



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

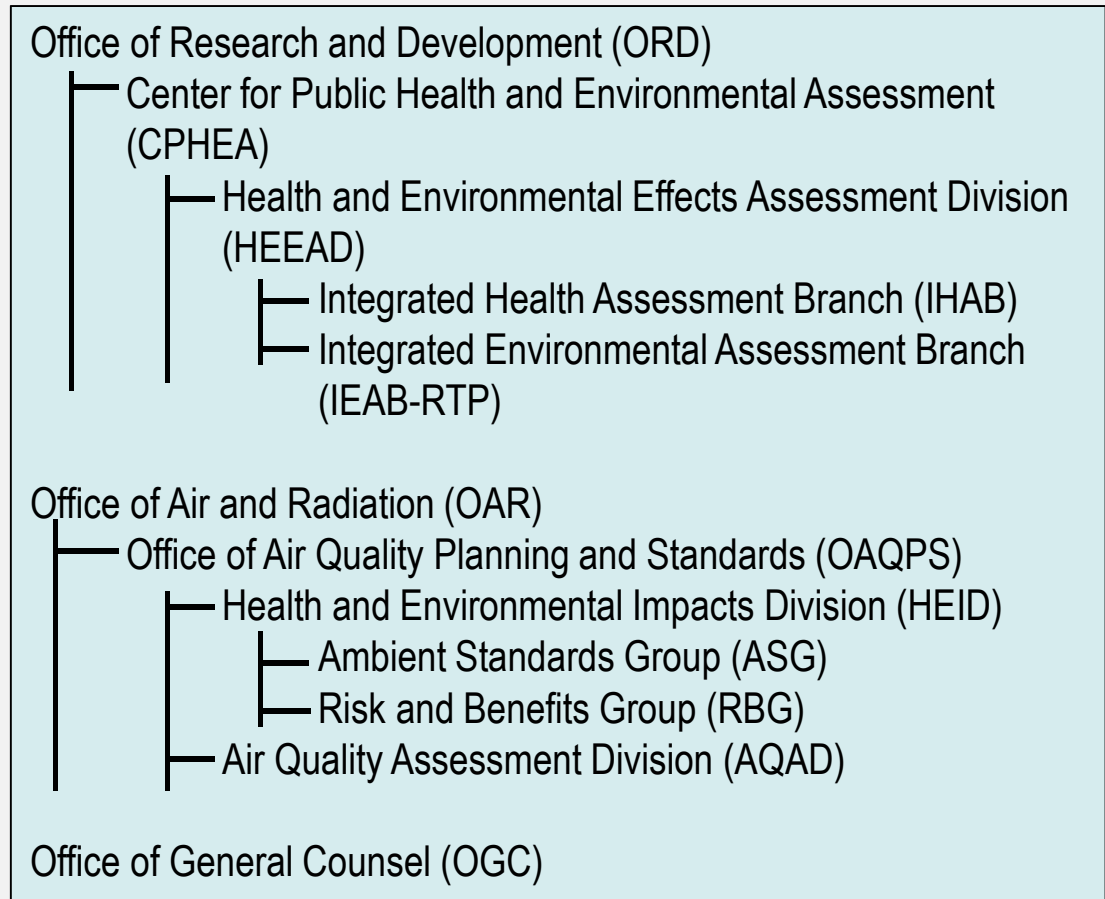
**Review of the Integrated Science Assessment
for Ozone
(External Review Draft)**

**Center for Public Health and Environmental Assessment
Office of Research and Development
December 4, 2019**

EPA Speakers

- ORD/CPHEA
 - John Vandenberg, Director, HEEAD
 - Tom Luben, ISA Health Lead
 - Meredith Lassiter, ISA Welfare Lead

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 - Robert Wayland, Group Leader (HEID/RBG)
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 - Stephen Graham (HEID/RBG)



Outline for Presentation

- Introduction and Background
 - Statutory requirements
 - Current Ozone 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

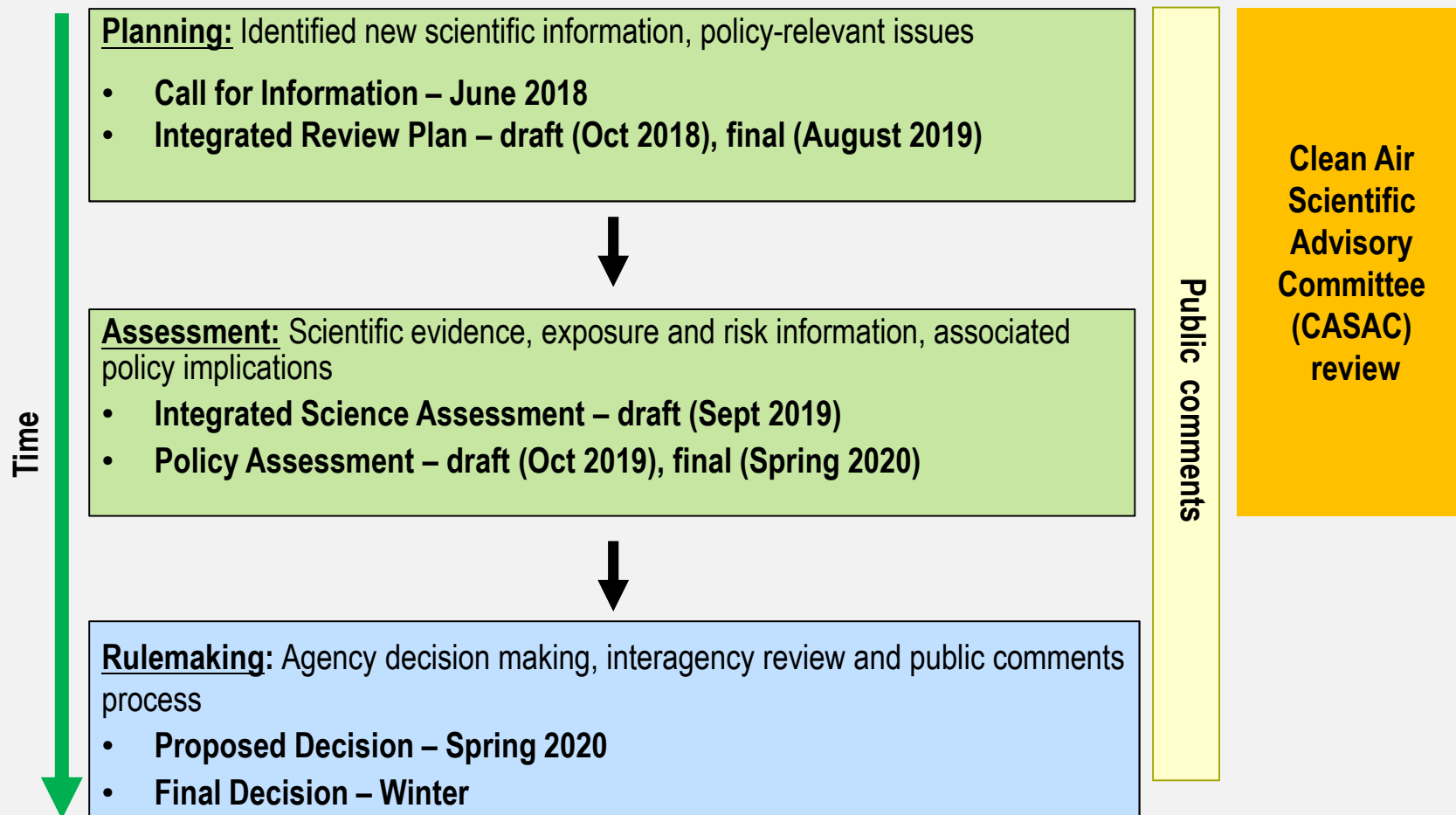
Introduction and Statutory Requirements

- EPA sets national ambient air quality standards (NAAQS) for six pollutants
 - Particulate matter (PM)
 - Ground-level ozone (O₃)
 - Lead (Pb)
 - Carbon monoxide (CO)
 - Nitrogen dioxide (NO₂)
 - Sulfur dioxide (SO₂)
- 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 (the “criteria”) and NAAQS for each criteria pollutant every five years, and to obtain advice from the Clean Air Scientific Advisory Committee (CASAC) on each review.
 - 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.

Process and Schedule for this Review of the Ozone NAAQS



Initiation of Expedited Review (May 2018 memo)

May 9, 2018 memo from the EPA Administrator:

- Directed the initiation of an expedited review of the Ozone NAAQS, targeting completion by the end of 2020
 - Also specified expedited review of NAAQS for PM
- 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

Overview of Current Ozone NAAQS

Current Standards – Last Review Completed in 2015*					Decision in 2015 Review
Indicator	Averaging Time	Primary/Secondary	Level	Form	
Ozone (O ₃)	8 hours	Primary and Secondary	0.070 ppm	Annual fourth-highest daily maximum 8-hour concentration, averaged over 3 years	Revised from 0.075 ppm to 0.070 ppm

*Final rule signed October 1, 2015, and effective December 28, 2015. The previous (2008) ozone standards additionally remain in effect in some areas. Revocation of the previous (2008) ozone standards and transitioning to the current (2015) standards will be addressed in the implementation rule for the current standards.

