Air pollution and Health: Recent Advances to Inform the European Green Deal

Current knowledge on adverse effects of ambient air pollution: have we filled the gap? What more do we need to know?

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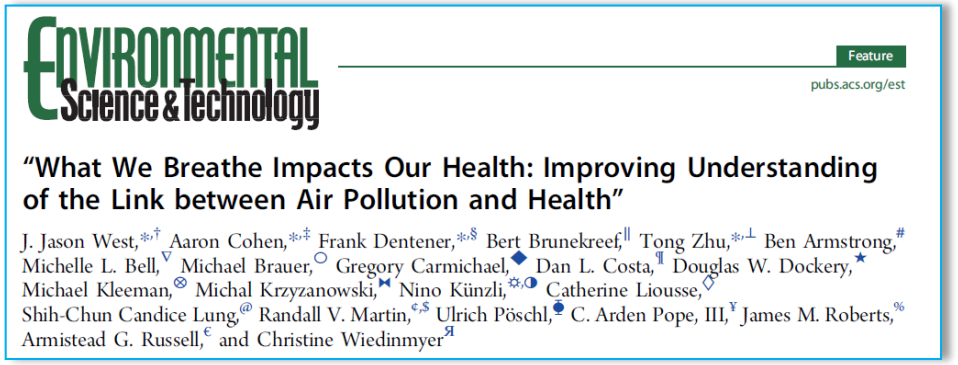
Outline



- ***Do we know enough to act? YES, definitively!***
- ***Further Strengthening the Policy-Relevant Scientific Base***
  - Priorities for policy-relevant questions: how, why and for whom the effect exists?
  - Methodology in exposure assessment, study design and evidence synthesis and evaluation
  - Priorities for biologically-relevant mechanism research questions: does the effect exist?
- ***Enhancing Analysis for Policy Decisions***
  - Progress in Health Burden Assessment
  - Accountability research in EU
  - Policy implications

Strength of evidence on health effects of $PM_{2.5}$, NO_2 and O_3

ST: short-term, LT: Long-term

C – causal

Lc – likely causal

S – suggestive for causal

Systematic reviews:

for $PM_{2.5}$ US EPA 2019
for NO_2 US EPA 2016
for O_3 US EPA 2013/2019

Outcome	$PM_{2.5}$		NO_2		O_3	
	LT	ST	LT	ST	LT	ST
Mortality	**C**	**C**	**S**	**S**	**S**	**Lc/S**
Cardiovascular Effects	**C**	**C**	**S**	**S**	**S**	**Lc/S**
Respiratory Effects	**Lc**	**Lc**	**Lc**	**C**	**C**	**C**
Cancer	**Lc/[1]**	**---**	**S**	**---**	**Lc**	**---**
Nervous System	**Lc**	**S**	**---**	**---**	**S**	**S**

