



**U.S. Environmental Protection Agency  
Clean Air Scientific Advisory Committee  
(CASAC)  
Public Meeting**

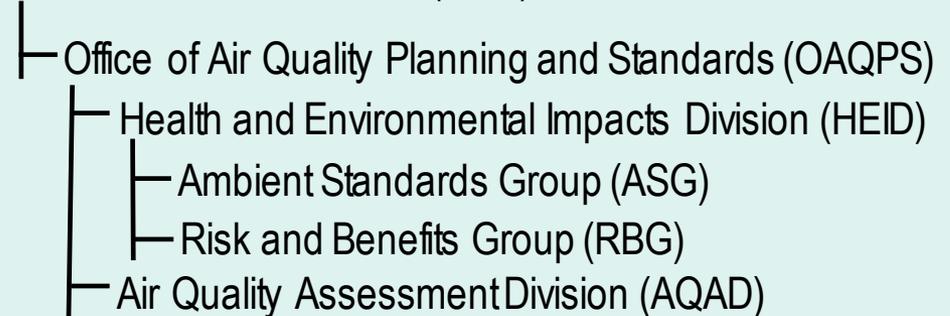
**Review of the Integrated Science Assessment  
for Particulate Matter  
External Review Draft**

**National Center for Environmental Assessment  
Office of Research and Development  
Washington, DC, December 12-13, 2018**

# EPA Speakers

- ORD/NCEA
  - John Vandenberg, Director, NCEA-RTP
  - Jason Sacks, Staff lead on the ISA (EMAG)
- OAR/OAQPS/HEID
  - Erika Sasser, Director
- Additional EPA staff
  - Karen Wesson, Group Leader (HEID/ASG)
  - Robert Wayland, Group Leader (HEID/RBG)
  - Scott Jenkins, Staff lead on PM NAAQS (HEID/ASG)
  - Zachary Pekar (HEID/RBG)
  - Sheila Igoe and David Orlin (OGC)

## Office of Air and Radiation (OAR)



## Office of Research and Development (ORD)



## Office of General Counsel (OGC)

# Outline for Presentation

- Introduction and Background
  - Statutory requirements
  - Current PM NAAQS
  - Initiation of expedited review
  - Timeline and role of CASAC in the current review
- Overview of the Draft ISA
  - Process for evaluating the scientific evidence
  - Scope of the ISA
  - Conclusions

# Introduction and Statutory Requirements

- EPA sets national ambient air quality standards (NAAQS) for six pollutants
  - Ground-level ozone
  - Carbon monoxide
  - Nitrogen dioxide
  - Particulate matter
  - Lead
  - Sulfur dioxide
- Sections 108 and 109 of the Clean Air Act govern the establishment, review, and revision (as appropriate) of NAAQS, including:
  - **Primary (health-based) standards** which in the “judgment of the Administrator” are “requisite to protect the public health”, including at-risk populations, with an “adequate margin of safety”
  - **Secondary (welfare-based) standards** which in the “judgment of the Administrator” are “requisite to protect the public welfare from any known or anticipated adverse effects”
- The law requires EPA to review the scientific information and NAAQS for each criteria pollutant every five years, and to obtain advice from the Clean Air Scientific Advisory Committee (CASAC) on each review.
- Court decisions provide additional guidance on aspects of EPA decision-making
  - EPA is required to engage in “reasoned decision making” to translate scientific evidence into standards
  - EPA may not consider cost in setting standards; however, cost is considered in developing control strategies to meet the standards (implementation phase)

# Statutory Requirements: CASAC

- Section 109(d)(2) addresses the appointment and advisory functions of an independent scientific review committee
- Section 109(d)(2)(B) provides that, at 5-year intervals, this committee “shall complete a review of the criteria...and the national primary and secondary ambient air quality standards...and shall recommend to the Administrator any new...standards and revisions of existing criteria and standards as may be appropriate...”.
- Section 109(d)(2)(C) reads: “Such committee shall also
  - (i) advise the Administrator of areas in which additional knowledge is required to appraise the adequacy and basis of existing, new, or revised national ambient air quality standards,
  - (ii) describe the research efforts necessary to provide the required information,
  - (iii) advise the Administrator on the relative contribution to air pollution concentrations of natural as well as anthropogenic activity, and
  - (iv) advise the Administrator of any adverse public health, welfare, social, economic, or energy effects which may result from various strategies for attainment and maintenance of such national ambient air quality standards.

# Overview of Current PM NAAQS

Current Standards – Last Review Completed in 2012*					Decisions in 2012 Review
Indicator	Averaging Time	Primary/Secondary	Level	Form	
PM <sub>2.5</sub>	Annual	Primary	12.0 µg/m <sup>3</sup>	Annual arithmetic mean, averaged over 3 years	Revised level from 15 to 12 µg/m <sup>3</sup> **
		Secondary	15.0 µg/m <sup>3</sup>		Retained**
	24-hour	Primary and Secondary	35 µg/m <sup>3</sup>	98th percentile, averaged over 3 years	Retained
PM <sub>10</sub>	24-hour	Primary and Secondary	150 µg/m <sup>3</sup>	Not to be exceeded more than once per year on average over a 3-year period	Retained

\*Prior to 2012, PM NAAQS were reviewed and revised several times – established in 1971 (total suspended particulate – TSP) and revised in 1987 (set PM<sub>10</sub>), 1997 (set PM<sub>2.5</sub>), 2006 (revised PM<sub>2.5</sub>, PM<sub>10</sub>)

\*\*EPA eliminated spatial averaging for the annual standards

# Initiation of Expedited Review (May 2018 memo)

## May 9, 2018 memo from the EPA Administrator:

- Directed the initiation of an expedited review of the PM NAAQS, targeting completion by the end of 2020
  - Also specified expedited review of NAAQS for ozone
- Identified ways to streamline the review process (e.g., increased focus on policy-relevant information and avoiding multiple drafts of documents)
- Identified standardized set of charge questions for CASAC including:
  - General charge questions for NAAQS reviews, to be supplemented with more detailed requests as necessary
  - Two additional charge questions that may elicit information not relevant to the standard-setting process.
    - EPA may consider an appropriate mechanism, including after receiving CASAC's final advice on the standards, to facilitate robust feedback on these topics

# Timeline and CASAC Role in the Current Review

Date	EPA	CASAC
Dec 2014	Call for Information	
Feb 2015	Kickoff Workshop	
April 2016	Draft IRP	<b>Reviewed</b> the draft IRP, which presented the plan for reviewing the air quality criteria and the NAAQS for PM
Dec 2016	Final IRP	
Oct-Dec 2018	<b>Draft ISA</b>	<b>Review</b> draft ISA, which provides an assessment of the currently available scientific information on public health and welfare effects of PM and is the science foundation for the review ( <i>the air quality criteria</i> )
Summer 2019	<b>Draft PA</b> (with REA analyses)	<b>Review</b> draft PA, which presents an evaluation of the policy-relevant aspects of the current scientific evidence and quantitative risk and air quality analyses, focusing on implications with regard to the adequacy of the current standards and, as appropriate, potential alternatives
2019-2020	<b>Final ISA</b>	
	<b>Final PA</b>	
Spring 2020	<b>Proposed decision</b>	
Dec 2020	<b>Final decision</b>	

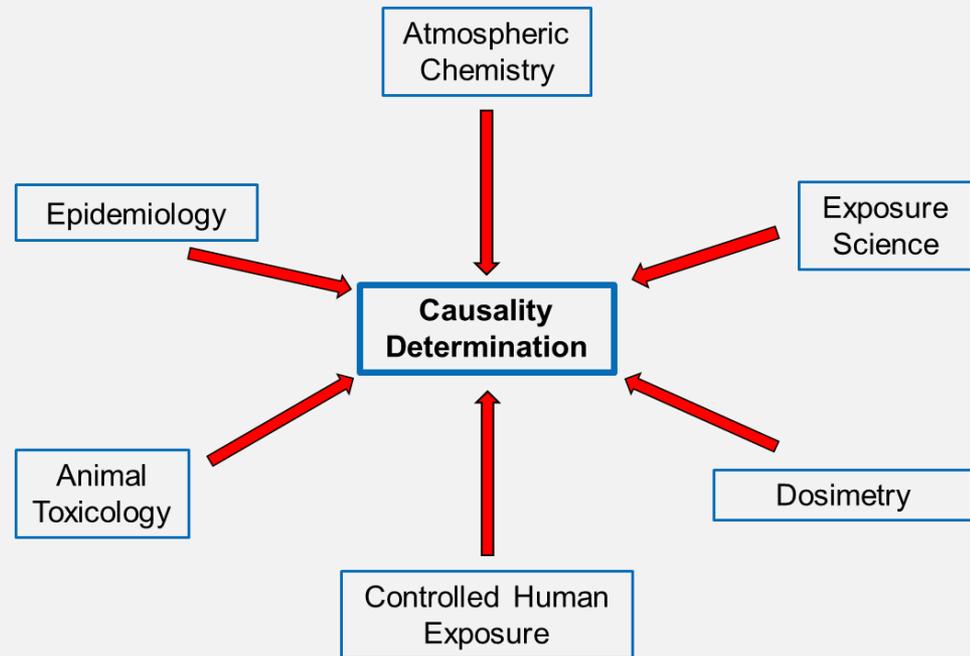
# Weight-of-Evidence Approach for Causality Determinations for Health and Welfare Effects