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

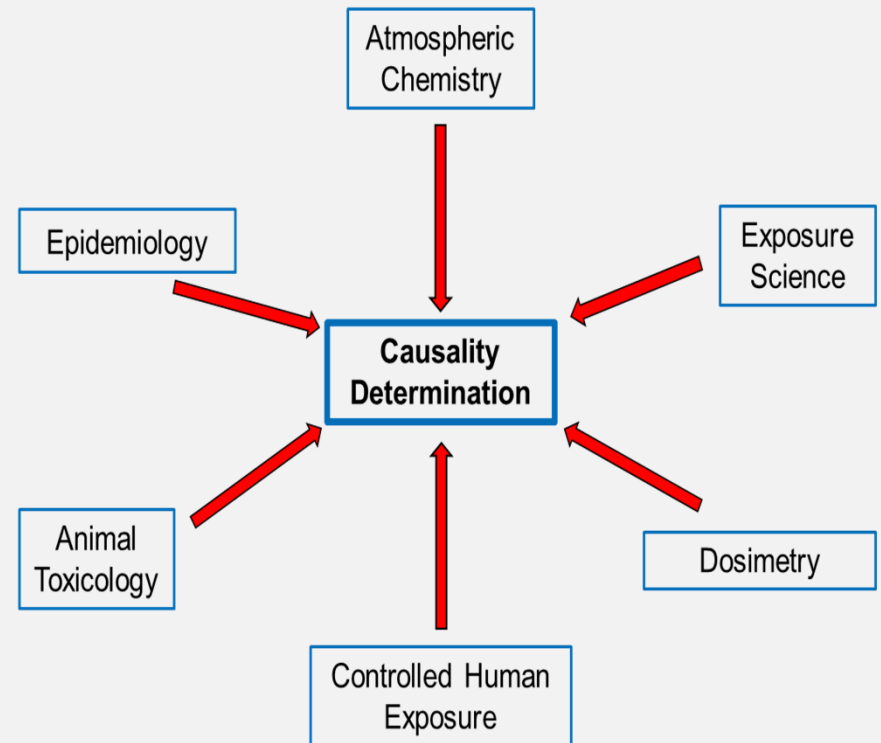
- Provides transparency through structured framework
- Developed and has been applied to ISAs for all criteria pollutants
- Emphasizes synthesis of evidence across scientific disciplines
 - E.g., controlled human exposure, epidemiologic, and toxicological studies, dosimetry, exposure science, atmospheric sciences, ecology
- 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 a causal relationship
 - Not likely to be a causal relationship

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

- [ISA Preamble](#) describes this framework
- Appendix 10 to the draft Ozone ISA provides supplemental information to the preamble
- 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**

Approach for Evaluation of the Scientific Evidence

- Organize relevant literature for broad outcome categories
- Evaluate studies, characterize results, extract relevant data
- Integrate evidence across disciplines for outcome categories
- Develop health and welfare causality determinations using established framework described in the [Preamble](#)
- Synthesize evidence for populations potentially at increased risk (health only)



Illustrative Example: Evidence Integration for Health

Framework for Causality Determinations in the ISA

	Health Effects	Ecological and Other Welfare Effects
Causal relationship	<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. For example: (1) controlled human exposure studies that demonstrate consistent effects, or (2) observational studies that cannot be explained by other lines of evidence (e.g., animal studies or mode of action information). 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 determination is based on multiple studies conducted by multiple research groups, and evidence that is considered sufficient to infer a causal relationship is usually obtained from the joint consideration of many lines of evidence that reinforce each other.</p>
Likely to be a causal relationship	<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 show an association, but exposures are difficult to address and/or other lines of evidence (e.g., animal studies or mode of action information) 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>
Suggestive of, but not sufficient to infer, a causal relationship	<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 toxicologic 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>
Inadequate to infer a causal relationship	<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>
Not likely to be a causal relationship	<p>Evidence indicates there is no causal relationship with relevant pollutant exposures. Several adequate studies, covering a full range of levels of 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 exposures are consistent in failing to show an effect at any level of exposure.</p>

Purpose and Contents of ISA

- **Purpose:** To identify, evaluate, and communicate the scientific information representing the “air quality criteria” per Section 108; Make causality determinations for health and welfare effects; Serves as the scientific foundation for the NAAQS
- **Contents of the Ozone ISA:**
 - Preface: Legislative Requirements, History
 - Executive Summary**
 - Integrated Synthesis**
 - Appendix 1: Atmospheric Source, Chemistry, Meteorology, Trends, and Background Ozone
 - Appendix 2: Exposure to Ambient Ozone
 - Appendix 3-7: Health Effects- Respiratory, Cardiovascular, Metabolic, Mortality, Other Endpoints
 - Appendix 8-9: Welfare Effects- Ecological, Climate
 - Appendix 10: Process

Improvements to the Assessment Process for Ozone ISA

- Utilized feedback from previous CASAC reviews (e.g., PM, NO_x/SO_x/PM-eco) and recent advances in systematic review approaches to update the process
 - Modernized systematic review methodologies
 - Improved literature search and screen methods (e.g., machine learning)
 - PECOS tool supports systematic screening
 - Improved documentation
 - Process Appendix (Appendix 10)
 - Study quality evaluation
 - Quality assurance
 - Revised overall format (focus on Integrated Synthesis)

Ozone ISA: Overall Observations

- Ozone Concentrations and Background Ozone
 - Median design value (4th highest daily max) ozone concentrations in the U.S. decreased from >80 ppb in 2000 to <70 ppb in 2013, and have remained relatively constant since
 - Three-month mean U.S. background ozone concentration estimates typically range from 20-50 ppb depending on elevation, meteorology, and precursor sources
- Health Effects
 - Recent studies support and expand strong body of evidence that short-term ozone exposure causes respiratory effects; Emerging evidence that short- and long-term ozone exposure is likely to cause metabolic disease, such as diabetes
 - Overall, recent evidence for short-term ozone exposure and cardiovascular effects, and between short-term ozone exposure and total (nonaccidental) mortality is suggestive of, but not sufficient to infer, a causal relationship
- Welfare Effects
 - Recent studies generally strengthen large body of scientific evidence demonstrating ozone effects on vegetation and ecosystems, and on radiative forcing and climate variables (e.g., temperature and precipitation)

Atmospheric Chemistry and Background Ozone

Appendix 1: Atmospheric Chemistry- Overall Concentrations and Trends

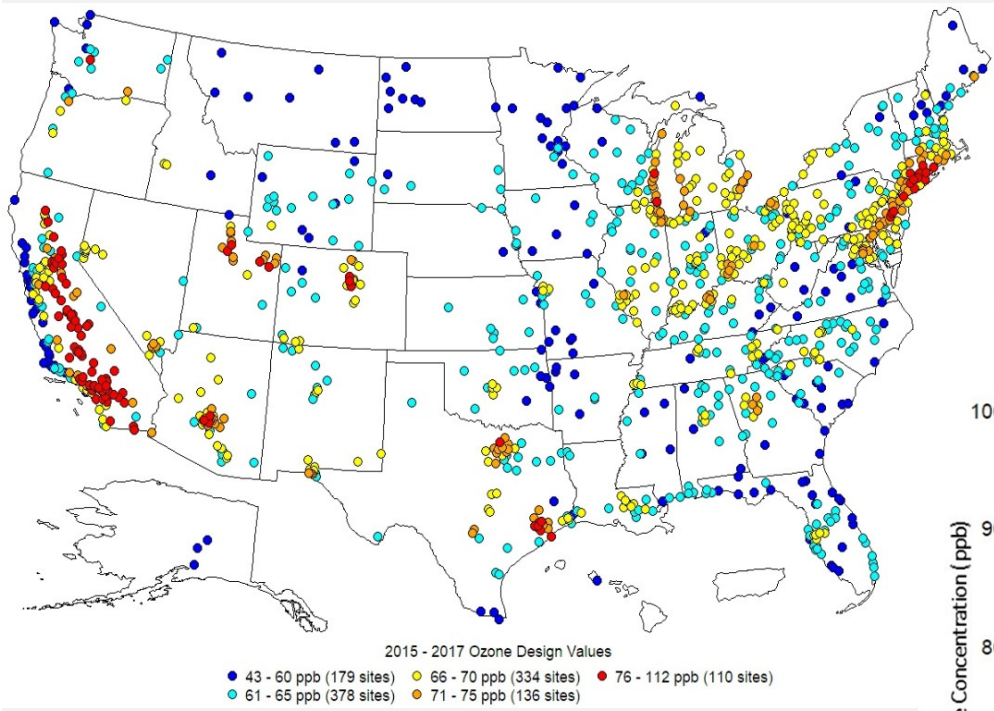


Figure 1-8 Individual monitor ozone concentrations in terms of design values for 2015–2017.