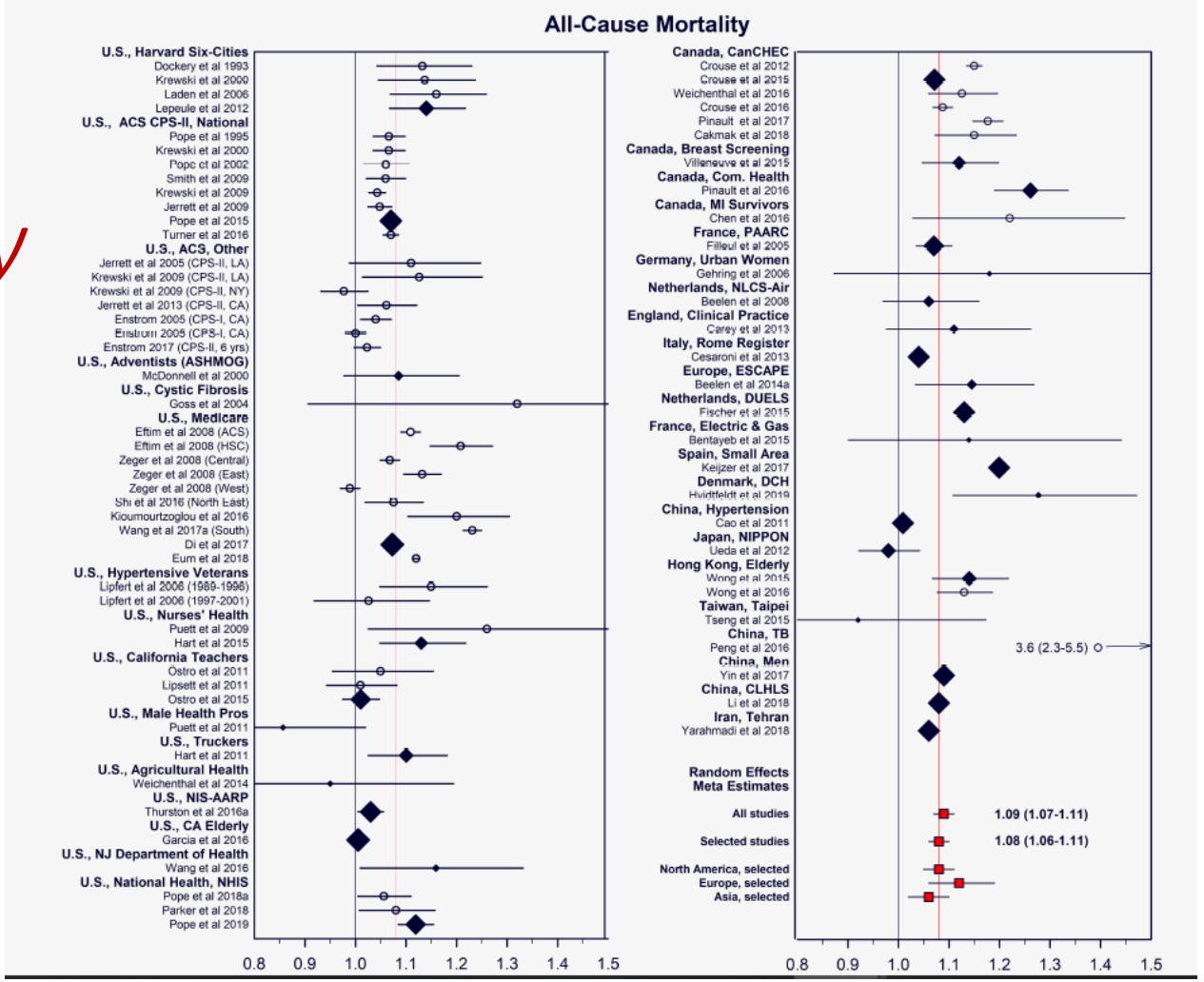
[1] *Group 1 carcinogen (Lung Cancer), IARC 2013*

Courtesy of Jason Sacks

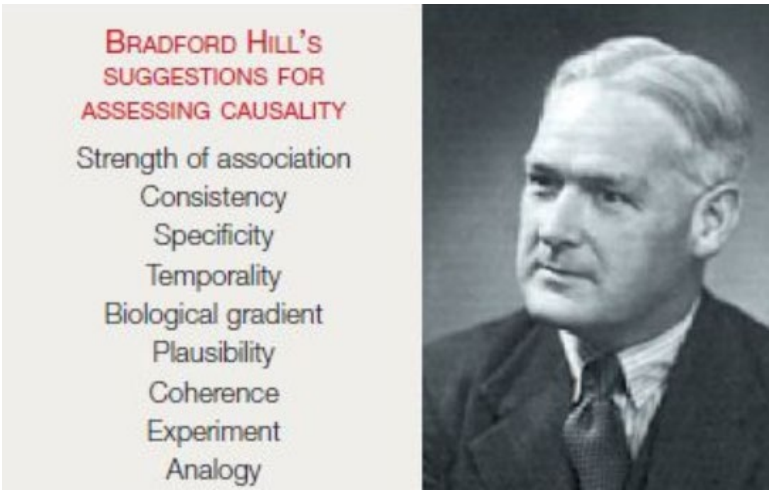
$PM_{2.5}$ and mortality, Pope et al, ER, 2019

$PM_{2.5}$ associated with all-cause, cardiopulmonary and lung-cancer mortality

RR=1.08 (1.06-1.11) per 10 ug/m^3



Hill AB. The environment and disease: association or causation? Proc Royal Soc Med 1965; 295-300