- Provides transparency through structured framework
- Developed and applied in ISAs for all criteria pollutants
- Emphasizes synthesis of evidence across scientific disciplines (e.g., controlled human exposure, epidemiologic, and toxicological studies)
- Five categories based on overall weight-of-evidence:
  - Causal relationship
  - Likely to be a causal relationship
  - Suggestive of, but not sufficient to infer, a causal relationship
  - Inadequate to infer the presence or absence of a causal relationship
  - Not likely to be a causal relationship
- ISA Preamble describes this framework
  - Preamble is now stand-alone document (<http://www.epa.gov/isa>)
- CASAC reviewed the Agency's causal framework **~13 times** by **~90** CASAC charter and ad hoc panel members in the process of reviewing ISAs from 2008 – 2015; its use was supported in all ISAs

# Evaluation of the Scientific Evidence

- Organize relevant literature for broad health outcome categories
- Evaluate studies, characterize results, extract relevant data
- Integrate evidence across disciplines for health outcome categories
- Develop causality determinations using established framework
- Evaluate evidence for populations potentially at increased risk
- Consideration of evidence spans many scientific disciplines from source to effect:

- Atmospheric chemistry
- Exposure
- Controlled human exposure studies
- Epidemiologic studies
- Animal toxicologic studies
- At-risk populations/lifestages



**\*\*Informs Hazard Identification step of Risk Assessment Process\*\***



# Framework for Causality Determinations in the ISA

	Health Effects	Ecological and Other Welfare Effects
<b>Causal relationship</b>	<p>Evidence is sufficient to conclude that there is a causal relationship with relevant pollutant exposures (e.g., doses or exposures generally within one to two orders of magnitude of recent concentrations) that have been shown to result in health effects and other biases could be ruled out with reasonable confidence. (1) controlled human exposure studies that demonstrate consistent effects, or (2) observational studies that cannot be explained by chance, confounding, and other biases. Generally, the determination is based on multiple high-quality studies conducted by multiple research groups.</p>	<p>Evidence is sufficient to conclude that there is a causal relationship with relevant pollutant exposures. That is, the pollutant has been shown to result in health effects in studies in which chance, confounding, and other biases could be ruled out with reasonable confidence. Controlled exposure studies (laboratory studies) provide the strongest evidence for causality, but the scope of inference may be limited. Generally, the relationship is usually obtained from the joint consideration of many lines of evidence that reinforce each other.</p>
<b>Likely to be a causal relationship</b>	<p>Evidence is sufficient to conclude that a causal relationship is likely to exist with relevant pollutant exposures. That is, the pollutant has been shown to result in health effects in studies where results are not explained by chance, confounding, and other biases, but uncertainties remain. For example: (1) observational studies where exposures are difficult to address and/or other lines of evidence are limited or inconsistent, or (2) animal toxicological evidence from multiple studies from different laboratories demonstrate effects, but limited or no human data are available. Generally, the determination is based on multiple high-quality studies.</p>	<p>Evidence is sufficient to conclude that there is a likely causal association with relevant pollutant exposures. That is, an association has been observed between the pollutant and the outcome in studies in which chance, confounding, and other biases are minimized but uncertainties remain. For example, field studies show a relationship, but suspected interacting factors and other lines of evidence are limited or inconsistent. Generally, the determination is based on multiple studies by multiple research groups.</p>
<b>Suggestive of, but not sufficient to infer, a causal relationship</b>	<p>Evidence is suggestive of a causal relationship with relevant pollutant exposures but is limited, and chance, confounding, and other biases cannot be ruled out. For example: (1) when the body of evidence is relatively small, at least one high-quality epidemiologic study shows an association with a given health outcome and/or at least one high-quality animal study shows effects relevant to humans in animal species, or (2) when the body of evidence is relatively large, evidence from studies of varying quality is generally supportive but not entirely consistent, and there may be coherence across lines of evidence (e.g., animal studies or mode of action information) to support the determination.</p>	<p>Evidence is suggestive of a causal relationship with relevant pollutant exposures, but chance, confounding, and other biases cannot be ruled out. For example, at least one high-quality study shows an effect, but the results of other studies are inconsistent.</p>
<b>Inadequate to infer a causal relationship</b>	<p>Evidence is inadequate to determine that a causal relationship exists with relevant pollutant exposures. The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an effect.</p>	<p>Evidence is inadequate to determine that a causal relationship exists with relevant pollutant exposures. The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an effect.</p>
<b>Not likely to be a causal relationship</b>	<p>Evidence indicates there is no causal relationship with relevant pollutant exposures. Several adequate studies examining relationships with relevant exposure that human beings are known to encounter and considering at-risk populations and lifestyles, are mutually consistent in failing to show an effect at any level of exposure.</p>	<p>Evidence indicates there is no causal relationship with relevant pollutant exposures. Several adequate studies examining relationships with relevant exposure are consistent in failing to show an effect at any level of exposure.</p>

# Contents of the Draft PM ISA

Preface: Legislative Requirements of the PM NAAQS, Purpose and Overview of the ISA, Process for Developing ISA

Executive Summary

Chapter 1. Integrated Synthesis

Chapter 2. Sources, Atmospheric Chemistry, and Ambient Concentrations

Chapter 3. Exposure to Ambient PM

Chapter 4. Dosimetry of PM

Chapters 5 - 11. Respiratory Effects, Cardiovascular Effects, Metabolic Effects, Nervous System Effects, Reproductive and Developmental Effects, Cancer, and Mortality

Chapter 12. Lifestages and Populations Potentially at Increased Risk of a PM-related Health Effect

Chapter 13. Welfare Effects

# Scope of PM ISA

- **Scope:** The ISA is tasked with answering the question “Is there an independent effect of PM on health and welfare at relevant ambient concentrations?”
  - Health Effects
    - Studies will be considered if they include a composite measure of PM (e.g., PM<sub>2.5</sub> mass, PM<sub>10-2.5</sub> mass, ultrafine particle (UFP) number)
      - Studies of source-based exposures that contain PM (e.g., diesel exhaust, wood smoke, etc.) if they have a composite measure of PM and examine effects with and without particle trap to assess the particle effect
      - Studies of components of PM if they include a composite measure of PM to relate toxicity of component(s) to current indicator
    - Studies will be considered if PM exposures are relevant to ambient concentrations (< 2 mg/m<sup>3</sup>; 1 to 2 orders of magnitude above ambient concentrations)

# Scope of PM ISA (cont.)

## – Welfare Effects

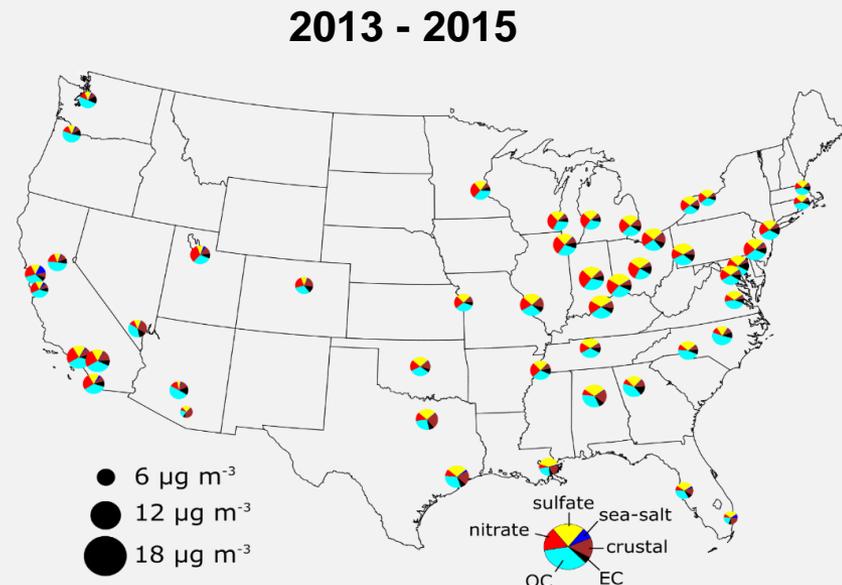
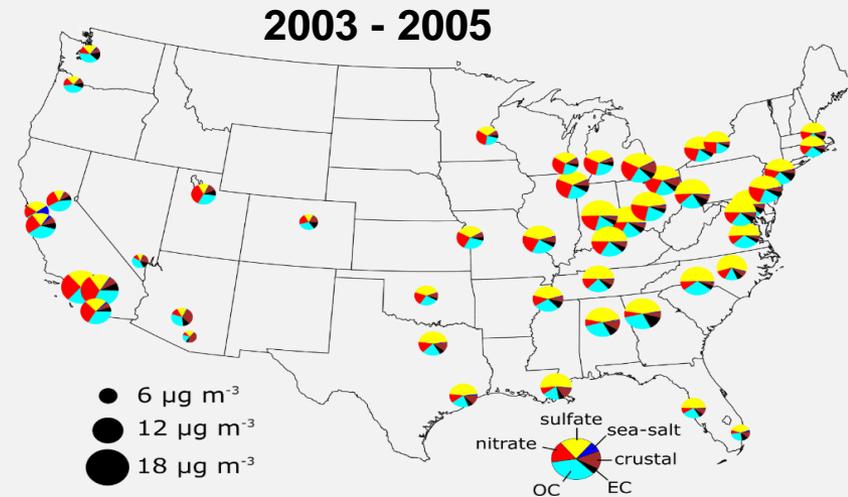
- Focus is on non-ecological welfare effects
  - Visibility Impairment
  - Climate Effects
  - Materials Effects
- Ecological effects resulting from the deposition of PM and PM components are being considered as part of the review of the secondary (welfare-based) NAAQS for oxides of nitrogen, oxides of sulfur and PM