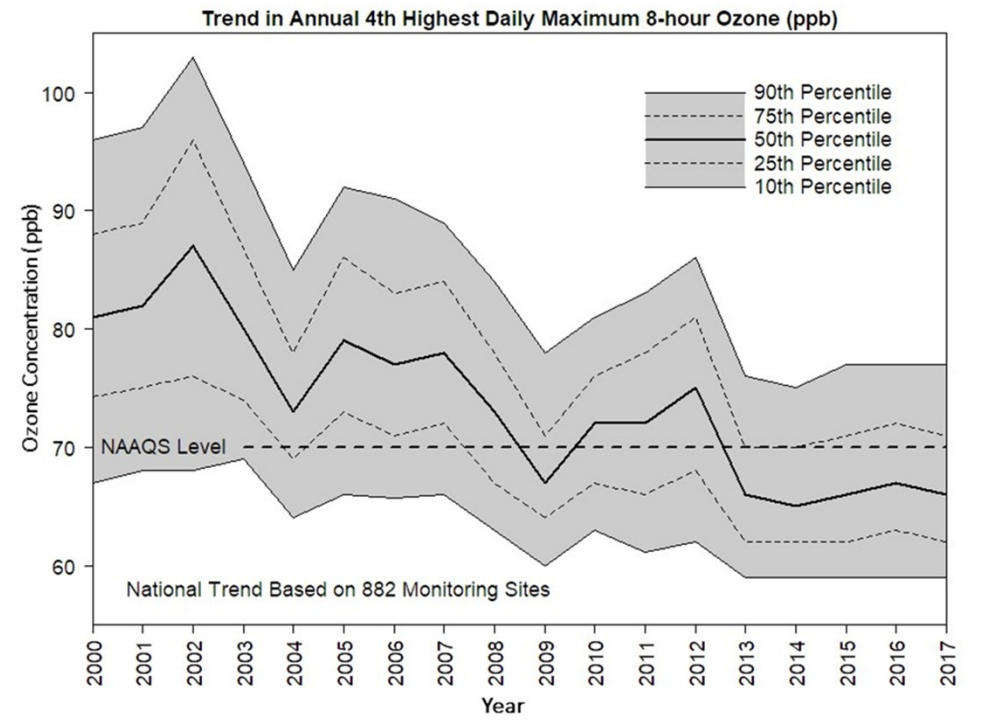


Figure 1-9 National 4th-highest 8-hour daily max ozone trend and distribution across 882 U.S. Ozone monitors 2000–2017 (concentrations in ppb).

Appendix 1: The Role of Background Ozone

- **U.S. Background Ozone (USB)**: *modeled ozone concentration that would occur if all U.S. anthropogenic precursor emissions were removed*
 - USB continues to account for large fraction of ambient ozone concentrations as a result of stratospheric exchange, international transport, wildfires, lightning, global methane emissions, natural biogenic and geogenic precursor emissions
 - Wider range of seasonal average USB concentration estimates (20-50 ppb) and poorer agreement between models than reported in 2013 Ozone ISA
 - Increasing trend of USB concentration estimates at high elevations in the western U.S. (before 2010) now shows signs of slowing or even reversing, attributed to decreasing Asian emissions

Appendix 2: Influence of Exposure Error on Epidemiology Study Outcomes

Sources of Exposure Measurement Errors	Fixed-site monitor	Data averaging	Inverse distance weighting	Kriging	Land use regression	Spatiotemporal model	Chemical transport model	Hybrid model	Microenvironmental model	Potential Influence on Effect Estimates	
										Time Series Studies <i>Errors mostly due to reduced correlation between surrogate and true exposure</i>	Long-Term Studies <i>Potential errors mostly due to differences between surrogate and true exposure</i>
Omission of time-activity data	X	X	X	X	X	X	X	X		((-))	((-))
Near road scavenging	X	X	X	X			X			((-))	((-))
Poorly characterized spatiotemporal variability	X	X								((-))	((-/++))
Over-smoothing			X	X							((-))
Exposure model misspecification					X	X		X			-/+
Spatial misalignment					X	X		X			-/+
Distributions of input data differ from true population distributions									X	(())	((-/++))

Health Effects

Summary

Causality Determinations - Health

Health Effects		
Short-term Exposure		
	<u>2013 Ozone ISA</u>	<u>Current Ozone ISA</u>
Respiratory Effects	Causal	Causal
Metabolic Effects	No Causality Determination	Likely to be Causal*
Cardiovascular Effects	Likely to be Causal	Suggestive of, but not sufficient to infer
Nervous System Effects	Suggestive of, but not sufficient to infer	Suggestive of, but not sufficient to infer
Mortality	Likely to be Causal	Suggestive of, but not sufficient to infer
Long-term Exposure		
Respiratory Effects	Likely to be Causal	Likely to be Causal
Metabolic Effects	No Causality Determination	Likely to be Causal*
Cardiovascular Effects	Suggestive of, but not sufficient to infer	Suggestive of, but not sufficient to infer
Nervous System Effects	Suggestive of, but not sufficient to infer	Suggestive of, but not sufficient to infer
Reproductive Effects – Fertility and Reproduction	Suggestive of, but not sufficient to infer	Suggestive of, but not sufficient to infer
Reproductive Effects – Pregnancy and Birth Outcomes		Suggestive of, but not sufficient to infer
Cancer	Inadequate	Inadequate
Mortality	Suggestive of, but not sufficient to infer	Suggestive of, but not sufficient to infer

Red text = new determination or change in causality determination from 2013 Ozone ISA

* New Causality Determination

Appendix 3: Respiratory Effects and Short-term Ozone Exposure

Recent evidence supports and extends the conclusions of the 2013 Ozone ISA that there is a causal relationship between short-term ozone exposure and respiratory effects.

- Evidence spanning decades from Controlled Human Exposure, Epidemiologic and Animal Toxicological studies
 - Controlled Human Exposure Studies: Well-established endpoints showing ozone-induced effects at 60-70 ppb and higher (e.g., lung function decrements, respiratory symptoms, inflammation)
 - Epidemiologic Studies: Panel studies and emergency department visit/hospital admission studies at ambient ozone concentrations
 - Animal Toxicological Studies: Large body of evidence demonstrates ozone-induced changes in lung function measures, inflammation, increased airway responsiveness, and impaired lung host defense

Appendix 3: Respiratory Effects and Short-term Ozone Exposure (Cont.)

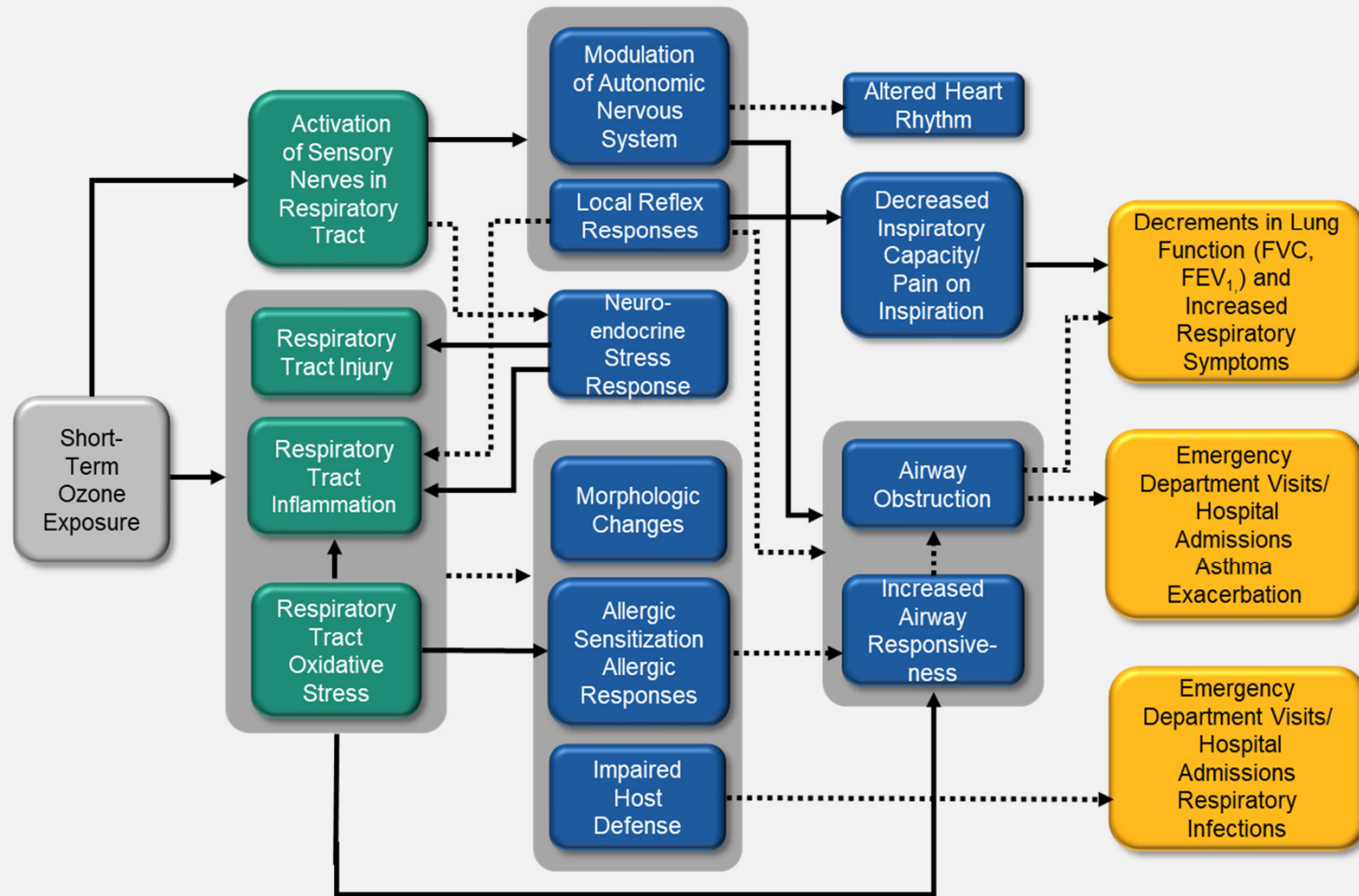


Figure 3-1

Potential biological pathways for respiratory effects following short-term ozone exposure.

