- Document reasons for exclusion; balancing need to be transparent with level of effort

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Researcher Reporting Checklist

Study Population

- ❑ Location
- ❑ Years of study
- ❑ Selection criteria

Exposure Assessment

- ❑ Units of measurement
- ❑ **Summary statistics + exposure distribution**
- ❑ Copollutant correlations
- ❑ **Exposure assessment technique**
- ❑ Averaging time
- ❑ Validation metrics

Comparator

- ❑ Exposure increments
- ❑ Categorical distributions

Outcome

- ❑ Description of outcome assessment
- ❑ Validation metrics

Statistical Methods

- ❑ Description of model
- ❑ Treatment of missing data
- ❑ **Considered confounders**

Other

- ❑ **Reporting of independent effect estimates for multipollutant/mixtures models**
- ❑ Numeric results corresponding to figures
- ❑ **Quantitative results for non-statistically-significant results**

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Key Scientific Conclusions: At-Risk and Causality Frameworks

Integration of Evidence and Determination of Causality

- The ISA's 5-category hierarchy to classify weight of evidence was endorsed by NASEM
- Each level of the causality hierarchy is delineated by the degree to which chance, confounding and other biases can be ruled out as explanations of study results with reasonable confidence.

Aspects to aid in judging causality include:

- Consistency, coherence of findings
- Experimental support, biological plausibility
- Temporal relationship between exposure and effect
- Exposure-response
- Strength and specificity of the relationship

Adapted From The ISA Preamble

Causal Relationship	Pollutant exposures have been shown to result in health effects in studies in which *chance, confounding, and other biases can be ruled out with reasonable confidence*
Likely to be a Causal Relationship	Pollutant exposures have been shown to result in health effects in studies where *results are not explained by chance, confounding, and other biases, but uncertainties remain in the evidence overall*
Suggestive of, but not sufficient to infer, a causal relationship	Pollutant exposures have been shown to result in health effects, but *chance, confounding, and bias cannot be confidently ruled out*
Inadequate to infer a causal relationship	Evidence is limited and available studies are of *insufficient quantity, quality, consistency, and/or statistical power to permit a conclusion regarding the presence or absence of an effect*
Not likely to be a causal relationship	Evidence indicates there is *no causal relationship with relevant pollutant exposures*

At-Risk Populations and Lifestages

- The ISAs apply a four-category hierarchy to convey the overall confidence in the scientific evidence as to whether certain populations and lifestages are at increased risk of a pollutant-related health effect.
- Per NASEM recommendations, increase transparency in how heterogeneity in exposure-response relationships is considered in causality determinations

Classification	Health Effects
Adequate evidence	There is substantial, consistent evidence within a discipline to conclude that a factor results in a population or lifestage being at increased risk of air pollutant-related health effect(s) relative to some reference population or lifestage. Where applicable, this evidence includes coherence across disciplines. Evidence includes multiple high-quality studies.
Suggestive evidence	The collective evidence suggests that a factor results in a population or lifestage being at increased risk of air pollutant-related health effect(s) relative to some reference population or lifestage, but the evidence is limited due to some inconsistency within a discipline or, where applicable, a lack of coherence across disciplines.
Inadequate evidence	The collective evidence is inadequate to determine whether a factor results in a population or lifestage being at increased risk of air pollutant-related health effect(s) relative to some reference population or lifestage. The available studies are of insufficient quantity, quality, consistency, and/or statistical power to permit a conclusion to be drawn.
Evidence of no effect	There is substantial, consistent evidence within a discipline to conclude that a factor does not result in a population or lifestage being at increased risk of air pollutant-related health effect(s) relative to some reference population or lifestage. Where applicable, the evidence includes coherence across disciplines. Evidence includes multiple high-quality studies.

Designing Studies to Inform Key Scientific Conclusions in the ISAs

- Studies to inform causality determinations for outcomes for which the evidence does not support a causal relationship:
  - Research to address uncertainties (e.g., exposure measurement error, biological plausibility, copollutant confounding, etc.)
- Studies to inform other key scientific conclusions:
  - Populations and lifestages potentially at increased-risk of air pollutant related health effects
  - Effects at low concentrations
  - Shape of the concentration-response or dose-response relationships
  - Critical windows of exposure
  - Lag structure
  - Etc.