# Executive Summary and Chapter 1

- Executive Summary
  - High-level overview of main conclusions of the entire ISA
  - Briefly captures strengths, limitations, and remaining uncertainties in the evidence base
- Integrated Synthesis (Chapter 1)
  - More detailed synthesis of the scientific evidence compared to the Executive Summary
    - Focus is on those health and welfare effects where it was concluded that a causal or likely to be causal relationship exists
    - Broad characterization of uncertainties and limitations in the evidence for PM<sub>10-2.5</sub> and UFPs that contributed to a suggestive of, but not sufficient to infer and inadequate causality determination
  - Integrated discussion of policy-relevant issues (e.g., copollutant confounding, concentration-response relationship, sources and components, etc.) spanning the health effects evidence
  - More detailed characterization of the strengths, limitations, and remaining uncertainties in the evidence base

# PM Concentrations and Trends (Chapter 2)

- $PM_{2.5}$ 
  - Steady declining trend 2000 to 2015, with most of the U.S. with annual average  $< 12 \mu\text{g}/\text{m}^3$
  - Annual average decreased from  $12 \mu\text{g}/\text{m}^3$  to  $8.6 \mu\text{g}/\text{m}^3$  from 2006 to 2014
- $PM_{10-2.5}$ 
  - Federal Reference Method (FRM) in 2011
  - Recent data indicates that the contribution of  $PM_{10-2.5}$  to  $PM_{10}$  is higher than previously reported
- UFPs
  - Highly variable concentration in space and over time due to physical and chemical processing in the atmosphere
  - UFP measured using multiple methods, varying in the size ranges examined
  - No U.S. monitoring network
- $PM_{2.5}$  Components
  - Organic carbon has replaced sulfate as the most abundant component of  $PM_{2.5}$  in many locations, specifically in the eastern U.S.



# Exposure to PM (Chapter 3)

- **Potential Errors and Uncertainty**

- Vary depending on the exposure assessment method used
- Evaluations more often occur for methods used in long-term exposure studies

- **Exposure Error**

- **Short-term exposure studies:** exposure error produces underestimation of health effects
- **Long-term exposure studies:** exposure error produces underestimation or overestimation of health effects
  - Overestimation of health effects occurs if the exposure model has low spatial resolution and underestimates exposures

- **Overall**

- Necessary to examine individual study details to evaluate potential errors and uncertainty as well as quality of the exposure assessment method used

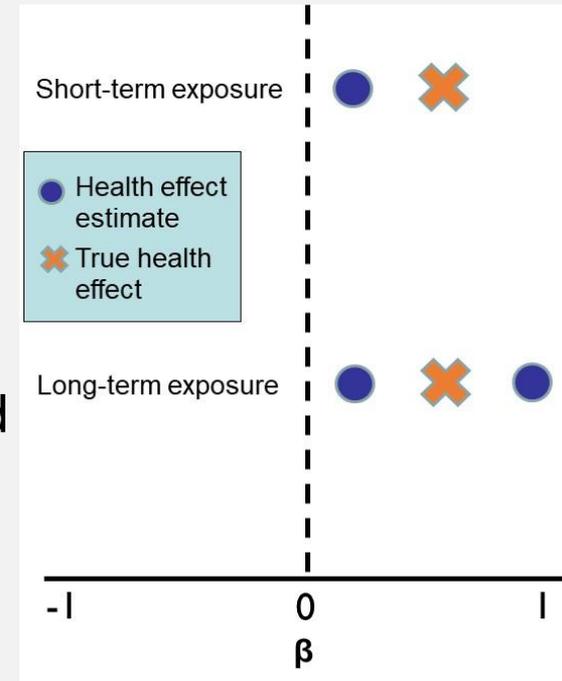
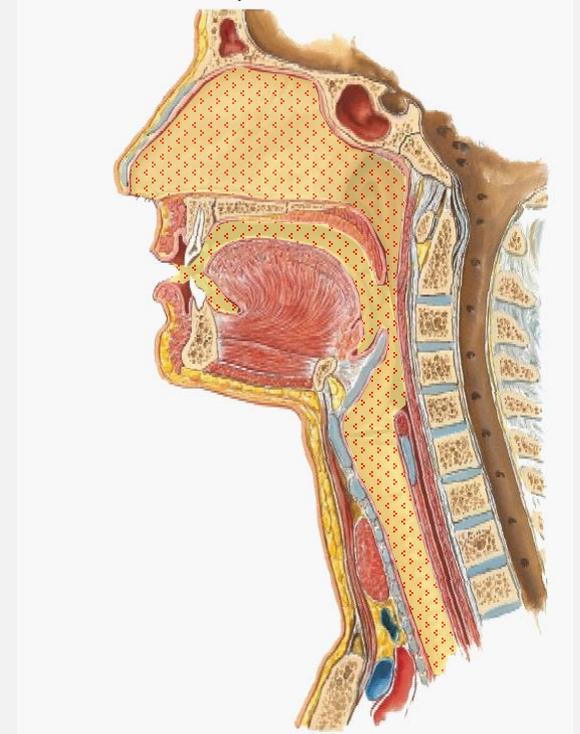


Figure. Influence of exposure error on health effects associations.

# Dosimetry of PM (Chapter 4)

- New information in this review:
  - Demonstrates that children inhale less through the nose and have lower nasal deposition efficiency than adults resulting in increased exposure of the lungs to inhaled PM
  - Shows the translocation of a small fraction of particles ( $\leq 0.2 \mu\text{m}$ ) out of the respiratory tract from the:
    - Olfactory mucosa to the brain
    - Alveolar region of the lung into blood
  - Indicates that  $\text{PM}_{10}$  overestimates the size of particles likely to enter the human lung



**Oronasal breathing**

# Draft PM ISA

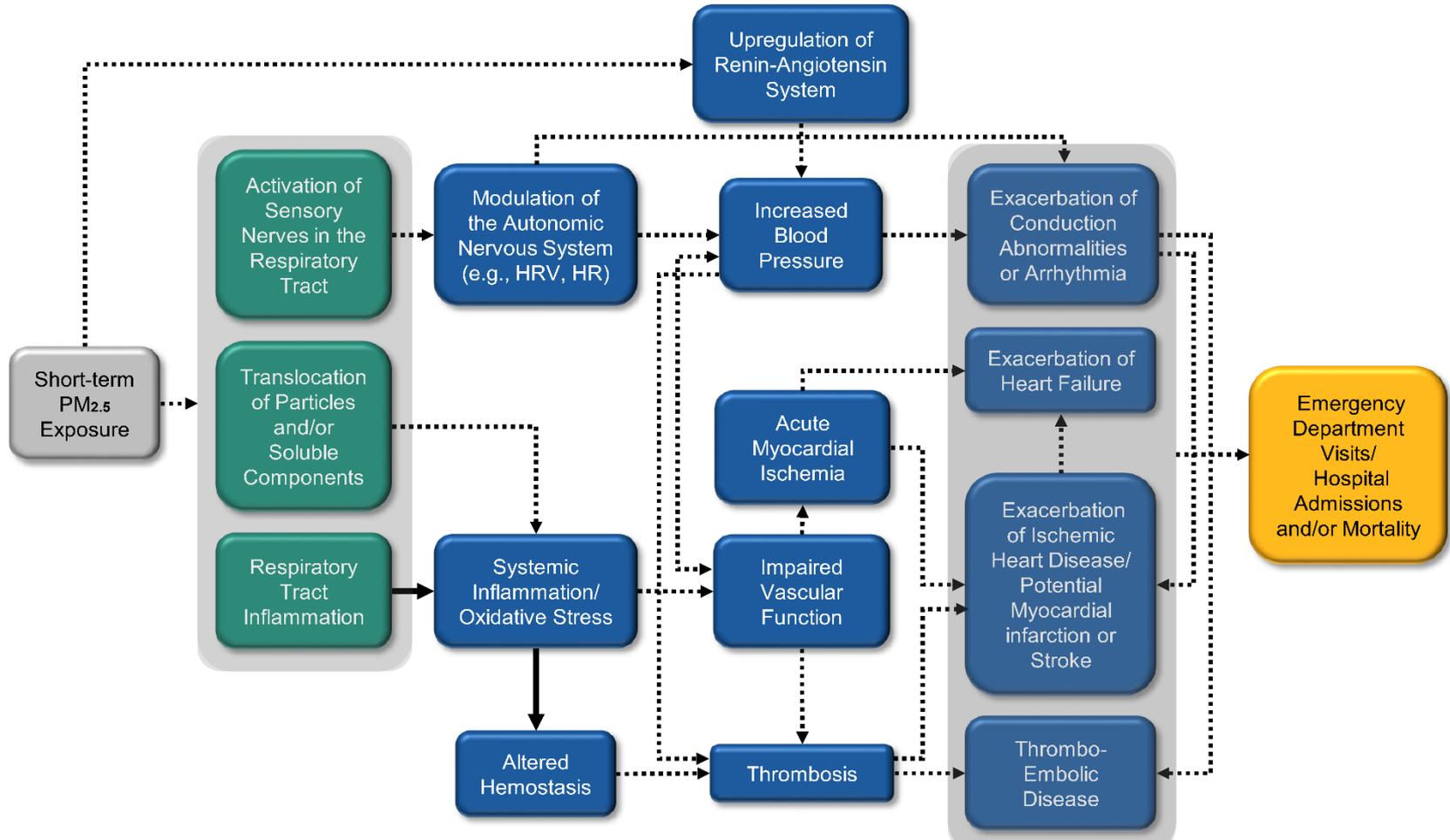
## Health Effects: Causality Determinations

HUMAN HEALTH EFFECTS					
ISA			Current PM Draft ISA		
Indicator			PM <sub>2.5</sub>	PM <sub>10-2.5</sub>	UFP
Health Outcome	Respiratory	Short-term exposure			
		Long-term exposure			
	Cardiovascular	Short-term exposure			
		Long-term exposure	*		
	Metabolic	Short-term exposure	*	*	*
		Long-term exposure	*	*	*
	Nervous System	Short-term exposure	*		*
		Long-term exposure	*	*	*
	Reproductive	Male/Female Reproduction and Fertility			
		Pregnancy and Birth Outcomes			
	Cancer	Long-term exposure	*	*	
	Mortality	Short-term exposure			
		Long-term exposure	*	*	

Causal
  Likely causal
  Suggestive
  Inadequate

\* = new determination or change in causality determination from 2009 PM ISA

# Example: Potential Biological Pathways Figure



Note: The boxes above represent the effects for which there is experimental or epidemiologic evidence, and the dotted arrows indicate a proposed relationship between those effects. Solid arrows denote direct evidence of the relationship as provided, for example, by an inhibitor of the pathway or a genetic knock-out model used in an experimental study. Shading around multiple boxes denotes relationships between groups of upstream and downstream effects. Progression of effects is depicted from left to right and color-coded (gray, exposure; green, initial event; blue, intermediate event; orange, apical event). Here, apical events generally reflect results of epidemiologic studies, which often observe effects at the population level. Epidemiologic evidence may also contribute to upstream boxes. When there are gaps in the evidence, there are complementary gaps in the figure.