Appendix 3: Respiratory Effects and Long-term Ozone Exposure

Recent evidence supports and extends the conclusions of the 2013 Ozone ISA, and continues to support that there is a likely to be causal relationship between long-term ozone exposure and respiratory effects.

- Animal toxicological studies in infant monkeys show postnatal ozone exposure results in respiratory effects, including alterations in structure and function of the developing lung that may underlie the development of asthma
- Epidemiologic studies demonstrate association between long-term ozone exposure and asthma development in children, including children with specific genetic variants

Appendix 5: Metabolic Disease Effects and Short-term Ozone Exposure

NEW conclusion: Recent evidence supports that there is a likely to be causal relationship between short-term ozone exposure and metabolic effects.

- Animal toxicological studies demonstrate that short-term ozone exposure results in metabolic effects
- Controlled human exposure study provides evidence that short-term ozone exposure results in neuroendocrine system activation
- Epidemiologic studies provide evidence for positive associations between short-term ozone exposure and metabolic indicators

Appendix 5: Metabolic Disease Effects and Long-term Ozone Exposure

NEW conclusion: Recent evidence supports that there is a likely to be causal relationship between long-term ozone exposure and metabolic effects.

- Animal toxicological studies demonstrate that long-term ozone exposure results in metabolic effects
 - Impaired insulin signaling
 - Induced glucose intolerance
 - Insulin resistance
- Epidemiologic studies demonstrate that long-term ozone exposure is associated with:
 - Increased incidence of diabetes
 - Development of gestational diabetes
 - Mortality from diabetes and cardiometabolic diseases

Appendix 4: Cardiovascular Effects and Short-term Ozone Exposure

Recent evidence changes the causality determination from a likely to be causal relationship (2013 Ozone ISA) to a suggestive of, but not sufficient to infer, a causal relationship between short-term ozone exposure and cardiovascular effects.

- Recent controlled human exposure studies provide little evidence of cardiovascular effects, though there was limited evidence in the last review (e.g., vascular dysfunction).
- Animal toxicological studies demonstrate some evidence of cardiovascular effects
- Epidemiologic studies provide:
 - Strong evidence for cardiovascular mortality, but
 - Little, if any, evidence of cardiovascular morbidity

Appendix 4: Cardiovascular Effects and Short-term Ozone Exposure (Cont.)

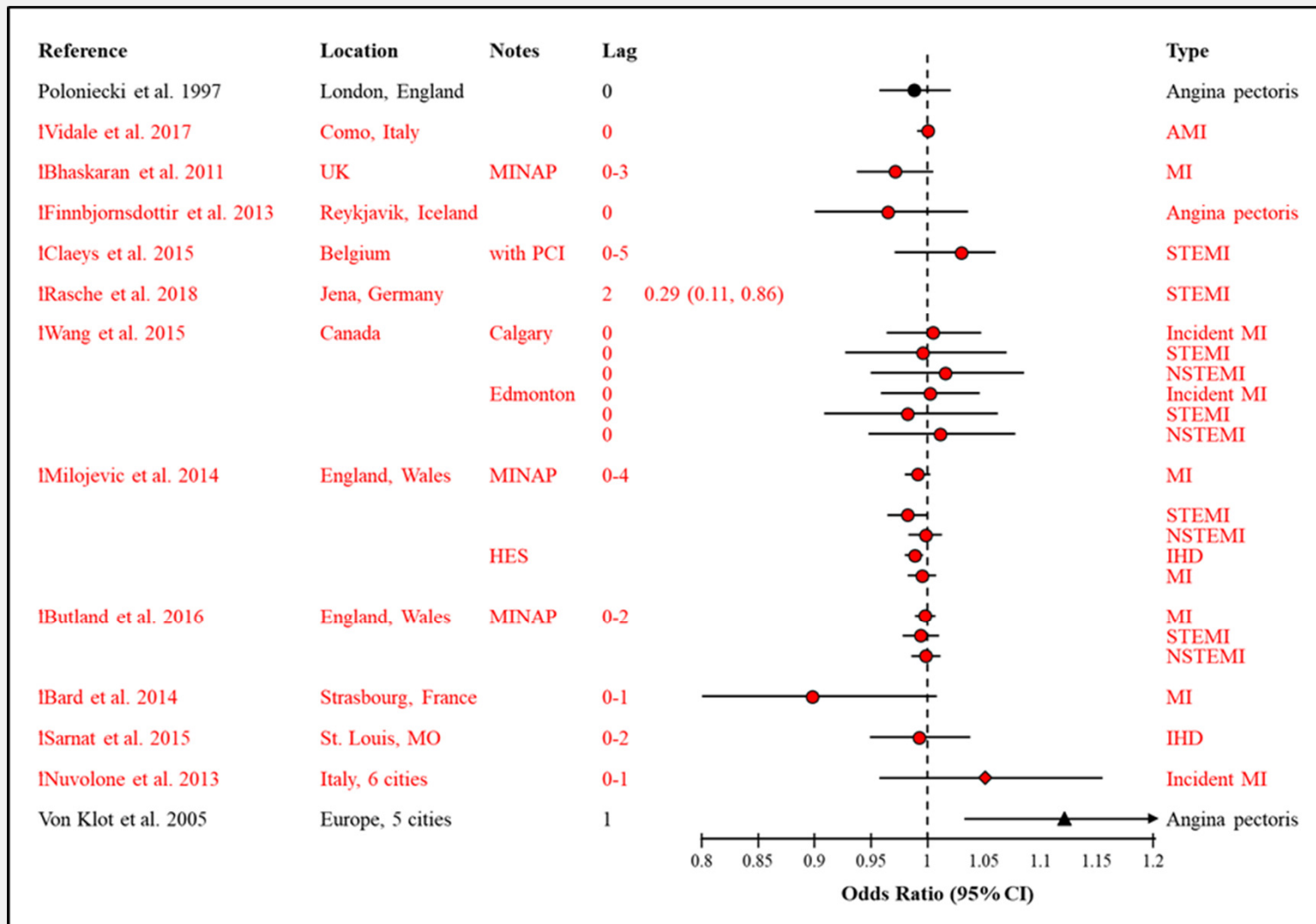


Figure 4-2. Associations between short-term exposure to ozone and ischemic heart disease-related emergency department visits and hospital admissions. Studies in red indicate recent studies (not included in 2013 Ozone ISA)



Cardiovascular Effects and Short-term Ozone Exposure

Recent evidence changes the causality determination from a likely to be causal relationship (2013 Ozone ISA) to a suggestive of, but not sufficient to infer, a causal relationship between short-term ozone exposure and cardiovascular effects.

Evidence Stream	2013 Ozone ISA	Current Draft ISA
Animal Toxicology	Evidence for CVD endpoints such as impaired vascular and cardiac function	Recent studies generally consistent with evidence in 2013 ISA
Controlled Human Exposure	Limited number of studies provide some evidence of changes in ECG measures, markers of inflammation	Expanded body of evidence evaluates greater number of cardiovascular endpoints. Recent studies provide little evidence for cardiovascular effects and are generally inconsistent with limited evidence from last review
Epidemiology - Morbidity	Little evidence for cardiovascular morbidity (e.g., MI, heart failure, stroke)	Expanded body of evidence is consistent with evidence from last review and provides little, if any, evidence for cardiovascular morbidity
Epidemiology - Mortality	Strong evidence for cardiovascular mortality	Limited number of recent studies consistent with evidence in 2013 ISA

Appendix 6: Mortality and Short-term Ozone Exposure

Recent evidence changes the causality determination from a likely to be causal relationship (2013 Ozone ISA) to a suggestive of, but not sufficient to infer, a causal relationship between short-term ozone exposure and mortality.