A Case for Action

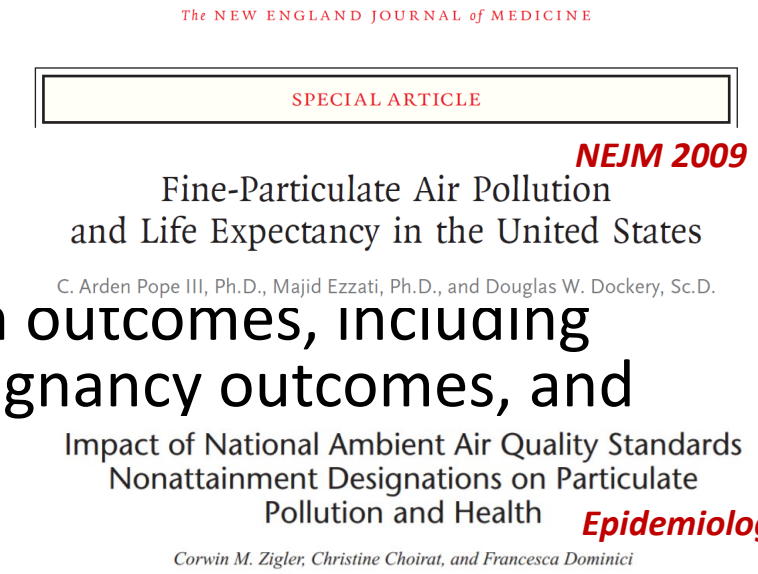
«In asking for very strong evidence I would, however, repeat emphatically that this does not imply crossing every 't', and swords with every critic, before we act.»

"All scientific work is incomplete - whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time."

What have we done so far? Isn't that enough?

Air quality actions across the globe – David Rich

- 1. Some evidence of health benefits of air quality actions, both short term/temporary and long term changes/improvements in air quality and health outcomes in Europe, US, and Asia


The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Fine-Particulate Air Pollution and Life Expectancy in the United States

C. Arden Pope III, Ph.D., Majid Ezzati, Ph.D., and Douglas W. Dockery, Sc.D.

NEJM 2009

- 2. Evidence of improvements in several health outcomes, including mortality, cause specific hospital admissions, pregnancy outcomes, and cardiovascular biomarkers

Impact of National Ambient Air Quality Standards Nonattainment Designations on Particulate Pollution and Health

Corwin M. Zigler, Christine Choirat, and Francesca Dominici

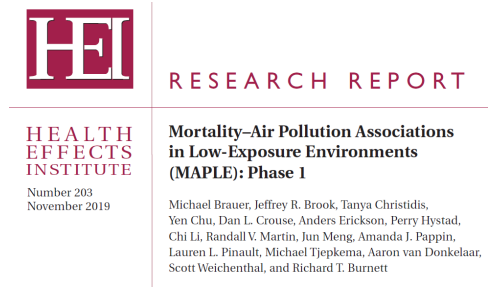
Epidemiology 2018

- 3. Effects observed following air quality policies targeting traffic emissions, industrial emissions, or mixtures of multiple sources

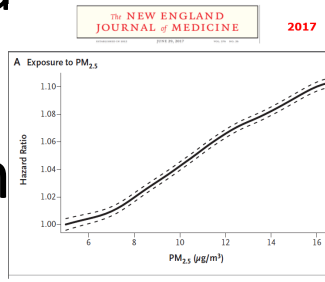
Priorities for policy-relevant questions: how, why and for whom the effect exists?

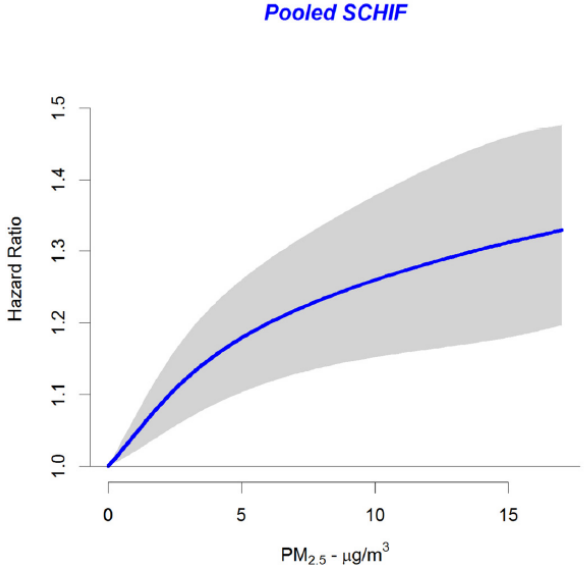
- Shape of the exposure-response at low levels *
- Health effects of different sources (e.g. tail and non-tailpipe emissions, industry, desert dust etc) *
- Health effects of different sizes (Coarse PM, UFP, metals) and combination of components *
- Sensitive subgroups of the population that need to be protected (e.g., pregnant women, elderly)
- Multipollutant exposure and interaction with related factors such as traffic noise, green space, and SES *