# Respiratory Effects (Chapter 5)

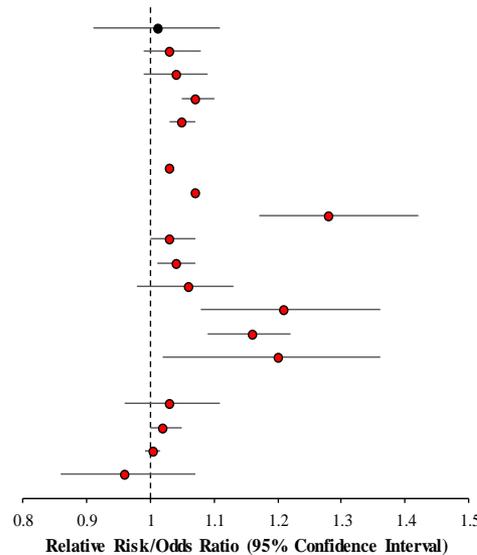
***Recent evidence supports the conclusions of the 2009 PM ISA, and continues to support a likely to be causal relationship between short- and long-term PM<sub>2.5</sub> exposure and respiratory effects***

- Short-term PM<sub>2.5</sub> Exposure **(Likely to be Causal)**
  - Epidemiologic evidence: consistent evidence for asthma exacerbation in children and COPD exacerbation in adults, as well as respiratory mortality.
  - Experimental evidence: worsening of allergic airways disease and/or subclinical effects related to COPD, provide biological plausibility for asthma and COPD exacerbations
- Long-term PM<sub>2.5</sub> Exposure **(Likely to be Causal)**
  - Epidemiologic evidence: consistent changes in lung function and lung function growth rate, increased asthma incidence, asthma prevalence and wheeze in children; acceleration of lung function decline in adults; and respiratory mortality
  - Experimental evidence: impaired lung development and development of allergic airways disease, biological plausibility for decrements in lung function growth in children and asthma development

# Respiratory Effects (Chapter 5)

## Example: Short-term PM<sub>2.5</sub> Exposure and Asthma

Study	Location	Age	Lag
Slaughter et al. (2005)	Spokane, WA	All ages	1
†Winqvist et al. (2012)	St. Louis, MO	All ages	0-4 DL
†Silverman et al. (2010)	New York, NY	All ages	0-1a
		All ages	0-1b
†Zhao et al. (2017)	Dongguan, China	All ages	0-3
†Yap et al. (2013)	Central Valley, CAc	1-9	0-2
	South Coast, CAc	1-9	0-2
†Chen et al. (2016)	Adelaide, Australia	0-17	0-4
†Li et al. (2011)d	Detroit, MI	2-18e	0-4
		2-18f	
†Winqvist et al. (2012)	St. Louis, MO	2-18	0-4 DL
†Silverman et al. (2010)	New York, NY	6-18	0-1a
		6-18	0-1b
†Iskandar et al. (2012)	Copenhagen, Denmark	6-18	0-4
†Silverman et al. (2010)	New York, NY	50+	0-1a
			0-1b
†Bell et al. (2015)	70 U.S. counties	65+	1
†Winqvist et al. (2012)	St. Louis, MO	65+	0-4 DL



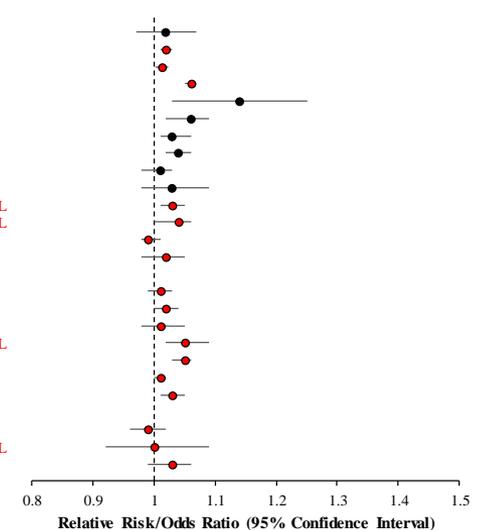
## Hospital Admissions

Red = recent studies;  
Black = U.S. study evaluated in the  
2009 PM ISA

## Emergency Department Visits

Red = recent studies;  
Black = U.S. and Canadian studies  
evaluated in the 2009 PM ISA

Study	Location	Age	Lag
Stieb et al. (2009)	7 Canadian cities	All	0
†Malig et al. (2013)	35 CA counties	All	0
†Ostro et al. (2016)	8 CA metro areas	All	0
†Weichenthal et al. (2016)	Ontario, Canada	All	0-2
Paulu et al. (2008)	Maine	All	0-1
ATSDR (2006)	Manhattan, NY	All	0-4
	Bronx, NY	All	0-4
Ito et al. (2007)	New York, NY	All	0-1
Peel et al. (2005)	Atlanta, GA	All	0-2
Slaughter et al. (2005)	Spokane, WA	All	1
†Winqvist et al. (2012)	St. Louis, MO	All	0-4 DL
†Sarnat et al. (2015)	St. Louis, MO	All	0-2 DL
†Byers et al. (2015)	Indianapolis, IN	All	0-2
†Kim et al. (2015)	Seoul, South Korea	All	0-2
†Gleason et al. (2014)	New Jersey	3-17	0-2
†Strickland et al. (2010)	Atlanta, GA	5-17	0-2
†Byers et al. (2015)	Indianapolis, IN	5-17	0-2
†Winqvist et al. (2012)	St. Louis, MO	2-18	0-4 DL
†Xiao et al. (2016)	Georgia	2-18	0-2
†Strickland et al. (2016)	Georgia	2-18	0
†Alhanti et al. (2015)	3 U.S. cities	5-18	0-2
†Byers et al. (2015)	Indianapolis, IN	45+	0-2
†Winqvist et al. (2012)	St. Louis, MO	65+	0-4 DL
†Alhanti et al. (2015)	3 U.S. cities	65+	0-2



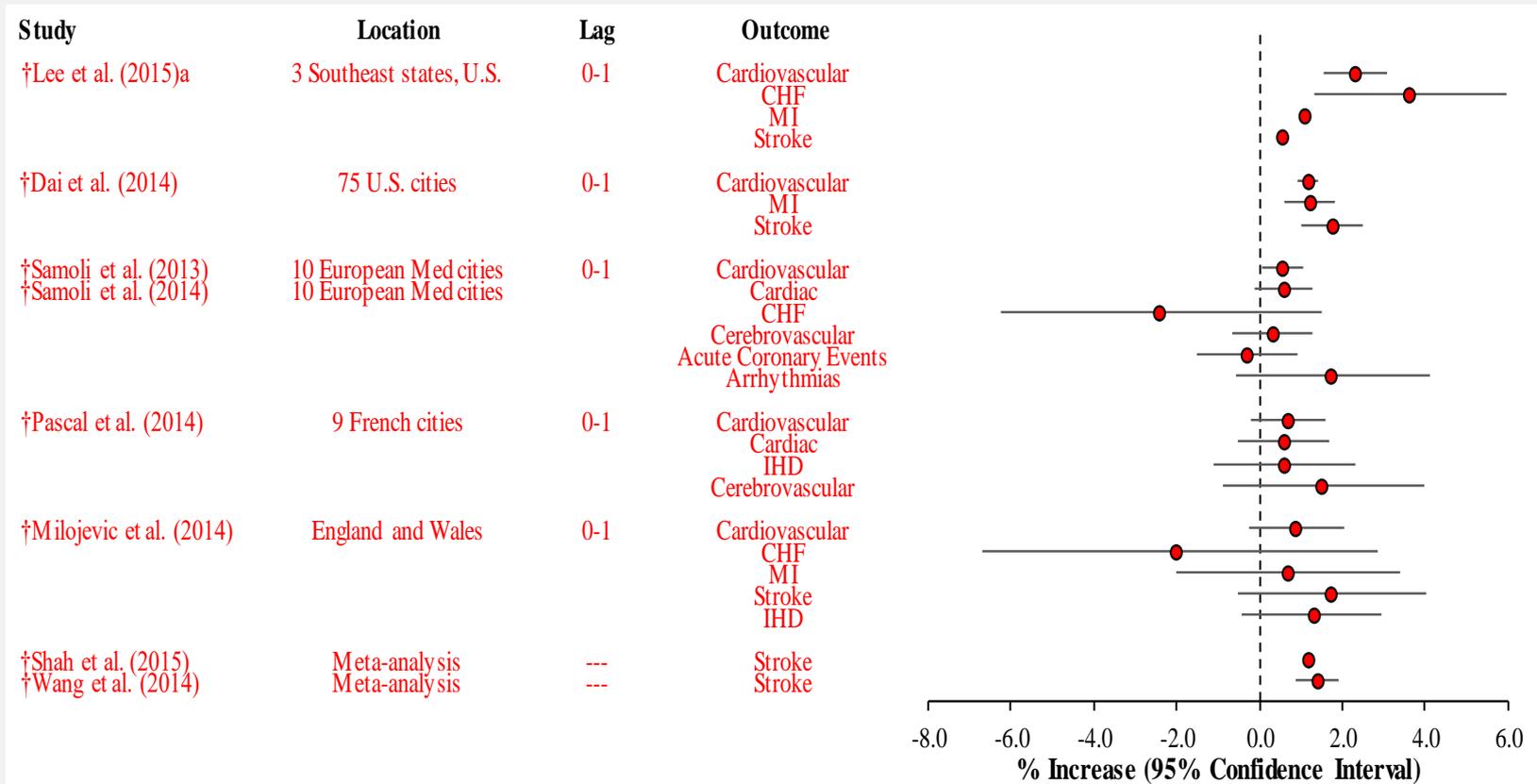
# Cardiovascular Effects (Chapter 6)