Optimizing Research to Inform the National Ambient Air Quality Standards (NAAQS):

How Science is Used to Inform Policy Options in EPA's Policy Assessments

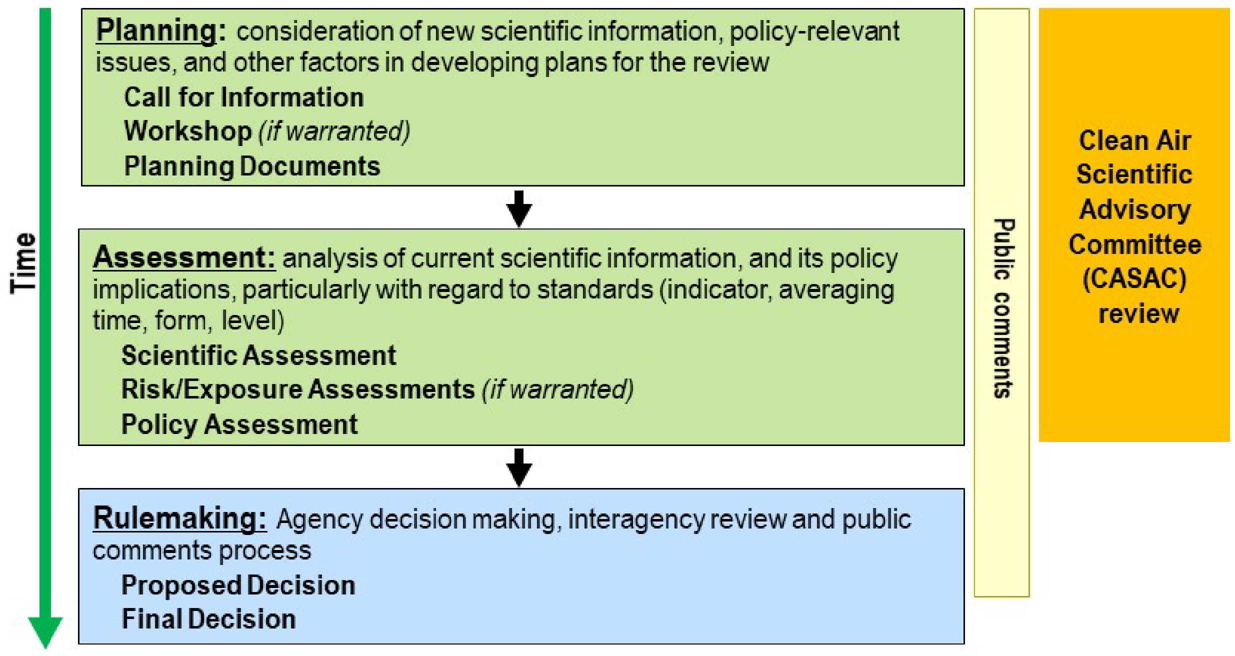
Health Effects Institute Annual Conference 2024
Philadelphia, PA

Lars Perlmutt
Office of Air Quality Planning and Standards
U.S. Environmental Protection Agency

April 30, 2024

From Scientific Assessments to Policy Options

- EPA creates the **Policy Assessment (PA)** document to bridge the gap between the scientific and quantitative assessments and the judgments required of the Administrator in determining whether it is appropriate to retain or revise the NAAQS
- To inform the Administrator's decisions on the adequacy of the standard, the PA evaluates the public health protection provided by the current standard (and any alternatives considered), with an emphasis on those most at risk for experiencing adverse effects
- The PA focuses on the health endpoints in the ISA where there is the strongest support for health effects to be associated with exposure
- Additionally, the PA gives particular attention to exposures and health risks to the at-risk populations identified in the ISA



The Key Policy Relevant Questions of the PA

- The PA evaluates the current scientific information regarding the health effects from exposure in ambient air and the potential for effects to occur under air quality conditions associated with the existing standard(s) (or any alternatives considered) by asking the following questions
  - ISA: What does the currently available scientific evidence tell us regarding the nature of health effects attributable to human exposure to the criteria pollutant from ambient air? What does the current available scientific evidence tell us regarding the exposure duration and concentrations associated with health effects?
  - Risk and Exposure Assessment (REA): What are the nature and magnitude of exposures and associated health risks associated with air quality conditions just meeting the current standard? To what extent are the estimates of exposures and risks to at-risk populations associated with air quality conditions just meeting the current standard (or alternatives considered) reasonably judged important from a public health perspective?
- The following slides give examples of how the PA uses information from scientific research to inform these policy-relevant questions