Research on low-levels (Hanna Boogaard)



- Decrease of levels of ambient air pollution over time in North America and Europe
- Epidemiologic studies reported consistent associations of air pollution with mortality at levels below current air quality standards
- A supralinear relationship appears in the Canadian investigation (Pappin et al, EHP, 2019)
- Strength the exposure-response curve at low levels
- The shape of the exposure-response should be investigated for other outcomes (e.g morbidity, asthma)



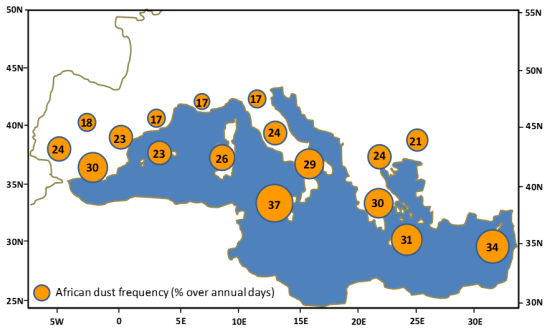


ELAPSE

Health effects of different sources

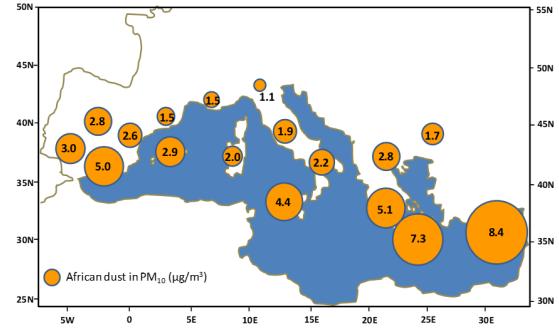
- Policy measures should be focussed on the wider spectrum of air pollution sources instead of on specific sources?
- What are the specific effects of traffic related air pollution (HEI traffic Review)?
- Other sources?
- Do we have long-term effects of desert dust?

Saharan dust: frequency ef events



Pey et al. *Atmos Chemistry Physics* (2013)

Saharan dust: PM_{10} contribution



Pey et al. *Atmos Chemistry Physics* (2013)

Health effects of different sizes (Coarse PM, UFP) and components (or combination of components)

A case for UFP (from Annette Peters)

- Exposures to ultrafine and fine particles differ in space and time
- Experimental and epidemiological studies suggest independent short-term health effects
- Studies on long-term health effects of UFP are missing