***A large body of recent evidence supports and extends the conclusions of the 2009 PM ISA that there is a causal relationship between short- and long-term PM<sub>2.5</sub> exposure and cardiovascular effects***

- Short-term PM<sub>2.5</sub> Exposure **(Causal)**
  - Epidemiologic evidence: generally consistent positive associations for hospital admissions and ED visits, particularly for ischemic heart disease (IHD) and heart failure (HF), as well as cardiovascular mortality
  - Experimental evidence: endothelial dysfunction, effects indicating impaired cardiac function, arrhythmia, changes in heart rate variability (HRV), increases in blood pressure (BP), and indicators of systemic inflammation, oxidative stress, and coagulation
- Long-term PM<sub>2.5</sub> Exposure **(Causal)**
  - Epidemiologic evidence: consistent positive associations for cardiovascular mortality; evidence for coronary heart disease (CHD) and stroke particularly in populations with pre-existing disease; evidence for coronary artery calcification (CAC)
  - Experimental evidence: impaired heart function, increased blood pressure, endothelial dysfunction, and atherosclerotic plaque progression

# Cardiovascular Effects (Chapter 6)

## Example: Short-term PM<sub>2.5</sub> Exposure and Cardiovascular-related Mortality



Red = recent studies

**Figure 6-7. Percent increase in cause-specific cardiovascular mortality outcomes for a 10 µg/m<sup>3</sup> increase in 24-hour average PM<sub>2.5</sub> concentrations observed in multicity studies and meta-analyses.**

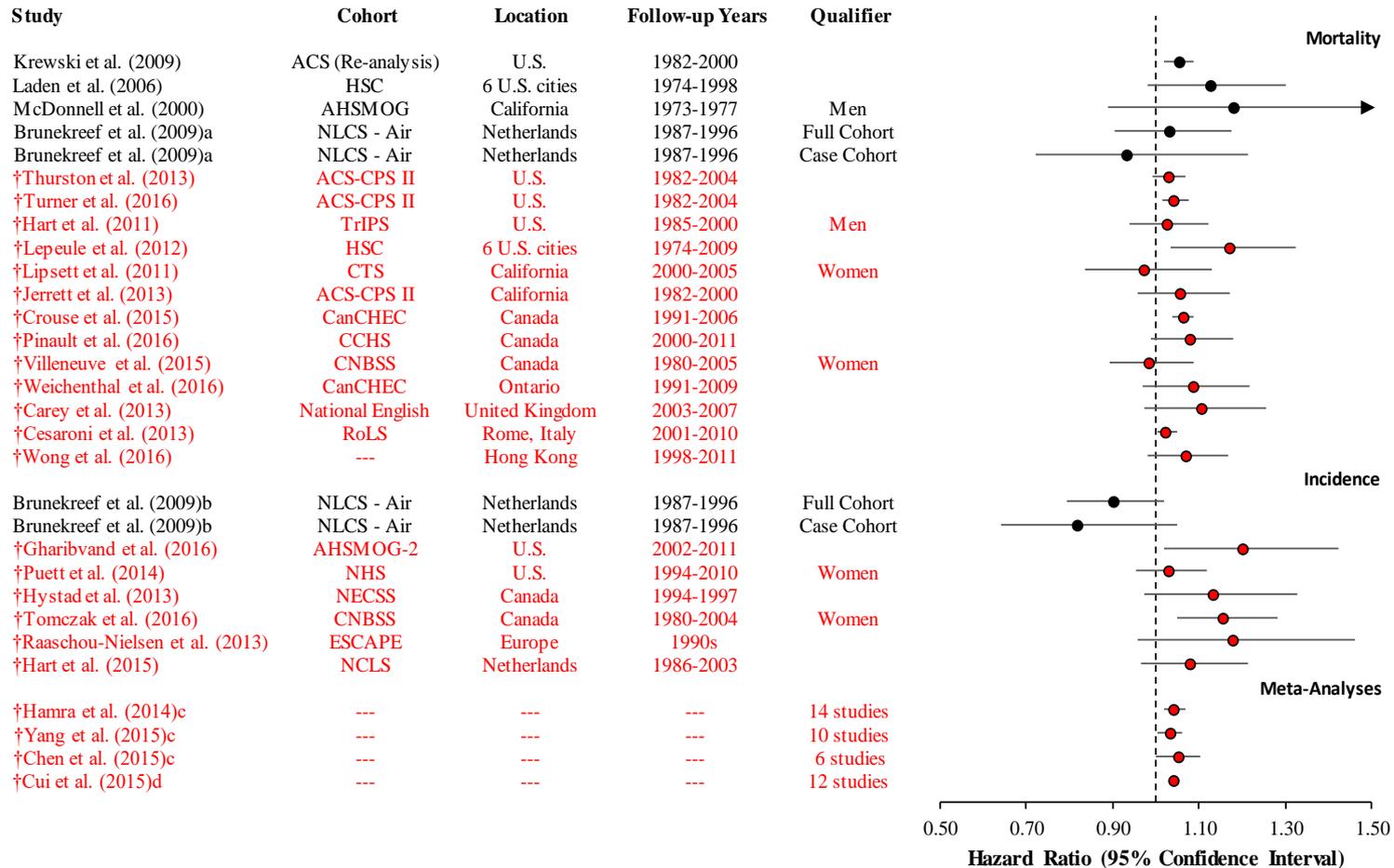
# Nervous System Effects (Chapter 8)

- Long-term PM<sub>2.5</sub> Exposure (**Likely to be Causal – NEW conclusion**)
  - Epidemiologic evidence
    - Consistent evidence for cognitive decline/impairment and decreased brain volume; more limited evidence for Alzheimer’s disease and dementia
  - Experimental evidence
    - Consistent evidence for inflammation, oxidative stress, morphologic changes, and neurodegeneration in multiple brain regions of adult animals
    - Limited evidence for early indicators of Alzheimer’s disease, impaired learning/memory, altered behavior in adult animals, and morphologic changes during development
- Long-term UFP Exposure (**Likely to be Causal – NEW conclusion**)
  - Epidemiologic evidence
    - Limited evidence for effects on cognitive development in children
  - Experimental evidence
    - Consistent evidence for inflammation, oxidative stress, and neurodegeneration in adult animals
    - Limited evidence of Alzheimer’s disease pathology in a susceptible animal model
    - Strong evidence, mainly from one laboratory, for inflammation, morphologic changes including persistent ventriculomegaly, and behavioral effects following pre/postnatal exposure

# Cancer (Chapter 10)

- Long-term PM<sub>2.5</sub> Exposure (**Likely to be Causal – NEW conclusion**)
  - Recent epidemiologic studies greatly expand upon the limited number of studies in the 2009 PM ISA that examined lung cancer incidence and mortality
    - Primarily positive associations, supported by analyses focusing on never smokers
  - Experimental and epidemiologic studies provide evidence for a relationship between PM<sub>2.5</sub> exposure and genotoxicity, epigenetic effects, and carcinogenic potential.
  - PM<sub>2.5</sub> exhibits several characteristics of carcinogens providing biological plausibility for PM<sub>2.5</sub> exposure contributing to cancer development