Example: How Clinical Studies Inform Policy-relevant Question in the Ozone NAAQS

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- 6.6 hr ozone exposures ≥ 60 ppb: report respiratory effects in healthy, exercising adults with 6.6 hr ozone exposures ≥ 60 ppb
- Shorter exposure periods (1 to 2-hrs) with heavy intermittent or very heavy continuous exercise: statistically significant respiratory effects at exposure to ≥ 120 ppb
- At-risk populations: people with asthma, children, older adults, and people who are active outdoors

Endpoint	Ozone Target Exposure Conc[A]	Statistically Significant Effect	Ozone-Induced Group Mean Response	Study
FEV_1 Reduction	80 ppb	Yes	-7.5%	Horstman et al. 1990
			-7.7%	McDonnell et al., 1991
			-6.5%	Adams, 2002
			-6.2% to -5.5%	Adams, 2003
			-7.0% to -6.1%	Adams, 2006b
			-7.8%	Schelegle et al., 2009
		ND	-3.5%	Kim et al., 2011 [F]
	70 ppb	Yes	-6.1%	Schelegle et al., 2009 [I]
	60 ppb	Yes	-2.9% -2.8%	Adams, 2006b; Brown et al., 2008
		Yes	-1.7%	Kim et al., 2011
		No	-3.5%	Schelegle et al., 2009
	40 ppb	No	-1.2%	Adams, 2002
		No	-0.2%	Adams, 2006b
Increased Respiratory Symptoms	80 ppb	Yes	Increased symptom scores	See 2020 PA Table 3-2
	70 ppb	Yes		
	60 ppb	No		
	40 ppb	No		
Airway Inflammation	80 ppb	Yes	Multiple indicators	Devlin et al. 1991; Alexis et al. 2010
	60 ppb	Yes	Increased sputum neutrophils	Kim et al., 2011
Increased Airway Resistance	80 ppb	Yes	Increased	Horstman et al., 1990

Example: How Clinical Studies Inform Policy-relevant Questions in the Ozone NAAQS (cont)

- Administrator Judgement: Informed by science, including uncertainties and limitations, on what ozone exposures should be judged important
- In the 2015 decision to revise the ozone standard, the Administrator:
  - Judged the evidence supporting the occurrence of adverse respiratory effects is strongest for exposures ≥ the 70 and 80 ppb benchmarks
  - Expressed less confidence that adverse effects will occur following exposures to ozone concentrations as low as 60 ppb, but noted the possibility, particularly for at risk populations
  - Recognized interindividual variability in responsiveness in the clinical studies, and focused on a standard that provides protection against repeated exposures of concern (e.g. 80, 70, 60 ppb)
- Based on this (and other information and scientific advice), the Administrator focused on a standard that would eliminate the occurrence of ≥ 2 exposures ≥ 80 ppb, virtually eliminate ≥ 2 exposures ≥ 70 ppb, and substantially limit the occurrence of ≥ 2 exposures ≥ 60 ppb for the general public and at-risk populations

2014 Risk and Exposure Assessment

Air Quality Scenario (Design Value, ppb)	Estimated average % of simulated children with at least one day per year at or above benchmark	Estimated average % of simulated children with at least two days per year at or above benchmark
Benchmark Exposure Concentration of 80 ppb		
75	0 – 0.3	0
70	0 – 0.1	0
65	0	0
Benchmark Exposure Concentration of 70 ppb		
75	0.6 – 3.3	0.1 – 0.6
70	0.1 – 1.2	0 – 0.1
65	0 – 0.2	0
Benchmark Exposure Concentration of 60 ppb		
75	9.5 – 17.0	3.1 – 7.6
70	3.3 – 10.2	0.5 – 3.5
65	0 – 4.2	0 – 0.8

2014 HREA Benchmark analysis for percent of children estimated to experience at least one, or two, days with an exposure at or above benchmarks while at moderate or greater exertion.