- Limited evidence for a biologically plausible mechanism by which ozone exposure could lead to mortality given the limited evidence for cardiovascular morbidity
- Limited coherence with controlled human exposure and epidemiologic studies of subclinical cardiovascular effects and cardiovascular morbidity
- Consistent, positive associations between short-term ozone exposure and total mortality reported in U.S. and Canadian epidemiologic studies

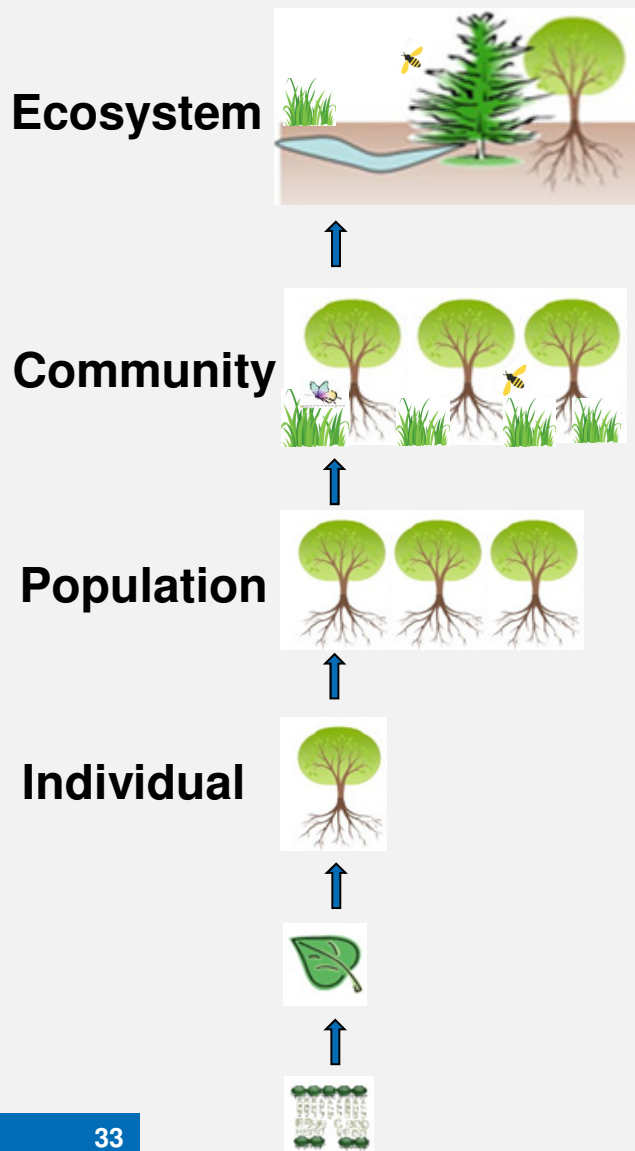
Policy-Relevant Considerations: Health

- Evidence across studies using a variety of statistical methods to examine potential deviations from linearity continues to support a linear concentration-response relationship but with less certainty in the shape of the curve at lower concentrations (i.e., below 30–40 ppb)
- Across recent studies examining various health effects and exposure durations, effects remain relatively unchanged in copollutant models
- Populations and life stages potentially at increased risk:
 - Children
 - Older adults
 - Pre-existing asthma
 - Outdoor workers

Welfare Effects

*Under the Clean Air Act section 302(h), effects on welfare include, but are not limited to, **“effects on soils, water, crops, vegetation,...animals, wildlife,...climate,...”***

Ecological Effects: Draft Causality Determinations



Causality Determinations for Ecological Effects of Ozone							
Scale of Ecological Response	Ecosystem	Belowground Biogeochemical Cycling		Causal			
		Water Cycling		Likely Causal			
		Carbon Sequestration		Likely Causal			
		Productivity		Likely Causal			
	Community	Biodiversity (Terrestrial Community Composition*)		Causal			
		Species Interactions (Plant Insect Signaling+)		Likely Causal			
	Population	Individual	Survival		Trees+		
			Growth		Plants	Herbivores +	
			Reproduction		Plants+	Herbivores +	
			Yield (Agricultural Crops)		Likely Causal		
Individual	Visible Foliar Injury		Likely Causal				

Causal Likely Causal

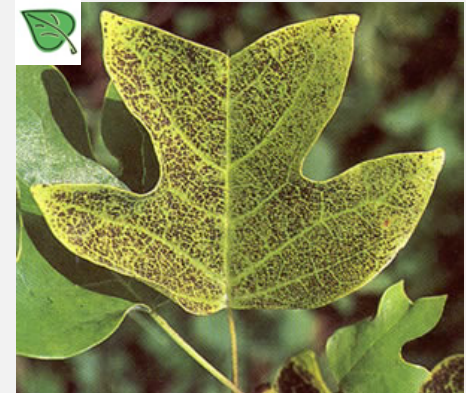
new determination (+) or change in causality determination (*) from 2013 Ozone ISA

Figure ES-5. Causality determinations for ozone across biological scales of organization and taxonomic groups

Ecological Effects

Recent evidence supports the conclusions of the 2013 Ozone ISA, and continues to support a causal relationship

- **Visible Foliar Injury**
 - Evidence for many tree, shrub, herbaceous and crop species from multiple experimental settings
- **Reduced Plant Growth**
 - Decreased growth and biomass accumulation in annual, perennial and woody plants, grasses, shrubs and trees
 - Robust exposure-response for some trees and major commodity crops
- **Reduced Crop Yield**
 - Several decades of research document losses in a variety of agricultural crops



Ecological Effects

Recent evidence supports the conclusions of the 2013 Ozone ISA, and continues to support a causal relationship

- **Reduced Productivity**
 - Much of the new research strengthens previous conclusions
- **Altered Belowground Biogeochemical Cycling**
 - Research continues to show ozone affects belowground processes



Recent evidence supports the conclusions of the 2013 Ozone ISA, and continues to support a likely to be causal relationship

- **Reduced Carbon Sequestration**
- **Altered Ecosystem Water Cycling**

Ecological Effects

NEW conclusion:
Recent evidence supports a causal relationship

- **Altered Terrestrial Community Composition**

2013 ISA: Likely Causal

- More evidence for shifts in community composition for: forest communities of trees and grassland communities of herbs, grasses and legumes



- **Reduced Plant Reproduction**

2013 ISA: included with growth causality determination

- Strong and consistent evidence for negative effects on reproduction in many species

Ecological Effects

NEW conclusion:

Recent evidence supports a likely to be causal relationship

- **Altered Plant-Insect Signaling**

- Altered/degraded emissions of plant signaling compounds
- Reduced detection of compounds by insect pollinators



- **Altered Herbivore Growth and Reproduction**

- Statistically significant effects in new and older studies

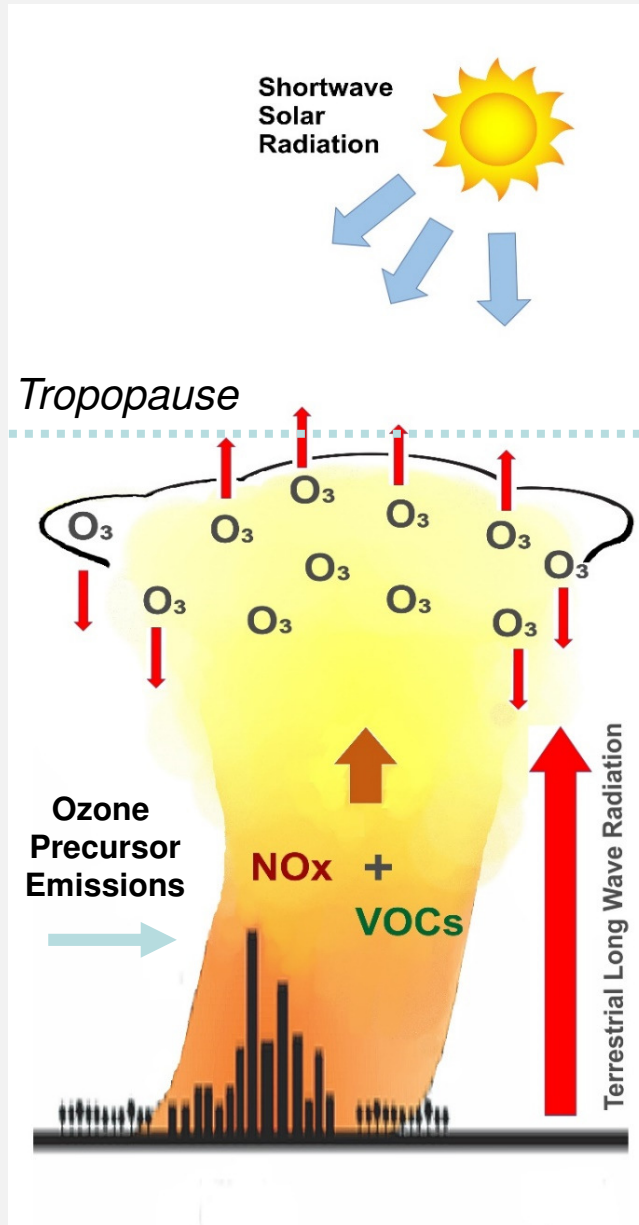
- **Increased Tree Mortality**

- Previous evidence for declines in conifer forests in several regions
- New analysis showing ozone significantly increased tree mortality in 7 of 10 plant functional types in eastern and central U.S.