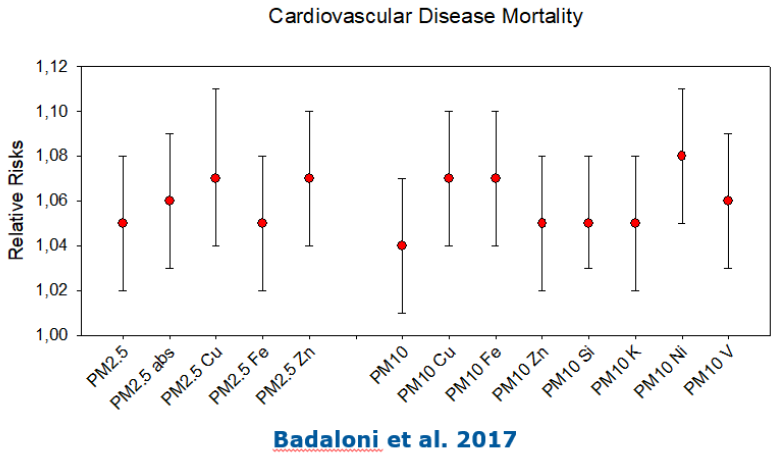
A case for components of PM

- Not great progress in the last two decades

  but need to continue to address the issue

  and search for better evidence

The Rome Longitudinal Study: Combustion Particles from all Sources and Mortality



Badaloni et al. 2017

Multipollutant exposure

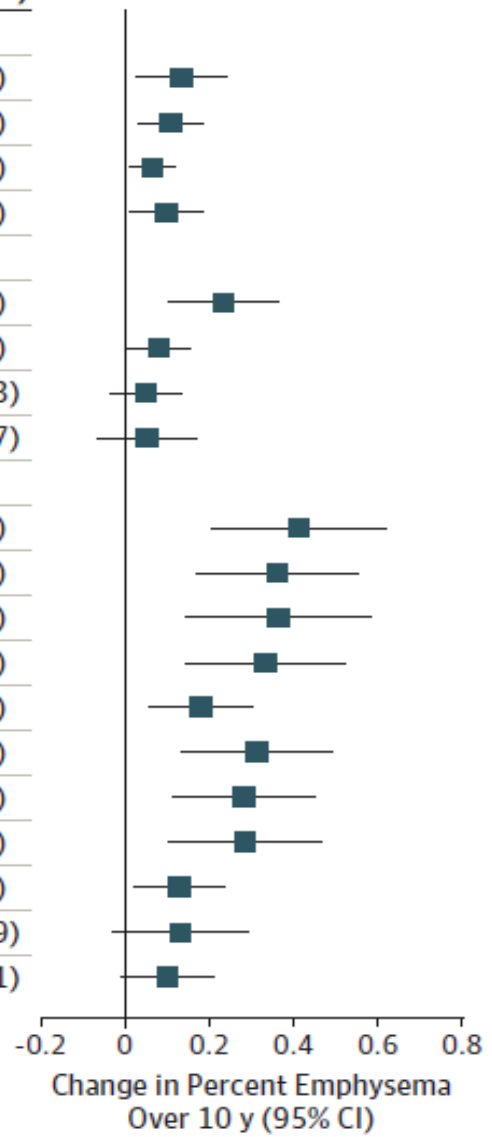
Association betwee long-term exposure to ambient air pollution and change in quantitatively assessed emphisema and lung functiom

Wang et al, Jama , 2019

Figure 4. Effect Estimates for the Associations Between Air Pollutants and Progression of Percent Emphysema

A Associations with baseline concentrations

	Change in Percent Emphysema (95% CI)
Single-pollutant model	
O_3 (per 3 ppb)	0.13 (0.03 to 0.24)
$PM_{2.5}$ (per 2 μg/m³)	0.11 (0.03 to 0.19)
NO_x (per 10 ppb)	0.06 (0.01 to 0.12)
BC (per 0.2 μg/m³)	0.10 (0.01 to 0.18)
Multipollutant model	
O_3 (per 3 ppb)	0.23 (0.10 to 0.36)
$PM_{2.5}$ (per 2 μg/m³)	0.08 (0.01 to 0.15)
NO_x (per 10 ppb)	0.05 (-0.04 to 0.13)
BC (per 0.2 μg/m³)	0.05 (-0.07 to 0.17)
Linear combination model	
$O_3 + PM_{2.5} + NO_x + BC$	0.41 (0.20 to 0.62)
$O_3 + PM_{2.5} + NO_x$	0.36 (0.17 to 0.55)
$O_3 + PM_{2.5} + BC$	0.36 (0.14 to 0.58)
$O_3 + NO_x + BC$	0.33 (0.14 to 0.52)
$PM_{2.5} + NO_x + BC$	0.18 (0.05 to 0.30)
$O_3 + PM_{2.5}$	0.31 (0.13 to 0.49)
$O_3 + NO_x$	0.28 (0.11 to 0.45)
$O_3 + BC$	0.28 (0.10 to 0.47)
$PM_{2.5} + NO_x$	0.13 (0.02 to 0.23)
$PM_{2.5} + BC$	0.13 (-0.03 to 0.29)
$NO_x + BC$	0.10 (-0.01 to 0.21)



Methodology in exposure assessment, study design and evidence synthesis and evaluation