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Ozone NAAQS: Examples of Research Gaps and Future Research Needs

- Additional controlled human exposure studies to more comprehensively assess risk of respiratory effects in at-risk individuals exposed to ozone at concentrations ≥ 70 ppb with varying levels of exertion
- Epidemiologic studies conducted in locations and during time periods with air quality at or below standards (e.g., in areas with design values at or below 70 ppb), as well as an improved understanding of copollutant exposures and effects on study results
- Studies assessing the influence of “long-term” versus “short-term” ozone exposures
- Continued improvements in modeling approaches to estimate personal and population exposure
- A better understanding of interindividual differences of responses (e.g., understand why some people are more responsive to ozone)
- More information to inform how to consider at risk populations, particularly asthmatics
- Collection of time-activity data over longer time periods, particularly for children (including under the age of five), to reduce uncertainty in the modeled exposure distributions

Example: How Epidemiological Studies Inform Policy-relevant Questions in the $PM_{2.5}$ NAAQS

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- The 2024 PM NAAQS included substantial new scientific evidence which indicated that both long-and short-term exposures to $PM_{2.5}$ are associated with adverse health effects
- Recognized the availability of a large number of epidemiologic studies reporting positive and significant associations between $PM_{2.5}$ exposures and mortality and morbidity effects
- 2019 ISA finds exposure to $PM_{2.5}$ causes mortality and cardiovascular effects and is likely to cause respiratory effects, cancer, and nervous system effects
- At-risk populations identified by the ISA: older adults, children, people with pre-existing cardiovascular or respiratory disease, minority populations, and low SES populations