# Cancer (Chapter 10)



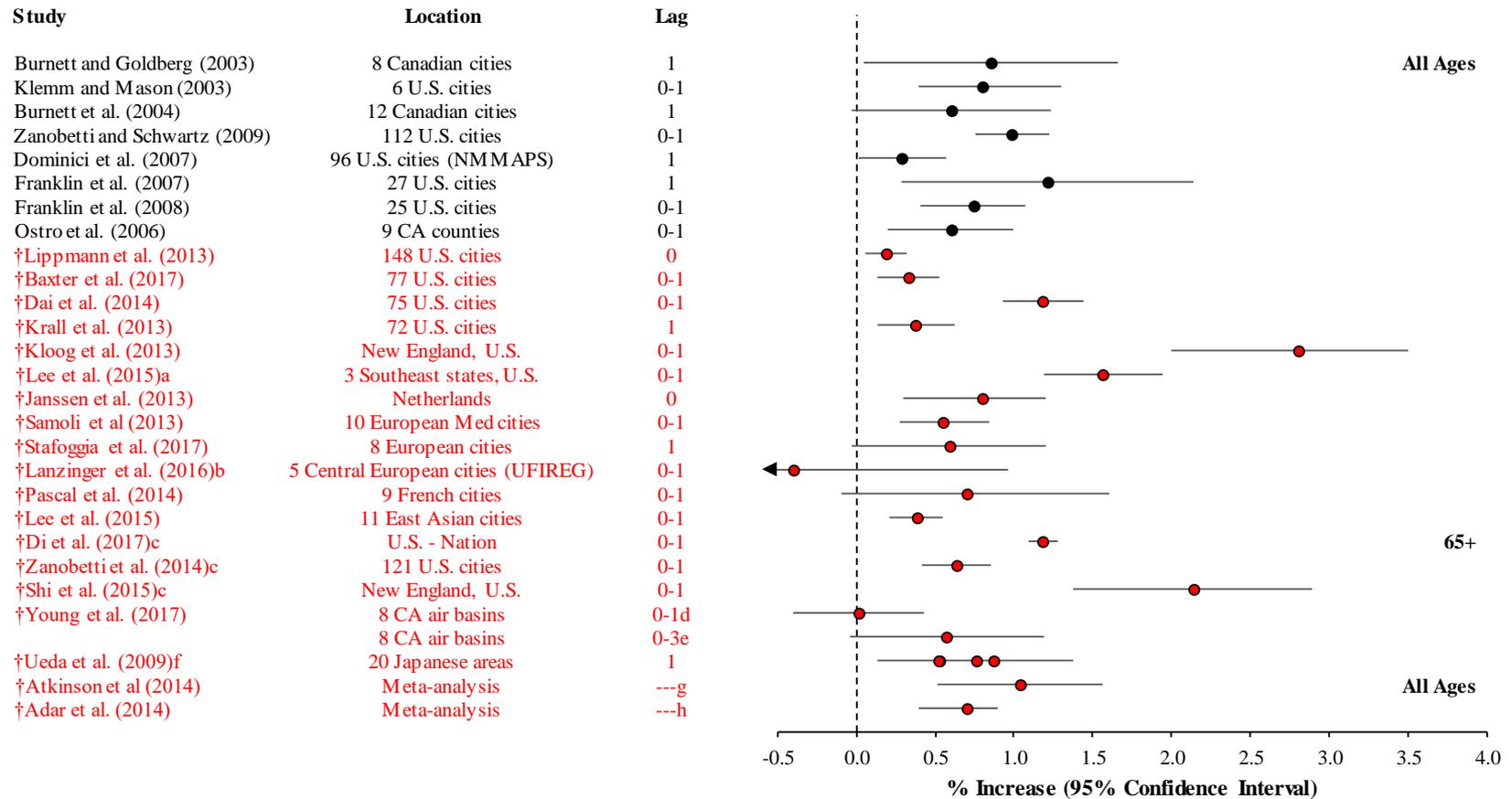
Note: Red = recent studies; Black = studies evaluated in the 2009 PM ISA

**Figure 10-3. Summary of associations reported in previous and recent cohort studies that examined long-term PM<sub>2.5</sub> exposure and lung cancer mortality and incidence.**

# Mortality – Short-term PM<sub>2.5</sub> Exposure (Chapter 11)

## (Causal)

***Recent evidence supports and extends the conclusions of the 2009 PM ISA that there is a causal relationship between short-term PM<sub>2.5</sub> exposure and mortality***



Note: Red = recent multi-city studies; Black = multi-city studies evaluated in the 2009 PM ISA

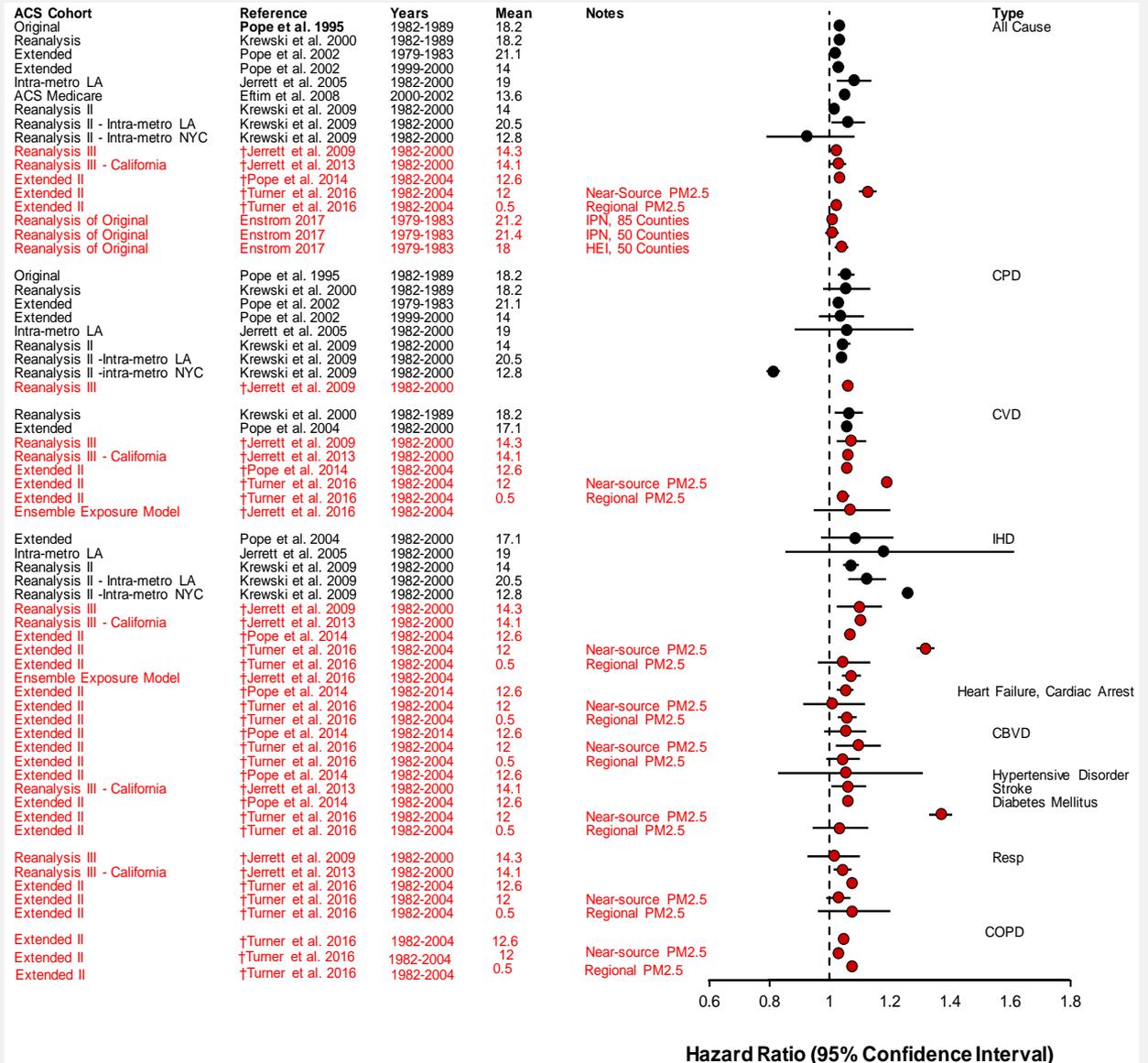
**Figure 11-1. Summary of associations between short-term PM<sub>2.5</sub> exposure and total (nonaccidental) mortality in multicity studies for a 10 µg/m<sup>3</sup> increase in 24-hour average concentrations.**

**Recent evidence supports and extends the conclusions of the 2009 PM ISA that there is a causal relationship between long-term PM<sub>2.5</sub> exposure and mortality**

**Figure 11-17.  
Associations  
between long-term  
exposure to PM<sub>2.5</sub>  
and total  
(nonaccidental)  
mortality in the  
American Cancer  
Society (ACS)  
cohort.**

Note: Associations are presented per 5 µg/m<sup>3</sup> increase in pollutant concentration.