- Improve exposure assessment methods
- Improve statistical methods for use in epidemiologic studies
- Expand the framework of causal inference *
- Improve the methodological aspects related to the synthesis of the scientific evidence and its overall evaluation *

Expand the framework of causal inference

- E.g. Propensity Score, Instrumental variables, difference-in-difference, regression discontinuity
- Methods of Causal Inference have been used in several applications in epidemiology, but to a limited extent in Environmental Health

"Causal Inference" methods are tools for:

- Formalizing thinking about what data can tell about cause and effect
- Forcing explicit definitions of familiar notions
- Clarifying common threats to validity in epidemiological studies
- Hopefully providing a remedy

HEI

RESEARCH REPORT

HEALTH EFFECTS INSTITUTE

Number 187
May 2016

Causal Inference Methods for Estimating Long-Term Health Effects of Air Quality Regulations

Corwin Matthew Zigler, Chanmin Kim, Christine Choirat, John Barrett Hansen, Yun Wang, Lauren Hund, Jonathan Samet, Gary King, and Francesca Dominici

Zigler and Dominici, HEI 2016

Improve the methodological aspects related to the synthesis of the scientific evidence and its overall evaluation

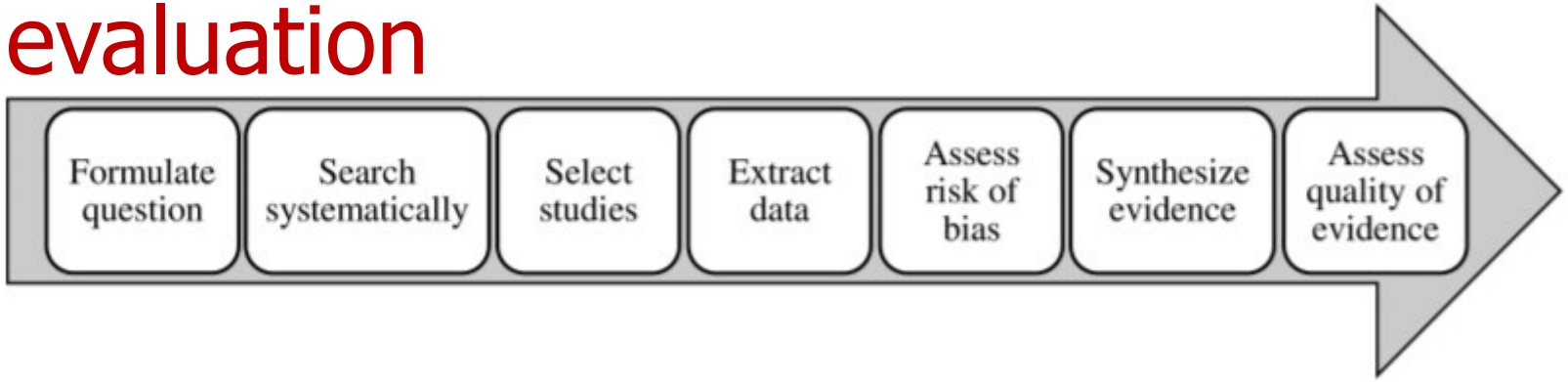


Fig. 1. Steps of the systematic review proces

IDEAS AND OPINIONS

Annals of Internal Medicine

GRADE Methods for Guideline Development: Time to Evolve? 2016

Susan L. Norris, MD, MPH, MSc, and Lisa Bero, PhD

Environmental health and clinical medicine are two different disciplines

- Clinical medicine
- Environmental health

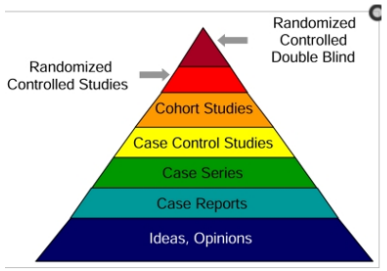


FIGURE 2-1 Evidentiary hierarchy of weighing evidence

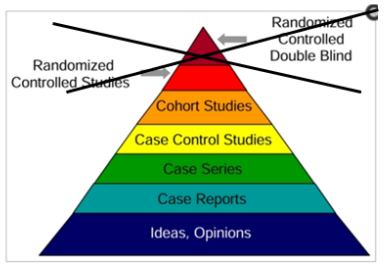


FIGURE 2-1 Evidentiary hierarchy of weighing evidence

EPA ISA NO2, 2016

- **Causal relationship:** the consistency and coherence of evidence integrated across scientific disciplines and related health outcomes are sufficient to rule out chance, confounding, and other biases with reasonable confidence.