Welfare Effects

*Under the Clean Air Act section 302(h), effects on welfare include, but are not limited to, “effects on soils, water, crops, vegetation,...animals, wildlife,...**climate**,...”*

Effects of Tropospheric Ozone on Climate: Draft Causality Determinations



Causality Determinations for Tropospheric Ozone and Climate Change	
Radiative Forcing	Causal
Temperature, precipitation and related climate variables	Likely Causal
Causal Likely Causal 	

Radiative forcing (RF)- *Perturbation in net radiative flux at the tropopause (or top of the atmosphere) caused by a change in radiatively active forcing agents (expressed as W/m²)*

Welfare: Effects on Climate

- **Radiative Forcing**

Recent evidence supports the causal conclusion of the 2013 Ozone ISA, and supports a causal relationship between tropospheric ozone and radiative forcing

- Modeling studies of tropospheric ozone reinforce previous estimates

- **Temperature, Precipitation and Climate-related Variables (referred to as “climate change” in the 2013 Ozone ISA)**

Recent evidence supports the likely to be causal conclusion of the 2013 Ozone ISA, and supports a likely to be causal relationship between tropospheric ozone and temperature, precipitation and climate related variables.

- Consistent with previous estimates, the effect of tropospheric ozone on global surface temperature, through its impact on radiative forcing, continues to be estimated at roughly 0.1 to 0.3° C since preindustrial times with larger effects regionally
- Tropospheric ozone changes have impacts on other climate metrics such as precipitation and atmospheric circulation patterns

Summary

Causality Determinations - Welfare

Ecological Effects		
	<u>2013 Ozone ISA</u>	<u>Current Ozone ISA</u>
Visible Foliar Injury	Causal	Causal
Reduced Vegetation Growth	Causal	Causal
Reduced Plant Reproduction	No separate causality determination; included with plant growth	Causal
Increased Tree Mortality	No Causality Determination	Likely to be Causal
Reduced Crop Yield	Causal	Causal
Altered Herbivore Growth and Reproduction	No Causality Determination	Likely to be Causal
Altered Plant-Insect Signaling	No Causality Determination	Likely to be Causal
Reduced Carbon Sequestration	Likely to be Causal	Likely to be Causal
Reduced Productivity	Causal	Causal
Alterations of Below-ground Biogeochemistry	Causal	Causal
Alteration of Terrestrial Community Composition	Likely to be Causal	Causal
Alteration of Ecosystem Water Cycling	Likely to be Causal	Likely to be Causal
Effects on Climate		
	<u>2013 Ozone ISA</u>	<u>Current Ozone ISA</u>
Radiative Forcing	Causal	Causal
Temperature, Precipitation and Climate-related Variables*	Likely to be Causal	Likely to be Causal

Summary - Key Science Points

- **U.S. Background Ozone**

- Estimates of U.S. background ozone concentrations remain highly uncertain, in part, due to challenges in representing the variability in natural and other contributing sources in current models

- **Health Effects Evidence**

- Recent studies support and expand upon strong body of evidence (from the last few decades) that short-term ozone exposure causes respiratory effects
- Emerging evidence indicates short- and long-term ozone exposure is likely to cause metabolic disease, including diabetes
- Recent studies expand the evidence base and support a change to suggestive of, but not sufficient to infer, a causal relationship between short-term ozone exposure and cardiovascular effects and total mortality

Summary - Key Science Points

- **Welfare Effects Evidence**

- Recent studies support and expand strong body of evidence that ozone induces damage in vegetation and ecosystems
- New research builds on previous evidence for tropospheric ozone effects on radiative forcing and climate variables including temperature and precipitation

Next Steps for the Ozone ISA

Milestone	Estimated Date
Release Draft ISA	September 2019
Public Comment Period	Through December 2, 2019
CASAC Review Meeting	December 4-6, 2019
Revise ISA	Winter-Spring 2020
Release Final ISA	April 2020

Ozone Team

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Dr. Ellen Kirrane	Dr. Benjamin Wells
Dr. Robert Kotchenruther	
Dr. David Lehmann	

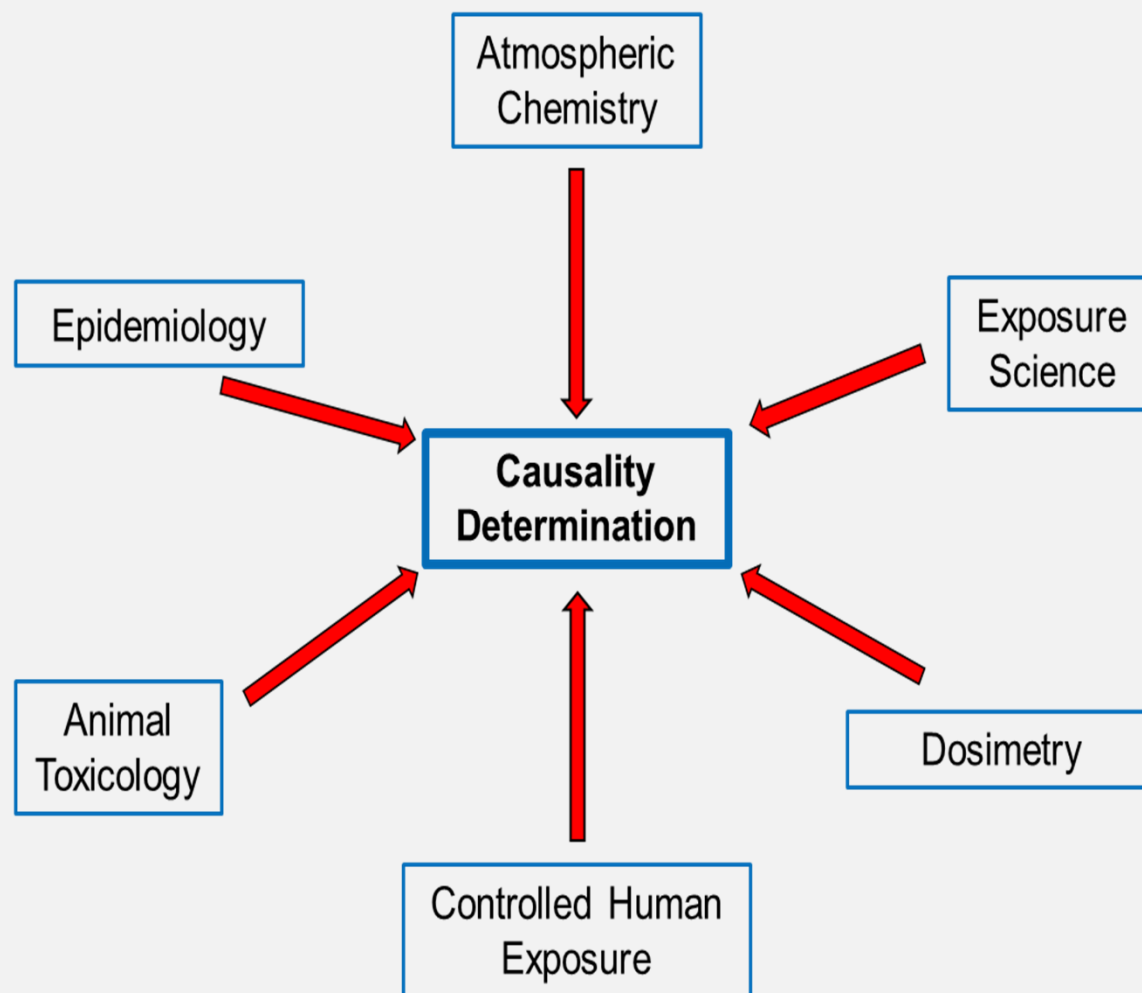
Executive Direction

Dr. John Vandenberg (Director)
Dr. Steven J. Dutton (Deputy Director)
Dr. Jennifer Nichols (Acting Branch Chief)
Dr. Tara Greaver (Acting Branch Chief)
Dr. Andrew Hotchkiss (Acting Branch Chief)