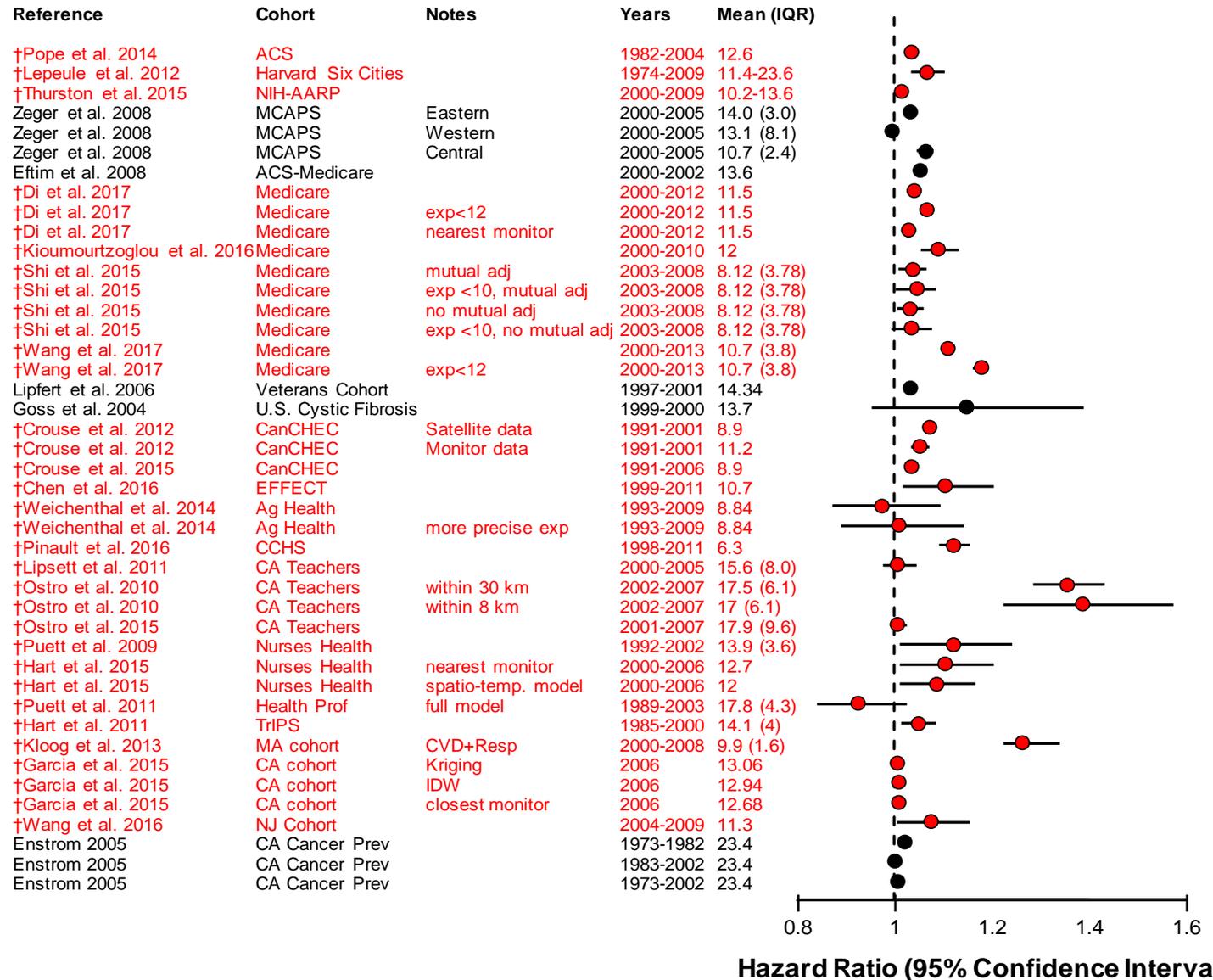
Red = recent studies;  
Black = studies evaluated in the  
2009 PM ISA



**Figure 11-18.**  
**Associations**  
**between long-term**  
**PM<sub>2.5</sub> and total**  
**(nonaccidental)**  
**mortality in recent**  
**North American**  
**cohorts.**

Note: Associations are presented per 5 µg/m<sup>3</sup> increase in pollutant concentration.

Red = recent studies;  
Black = studies evaluated in the 2009 PM ISA



# Other Causality Determinations (Chapters 5 – 10)

- Limitations and uncertainties in the evidence, along with few or no epidemiologic and experimental studies resulted in conclusions of:
  - Suggestive of, but not sufficient to infer, a causal relationship, for:
    - PM<sub>2.5</sub>: repro/dev, nervous system (ST)
    - PM<sub>10-2.5</sub>: mortality (ST), respiratory (ST), cardiovascular (ST/LT), metabolic (LT), cancer, nervous system (LT)
    - UFP: respiratory (ST), cardiovascular, (ST), nervous system (ST).
  - Inadequate to determine the presence or absence of a causal relationship, for:
    - PM<sub>10-2.5</sub>: respiratory (LT), metabolic (ST), repro/dev, nervous system (ST)
    - UFP: mortality (ST/LT), respiratory (LT), cardiovascular (LT), metabolic (ST/LT), repro/dev, cancer

# Policy-Relevant Considerations (Chapter 1)

- **Copollutant Confounding**: Across recent studies examining various health effects and both short- and long-term PM<sub>2.5</sub> exposures, associations remain relatively unchanged in copollutant models
- **Concentration-Response (C-R) Relationship**: Across studies evidence continues to support a linear, no-threshold C-R relationship
- **PM Components and Sources**: Many PM<sub>2.5</sub> components and sources are associated with many health effects, and the evidence does not indicate that any one source or component is more strongly related with health effects than PM<sub>2.5</sub> mass

# Populations Potentially at Increased Risk of a PM-related Health Effect (Chapter 12)

- The NAAQS are intended to protect both the population as a whole and those potentially at increased risk for health effects in response to exposure to criteria air pollutants
  - *Are there specific populations and lifestages at increased risk of a PM-related health effect, compared to a reference population?*
- The ISA identified and evaluated evidence for factors that may increase the risk of PM<sub>2.5</sub>-related health effects in a population or lifestage, classifying the evidence into four categories:
  - Adequate evidence; suggestive evidence; inadequate evidence; evidence of no effect
- Conclusions:
  - Adequate: children and nonwhite populations
  - Suggestive: pre-existing cardiovascular and respiratory disease, overweight/obese, genetic variants glutathione pathways, low SES
  - Inadequate: pre-existing diabetes, older adults, residential location, sex, diet, and physical activity

# Draft PM ISA

## Welfare Effects: Causality Determinations

NONECOLOGICAL WELFARE EFFECTS		
ISA		Current PM Draft ISA
		PM
Welfare Effect	Visibility	
	Climate	
	Materials	
<p> <span style="display: inline-block; width: 15px; height: 15px; background-color: #4b0082; border: 1px solid black;"></span> <b>Causal</b> <span style="display: inline-block; width: 15px; height: 15px; background-color: #8000ff; border: 1px solid black;"></span> <b>Likely causal</b> <span style="display: inline-block; width: 15px; height: 15px; background-color: #d8bfd8; border: 1px solid black;"></span> <b>Suggestive</b> <span style="display: inline-block; width: 15px; height: 15px; border: 1px solid black;"></span> <b>Inadequate</b> </p> <p>* = new determination or change in causality determination from 2009 PM ISA</p>		

# Welfare Effects (Chapter 13)

***Recent evidence supports and extends the conclusions of the 2009 PM ISA that there is a causal relationship between PM and welfare effects***

- Visibility Impairment **(Causal)**

- Long-term visibility improvements throughout the U.S as PM concentrations have decreased
- Regional and seasonal patterns in atmospheric visibility parallel PM concentration patterns
- More evidence supporting the relationship between visibility and PM composition

- Climate Effects **(Causal)**

- New evidence provides greater specificity about radiative forcing
- Increased understanding of additional climate impacts driven by PM radiative effects
- Improved characterization of key sources of uncertainty particularly with response to PM-cloud interactions

- Materials Effects **(Causal)**

- New information for glass and metals including modeling of glass soiling
- Progress in the development of quantitative dose-response relationships and damage functions for materials in addition to stone, including glass and metals
- Quantitative research on PM impacts on energy yield from photovoltaic systems

# PM ISA Team

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# Supplemental Materials

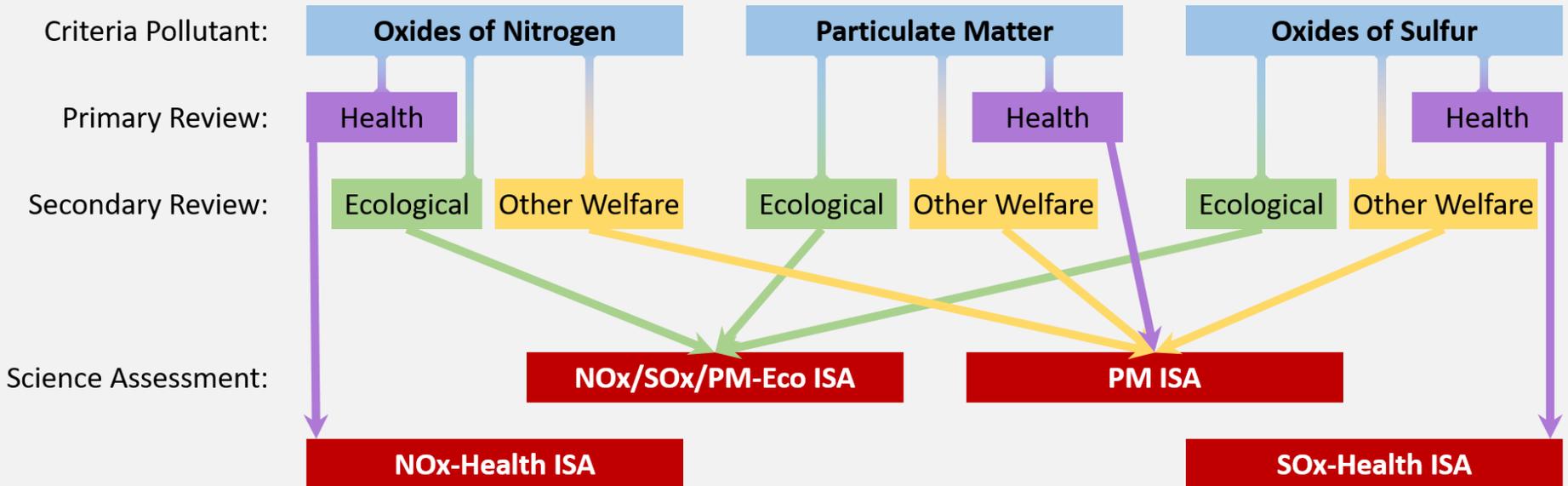
# May 2018 Memo: Standardized Charge Questions for CASAC

- The May 2018 memo identified general charge questions for CASAC in NAAQS reviews, to be supplemented with more detailed requests as necessary.
  - Are there areas in which additional knowledge is required to appraise the adequacy and basis of existing, new, or revised NAAQS? Please describe the research efforts necessary to provide the required information.
  - What scientific evidence has been developed since the last review to indicate if the current primary and/or secondary NAAQS need to be revised or if an alternative level or form of these standards is needed to protect public health and/or public welfare? Please recommend to the Administrator any new NAAQS or revisions of existing criteria and standards as may be appropriate. In providing advice, please consider a range of options for standard setting, in terms of indicators, averaging times, form, and ranges of levels for any alternative standards, along with a description of the alternative underlying interpretations of the scientific evidence and risk/exposure information that might support such alternative standards and that could be considered by the Administrator in making NAAQS decisions.
  - Do key studies, analyses, and assessments which may inform the Administrator's decision to revise the NAAQS properly address or characterize uncertainty and causality? Are there appropriate criteria to ensure transparency in the evaluation, assessment and characterization of key scientific evidence for this review?
- Two additional charge questions may elicit information not relevant to the standard-setting process. EPA may consider an appropriate mechanism, including after receiving CASAC's final advice on the standards, to facilitate robust feedback on these topics.
  - What is the relative contribution to air pollution concentrations of natural as well as anthropogenic activity? In providing advice on any recommended NAAQS levels, please discuss relative proximity to peak background levels.
  - Please advise the Administrator of any adverse public health, welfare, social, economic, or energy effects which may result from various strategies for attainment and maintenance of such NAAQS.