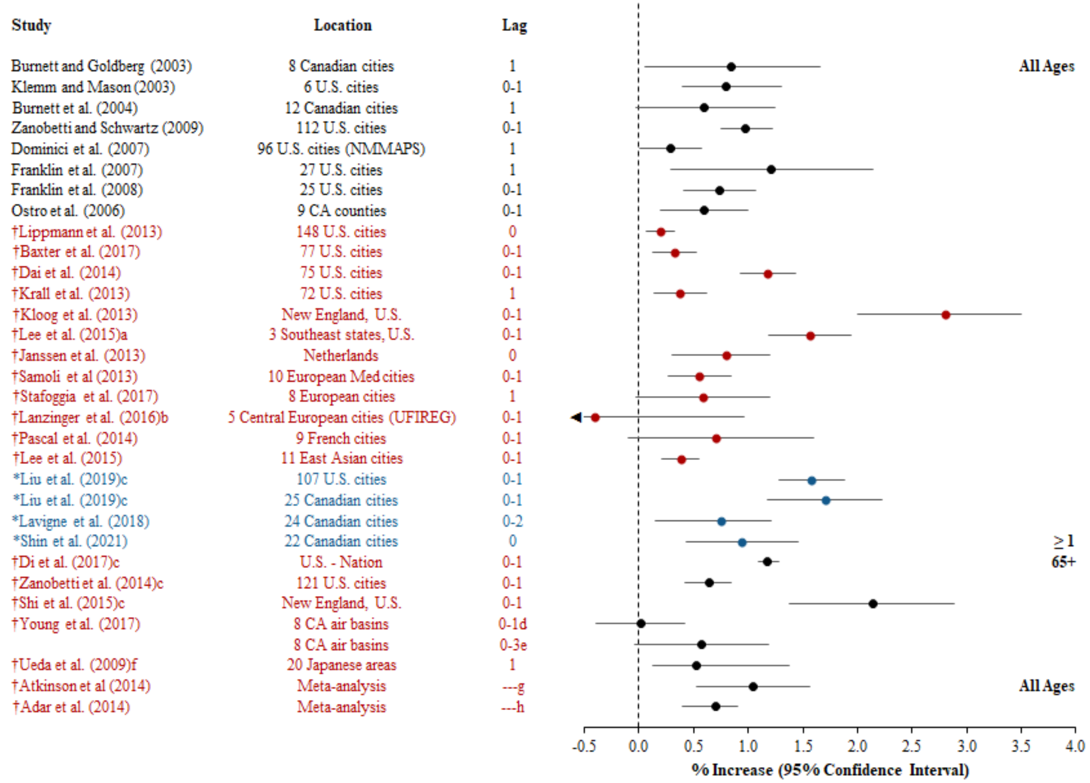


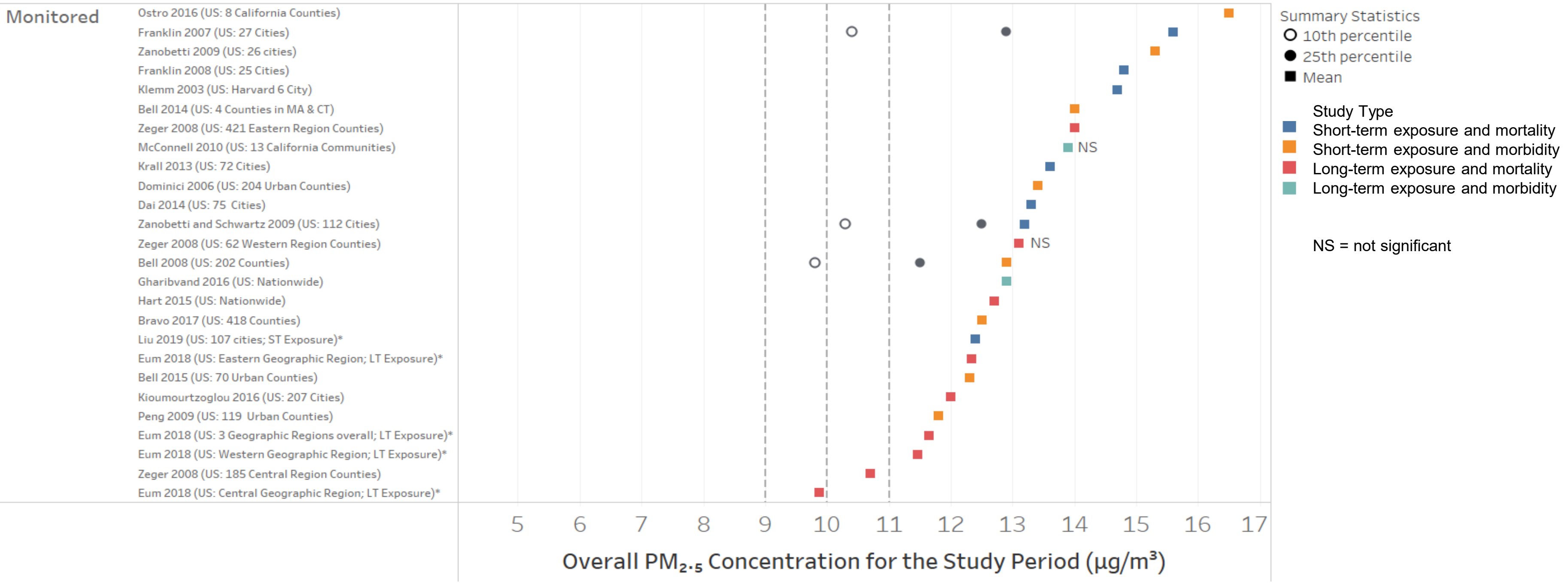
Figure 3-13. Summary of associations between short-term $PM_{2.5}$ exposure and total (nonaccidental) mortality in multicity studies