Management and Technical Support Staff

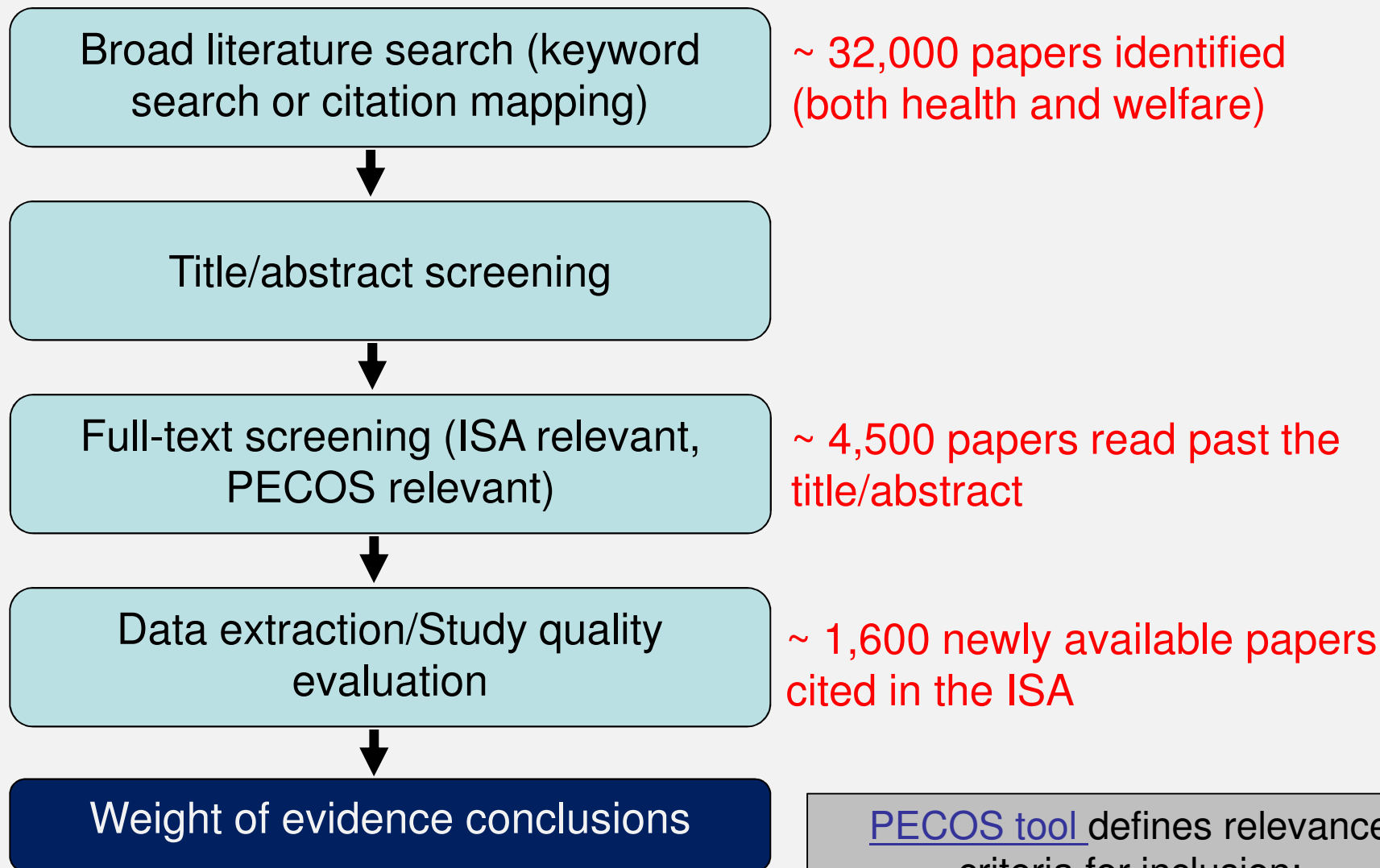
Ms. Rebecca Daniels (Project Manager)
Ms. Marieka Boyd
Mr. Ryan Jones
Mr. S. Shane Thacker
Mr. Lukas Kerr
Ms. Mckayla Lein
Mr. R. Byron Rice
HERO database team

Approach for Evaluation of the Scientific Evidence



Supplemental Slides

Literature Search/ Systematic Review

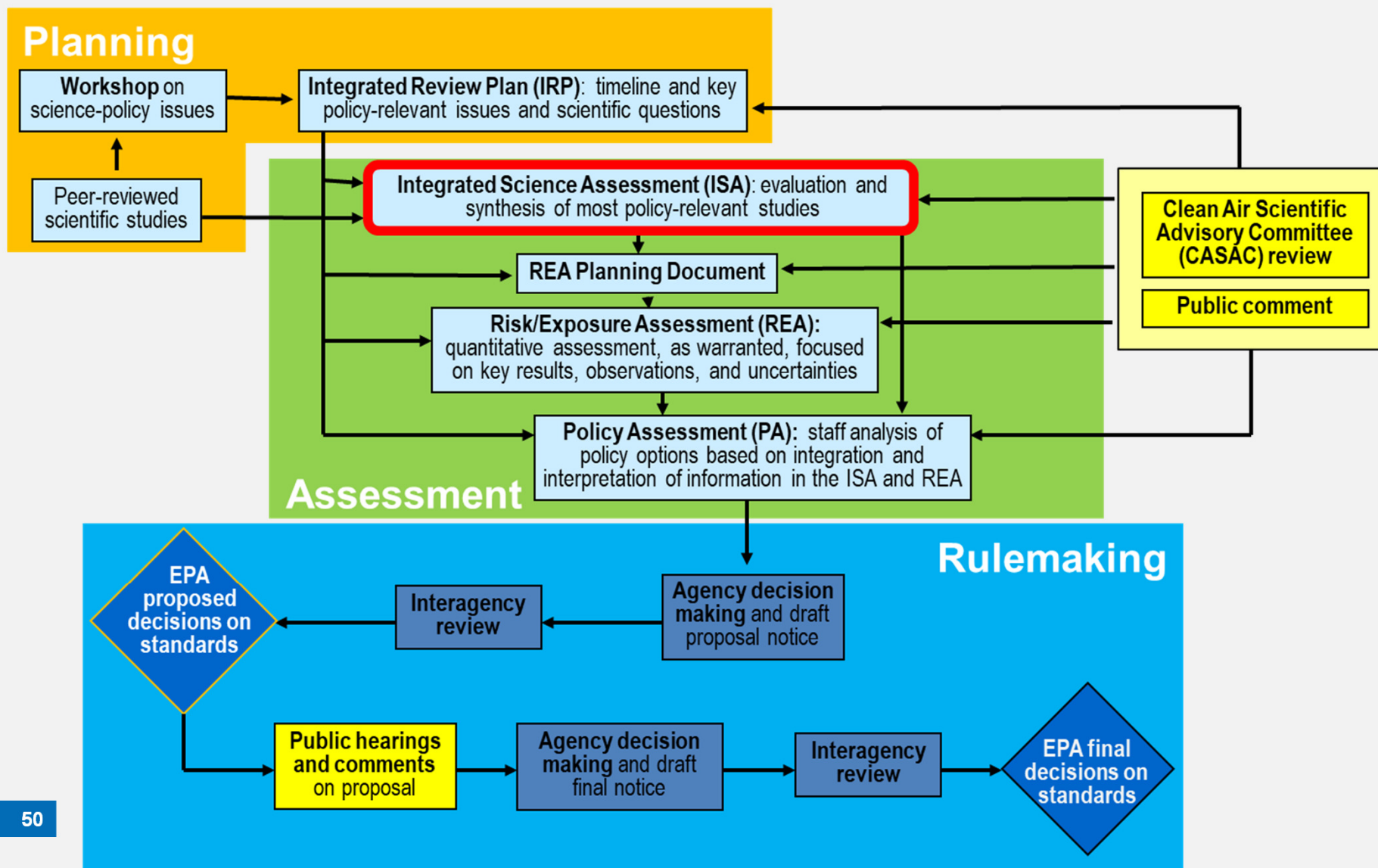


PECOS tool defines relevance criteria for inclusion:
Population, Exposure, Comparator, Outcome, Study Design









Statutory Requirements

- Section 108(a)(2): “Air quality criteria for an air pollutant shall accurately reflect the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health or welfare which may be expected from the presence of such pollutant in the ambient air, in varying quantities. The criteria for an air pollutant, to the extent practicable, shall include information on –
 - (A) those variable factors (including atmospheric conditions) which of themselves or in combination with other factors may alter the effects on public health or welfare such air pollutant;
 - (B) the types of air pollutants which, when present in the atmosphere, may interact with such pollutants to produce and adverse effect on public health or welfare; and
 - (C) any known or anticipated adverse effects on welfare.”

Overview of the NAAQS Review Process



CPHEA/ORD and OAQPS/OAR Interactions: NAAQS Review

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

Example PECOS tool

Short-term Ozone Exposure and Respiratory Effects

- **Experimental studies:**

Population: Study populations of any controlled human exposure or animal toxicological study of mammals at any lifestage

Exposure: Short-term (on the order of minutes to weeks) inhalation exposure to relevant ozone concentrations (i.e., ≤ 0.4 ppm for humans, ≤ 2 ppm for other mammals); while ozone concentrations in animal toxicological studies appear high, it should be noted that deposition of ozone resulting from exposure to 2 ppm ozone in a resting rat is roughly equivalent to deposition of ozone resulting from exposure to 0.4 ppm ozone in an exercising human.