# NCEA/ORD and OAQPS/OAR Interactions: NAAQS Review

NAAQS Activity	NCEA/ORD	OAQPS/OAR
<b>Workshop on science-policy issues</b>	Co-lead development	Co-lead development
<b>Integrated Review Plan</b>	Lead development of chapter on the ISA	Lead development of other chapters (e.g., REA, PA)
<b>Integrated Science Assessment</b>	<u>Lead development</u>	Review draft materials with focus on identifying areas where clarification is needed
<b>Risk/Exposure Assessment</b>	Review draft materials and provide comments on interpretation of science	<u>Lead development</u>
<b>Policy Assessment</b>	Review draft materials and provide comments on interpretation of science	<u>Lead development</u>
<b>Rule-making materials</b>	Provide technical and scientific support	<u>Lead development</u>

# Relationship among Integrated Science Assessments



- Notes:
- Primary (health-based) review of effects on public health = **Health**
  - Secondary (welfare-based) review of effects on public welfare = **Ecological** + **Other Welfare**
  - Ecological** = effects on soil, water, crops, vegetation, animals, wildlife
  - Other Welfare** = effects on manmade materials, weather, visibility, climate

# Example: Evaluation of PM Components Studies

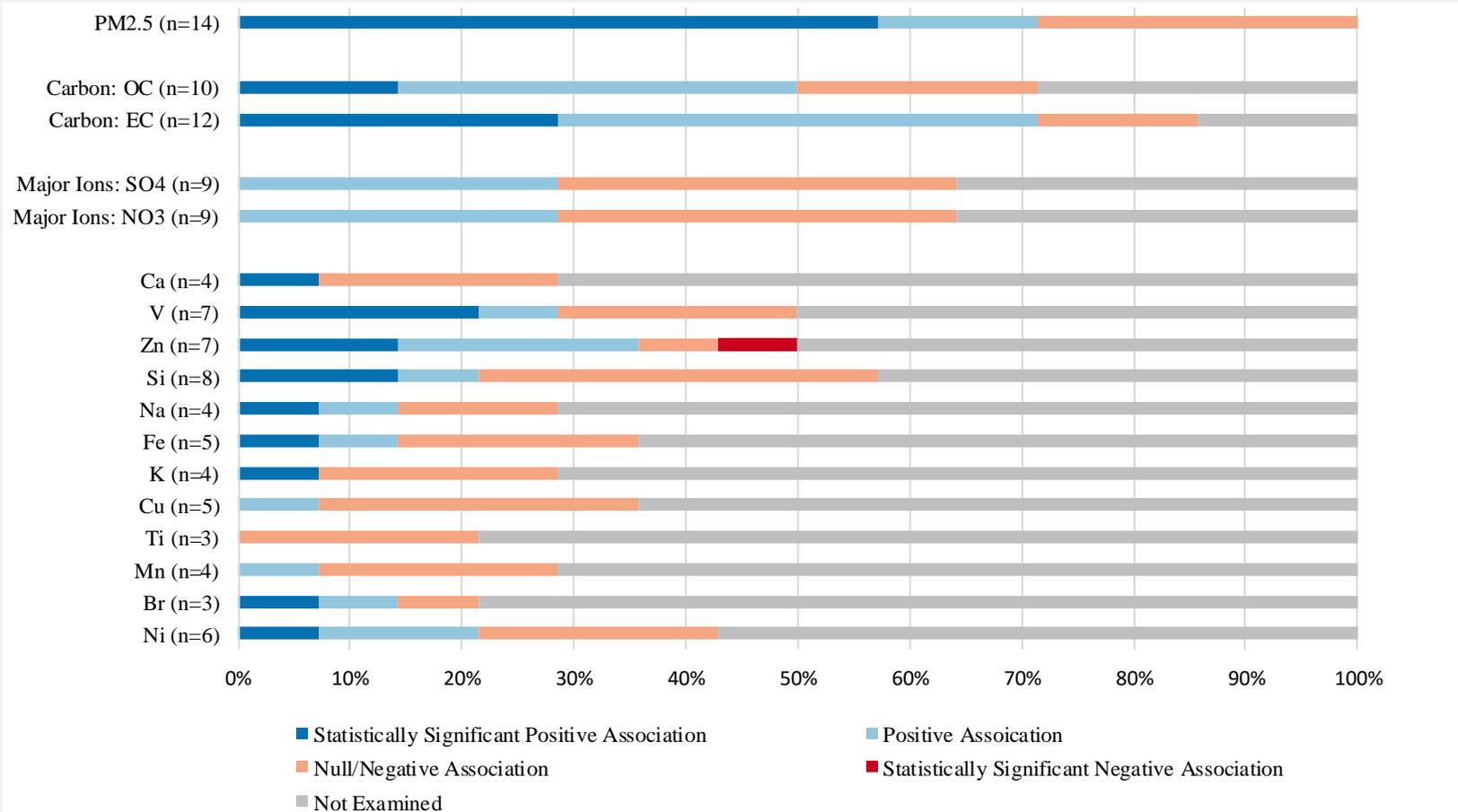
## Short-term PM<sub>2.5</sub> and PM<sub>2.5</sub> Components Exposure and Cardiovascular Effects: Hospital Admissions and Emergency Department (ED) visits – Heat Map

	<i>Ito et al. (2013)</i>	<i>Lal et al. (2011)</i>	<i>Koumartzoglou et al. (2013)</i>	<i>Osato et al. (2016)</i>	<i>Kim et al. (2012)</i>	<i>Sarmat et al. (2015)</i>	<i>Zanobetti et al. (2009)</i>	<i>Peng et al. (2009)</i>	<i>Levy et al. (2012)</i>	<i>Ballester et al. (2014)</i>	<i>Ito et al. (2011)</i>	<i>Lai et al. (2016)</i>	<i>Baloghazi et al. (2014)</i>	<i>Sarnoi et al. (2016)</i>	
	CVD	CVD	CVD	CVD	CVD	CVD	CVD	CVD	CVD	CVD	CVD	CVD	CVD	CVD	
PM <sub>2.5</sub>	0-3	0, 0-3	0-1	2	0-1	0-2	0-1	0	0	0	0	0	0	0	1, 0-6
Carbon															
OC	0-3		0-1	0,1,2	0	0-2		0,1,2	0		0	0	0	0	
EC	0-3	0	0-1	0,2	0	0-2		0,1,2	0		0	0	0	0	1
Major Ions															
SO <sub>4</sub> <sup>2-</sup>	0-3			0,1,2	0	0-2		0,1,2	0		0	0	0	0	
NO <sub>3</sub> <sup>-</sup>	0-3			2	0	0-2		0,1,2	0		0	0	0,1,2		
Metals, Metalloids, Non-Metals															
Ca						0-2				0		0	0,1,2		
V	0-3			0,1,2			0-1			0	0	0	0,1,2		
Zn	0-3			0		0-2				0	0	0	1		
Si	0-3	1,2		1		0-2		0,1,2			2,3	0	0,1,2		
Na							0-1	0,1,2			0	0			
Fe	0-3			0,1,2		0-2						0	0		
K				2		0-2						0	0,1,2		
Cu	0-3			0,1,2		0-2						0	0,1,2		
Ti				0,1,2								0	0,1,2		
Mn		0,1,2,3		0,1,2								0	0		
Br							0-1				0	0			
Ni		3		0,1,2			0-1				0	0	0,1,2		

- Numbers represent lags for which associations observed.
- PM<sub>2.5</sub> mass or PM<sub>2.5</sub> components associations categorized by results that are statistically significant positive (dark blue), positive/null (light blue), null/negative (light orange), statistically significant negative (red), or not examined (gray).

# Example: Evaluation of PM Components Studies

## Short-term PM<sub>2.5</sub> and PM<sub>2.5</sub> Components Exposure and Cardiovascular Effects: Hospital Admissions and ED visits – Distribution of Risk Estimates



Bars represent the percent of associations across studies for PM<sub>2.5</sub> mass or PM<sub>2.5</sub> components that are statistically significant positive (dark blue), positive (light blue), null/negative (light orange), statistically significant negative (red), or not examined (gray). n = number of studies that provided an estimate for PM<sub>2.5</sub> mass and individual PM<sub>2.5</sub> components.

# At-Risk Framework Description

Classification	Health Effects
<b>Adequate evidence</b>	<p>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.</p>
<b>Suggestive evidence</b>	<p>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.</p>
<b>Inadequate evidence</b>	<p>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.</p>
<b>Evidence of no effect</b>	<p>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.</p>