Key:
Studies in 2009 PM ISA
Studies in 2019 PM ISA
Recent studies

Note: Results are for a 10 µg/m³ increase in 24-h avg $PM_{2.5}$ concentrations

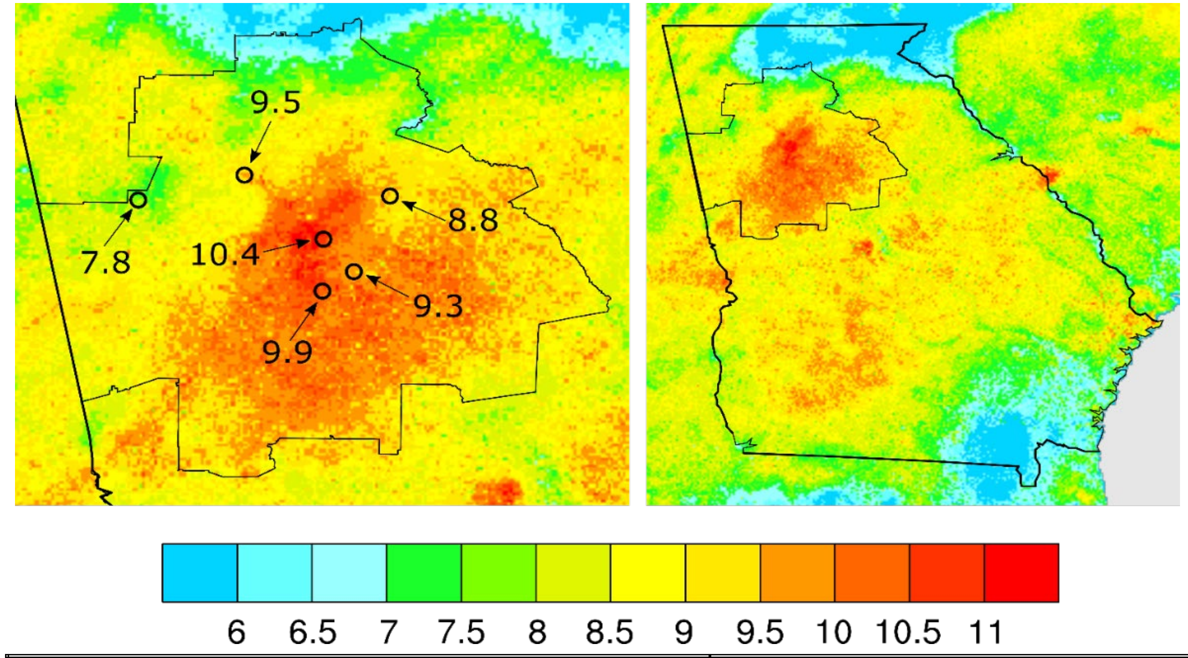
Example: How Epidemiological Studies Inform Policy-relevant Questions in the $PM_{2.5}$ NAAQS (cont)

- Epidemiologic studies provide the strongest scientific evidence when evaluating the adequacy of the level of the annual standard
- No Clear “Bright Line”: No specific air quality point in epidemiologic studies distinctly separates observed effects from non-observed effects.
- Judgements are required by the Administrator in interpreting how those data inform the adequacy of the standard or any alternative standards
  - Highest confidence in reported associations near and somewhat below reported mean $PM_{2.5}$ concentrations
  - Diminished confidence in associations where fewer health events are observed (e.g.at lower concentrations)



Example: How Epidemiological Studies Inform Policy-relevant Questions in the PM2.5 NAAQS (cont)

- The PA also recognized that epidemiologic studies used various approaches to estimate exposure (e.g., monitors versus models)
  - The study reported mean could vary significantly based on the method used to estimate exposure
- Important for EPA to understand what those exposure estimates represented in each of the key epidemiologic studies
- Important to consider how such exposures patterns (and concentration gradients) compared to those that would be generated when meeting the current or alterative standards under consideration



Description of Calculation Approach	$PM_{2.5}$ Mean (µg/m^3)
Atlanta highest monitor	10.4
Atlanta monitored average	9.3
Atlanta spatial average using hybrid modeling data	9.2
Atlanta population-weighted average using hybrid modeling data	9.6
Georgia spatial average using hybrid modeling data	8.3
Georgia population-weighted average using hybrid modeling data	9.1

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PM NAAQS: Examples of Information/Research Gaps and Future Research Needs

Information Needs

- Clear information about how exposures are estimated and used in the epidemiological study, including information related to the air quality surface being used to estimate exposure
  - Monitored versus modeled exposure surface
  - In restricted analyses, more information on how study exposures are excluded
- Study means and methods on how study means calculated
  - Information on other aspects of the distribution of estimated exposures (e.g., minimum, 5th, 10th, 25th, 50th, 75th, 95th-99th, maximum, and average)
  - Information on the distribution of health events across the range of ambient or exposure concentrations (e.g., the concentration at which the minimum, 5th, etc of health events in a study occur)

Research Needs

- Distinguishing the health impacts of short-term exposures to high pollutant concentrations (including repeated exposures) from long-term exposures to average concentrations
- Experimental studies that further inform biological plausibility of adverse health effects, particularly at lower PM concentrations
- Research on how effect estimates might vary across different populations (e.g. epidemiologic studies that assess different populations, such as children and minority populations)

Closing thoughts

- Science is the backbone of the NAAQS – Thank you for all that you do!
  - These studies are also used to inform EPA's other assessments, including those in EPA's Regulatory Impact Analyses for the NAAQS and other national rules
- Every PA includes a section that identifies research gaps and future research needs and reflects CASAC's review and advice on those needs
  - CASAC letters also provide detailed advice on research gaps and future research needs in their reviews of the ISA, PA, and REA
- If you have any questions, please feel free to contact us!