Comparison: Human subjects serve as their own controls with an appropriate washout period or groups may be compared at the same or varied exposure concentrations; or, in toxicological studies of mammals, an appropriate comparison group is exposed to a negative control (i.e., clean air or filtered-air control)

Outcome: Respiratory effects

Study Design: Controlled human exposure studies and animal studies meeting the above criteria

- **Epidemiologic studies:**

Population: Any U.S. or Canadian population, including populations or lifestages that might be at increased risk

Exposure: Short-term exposure (on the order of hours to several days) to ambient concentrations of ozone

Comparison: Per unit increase (in ppb), or humans exposed to lower levels of ozone compared with humans exposed to higher levels

Outcome: Change in risk (incidence/prevalence) of respiratory effects

Study Design: Epidemiologic studies consisting of panel, case-crossover, time-series studies, and case-control studies, as well as cross-sectional studies with appropriate timing of exposure for the health endpoint of interest

Appendix 6: Short-term Ozone Exposure and Total Mortality

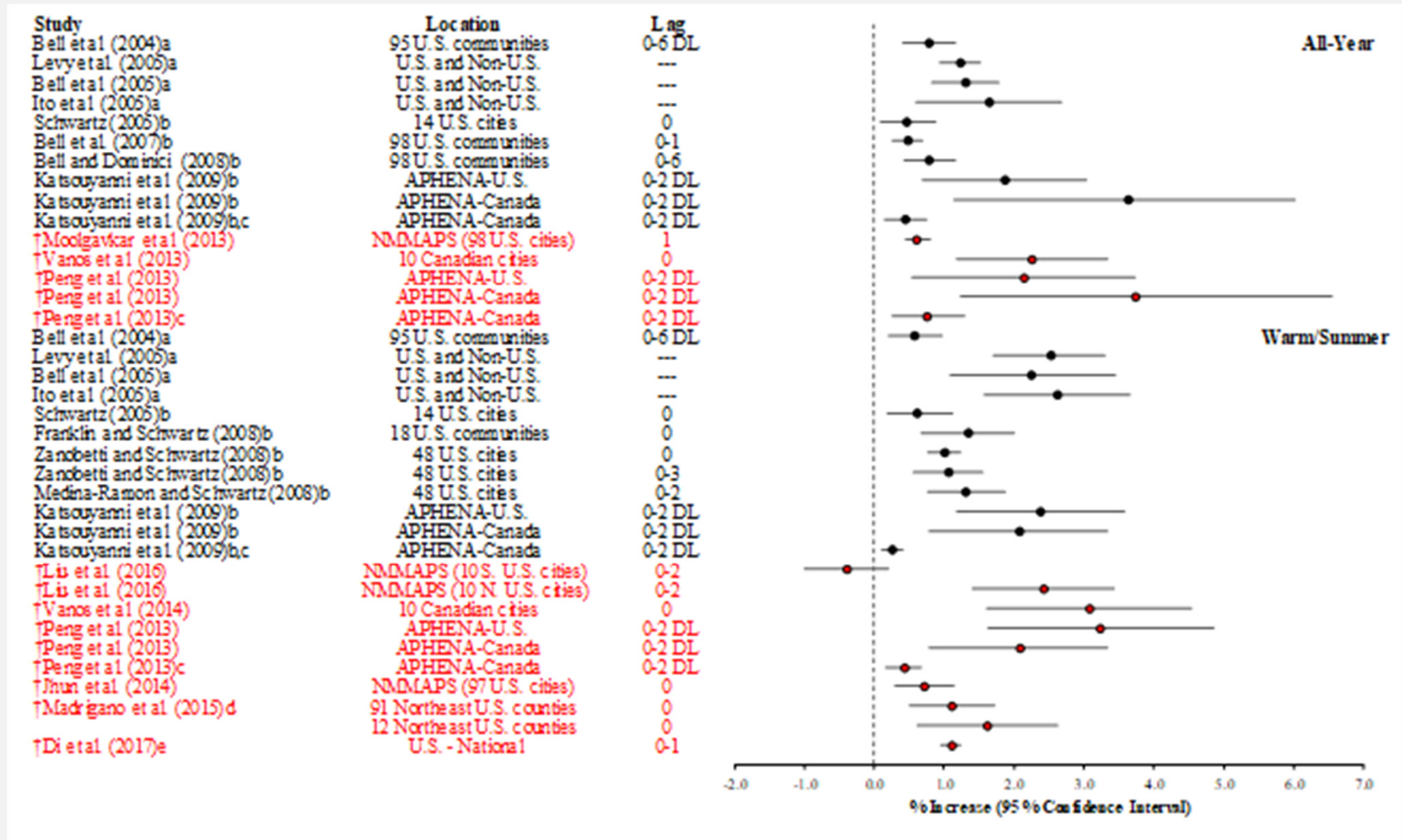


Figure 6-1. Summary of associations for short-term ozone exposure and total (nonaccidental) mortality from multicity U.S. and Canadian studies. Studies in red indicate recent studies (not included in 2013 Ozone ISA)

Appendix 6: Short-term Ozone Exposure and Cause-Specific Mortality

Study	Location	Ages	Lag
Bell et al (2005)a	U.S. and non-U.S.	All	--
†Vanos et al. (2014)	10 Canadian cities	All	0
Katsouyanni et al (2009)b	APHENA-US	≥75	0-2
Katsouyanni et al (2009)b	APHENA-CAN	≥75	0-2
Katsouyanni et al (2009)b	APHENA-US	<75	0-2
Katsouyanni et al (2009)b	APHENA-CAN	<75	0-2
Zanobetti and Schwartz(2008)b	48 U.S. cities	All	0-3
†Vanos et al. (2014)	10 Canadian cities	All	0
Katsouyanni et al (2009)b	APHENA-US	≥75	0-2
Katsouyanni et al (2009)b	APHENA-CAN	≥75	0-2
Katsouyanni et al (2009)b	APHENA-US	<75	0-2
Katsouyanni et al (2009)b	APHENA-CAN	<75	0-2
Bell et al (2005)a	U.S. and non-U.S.	All	--
Katsouyanni et al (2009)b	APHENA-US	All	0-2
Katsouyanni et al (2009)b	APHENA-CAN	All	0-2
†Vanos et al. (2014)	10 Canadian cities	All	0
Katsouyanni et al (2009)b	APHENA-US	≥75	0-2
Katsouyanni et al (2009)b	APHENA-CAN	≥75	0-2
Zanobetti and Schwartz(2008)b	48 U.S. cities	All	0-3
Katsouyanni et al (2009)b	APHENA-US	All	0-2
Katsouyanni et al (2009)b	APHENA-CAN	All	0-2
†Vanos et al. (2014)	10 Canadian cities	All	0
Katsouyanni et al (2009)b	APHENA-US	≥75	0-2
Katsouyanni et al (2009)b	APHENA-CAN	≥75	0-2

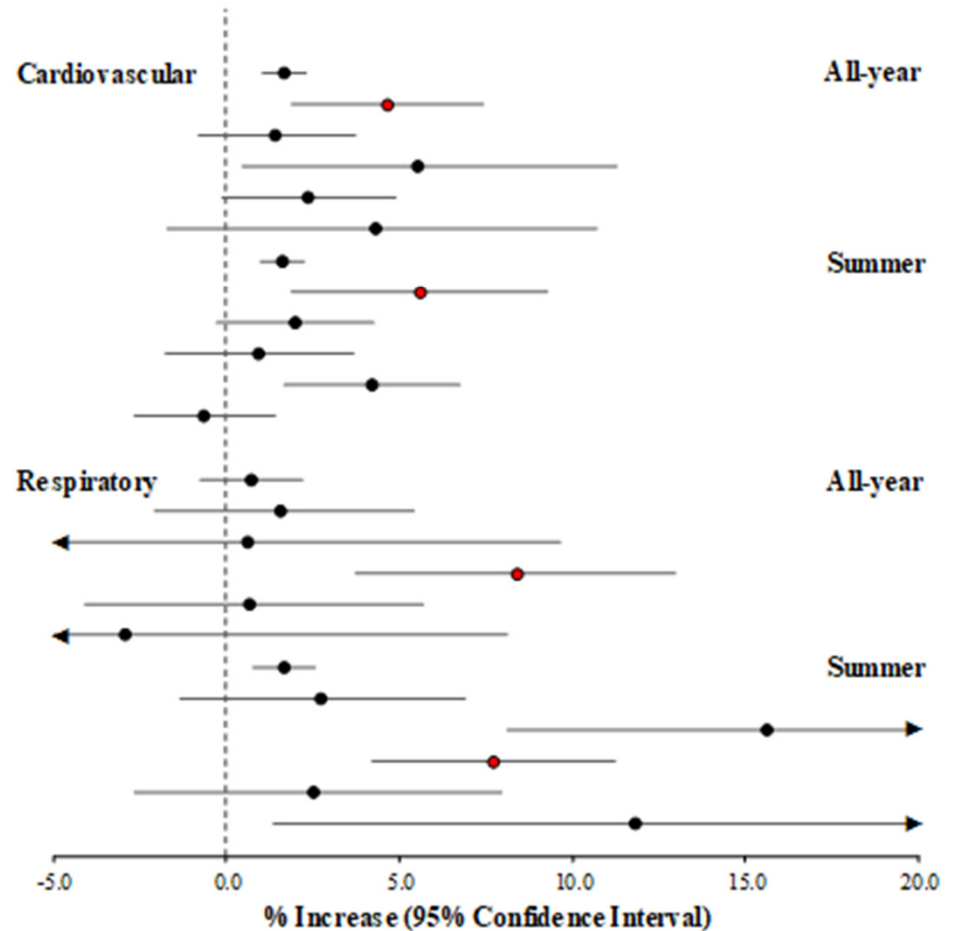


Figure 6-2. Summary of associations for short-term ozone exposure and cause-specific mortality from multicity U.S. and Canadian studies. Studies in red indicate recent studies (not included in 2013 Ozone ISA)

Full List of At-Risk Populations

- Adequate Evidence

- Pre-existing asthma
- Children
- Older adults
- Outdoor workers
- Genetic factors
- Diet

- Suggestive Evidence

- Sex
- Pre-existing obesity
- SES

- Inadequate Evidence

- Race/Ethnicity
- Pre-existing COPD
- Pre-existing CVD
- Pre-existing diabetes
- Smoking