- **Likely to be a causal relationship:** there are studies where results are not explained by chance, confounding, or other biases, but uncertainties remain in the evidence overall. For example, the influence of other pollutants is difficult to address, or evidence among scientific disciplines may be limited or inconsistent.
- **Suggestive of, but not sufficient to infer, a causal relationship:** evidence is generally supportive but not entirely consistent or overall is limited. Chance, confounding, and other biases cannot be ruled out.
- **Inadequate to infer a causal relationship:** there is insufficient quantity, quality, consistency, or statistical power of results from studies.
- **Not likely to be a causal relationship:** several adequate studies, examining the full range of human exposure concentrations and potential at-risk populations and lifestages, consistently show no effect.

Regular synthesis of the scientific evidence

- Review of evidence on health aspects of air pollution -REVIHAAP Project
- Health risks of air pollution in Europe- HRAPIE Project

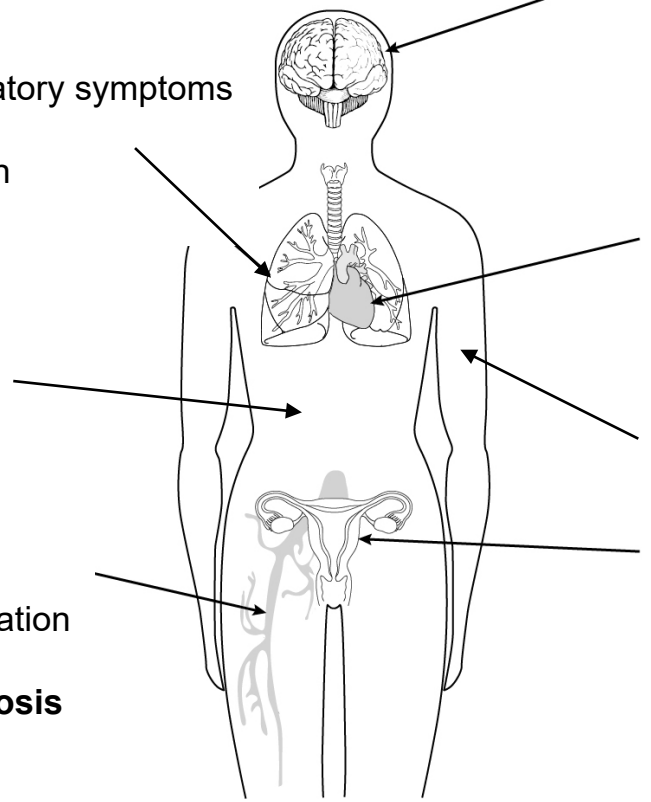
- **Need of continuous collection, evaluation, synthesis and dissemination of the evidence**

Priorities for biologically-relevant mechanism research questions: does the effect exist?

- **Respiratory Disease Mortality**
- **Respiratory Disease Morbidity**
- **Lung Cancer**
- **Pneumonia**
- Upper and lower respiratory symptoms
- Airway inflammation
- Decreased lung function
- Decreased lung growth

- Insulin Resistance
- **Type 2 diabetes**
- **Type 1 diabetes**
- Bone metabolism

- **High blood pressure**
- Endothelial dysfunction
- Increased blood coagulation
- Systemic inflammation
- **Deep Venous Thrombosis**



- **Stroke**
- Neurological development
- Mental Health
- **Neurodegenerative diseases**

- **Cardiovascular Disease Mortality**
- **Cardiovascular Disease Morbidity**
- **Myocardial Infarction**
- **Arrhythmia**
- **Congestive Heart Failure**
- Changes in Heart Rate Variability
- ST-Segment Depression

- Skin Aging

- **Premature Birth**
- **Decreased Birth Weight**
- Decreased foetal growth
- In uterine growth retardation
- Decreased sperm quality
- Preclampsia

ERS / ATS: Statement on Adverse Health Effects (Thurston et al, 2017)

Oxidative stress and the cardiovascular effects of air pollution (Miller et al, Free Radic Biol Med. 2020)

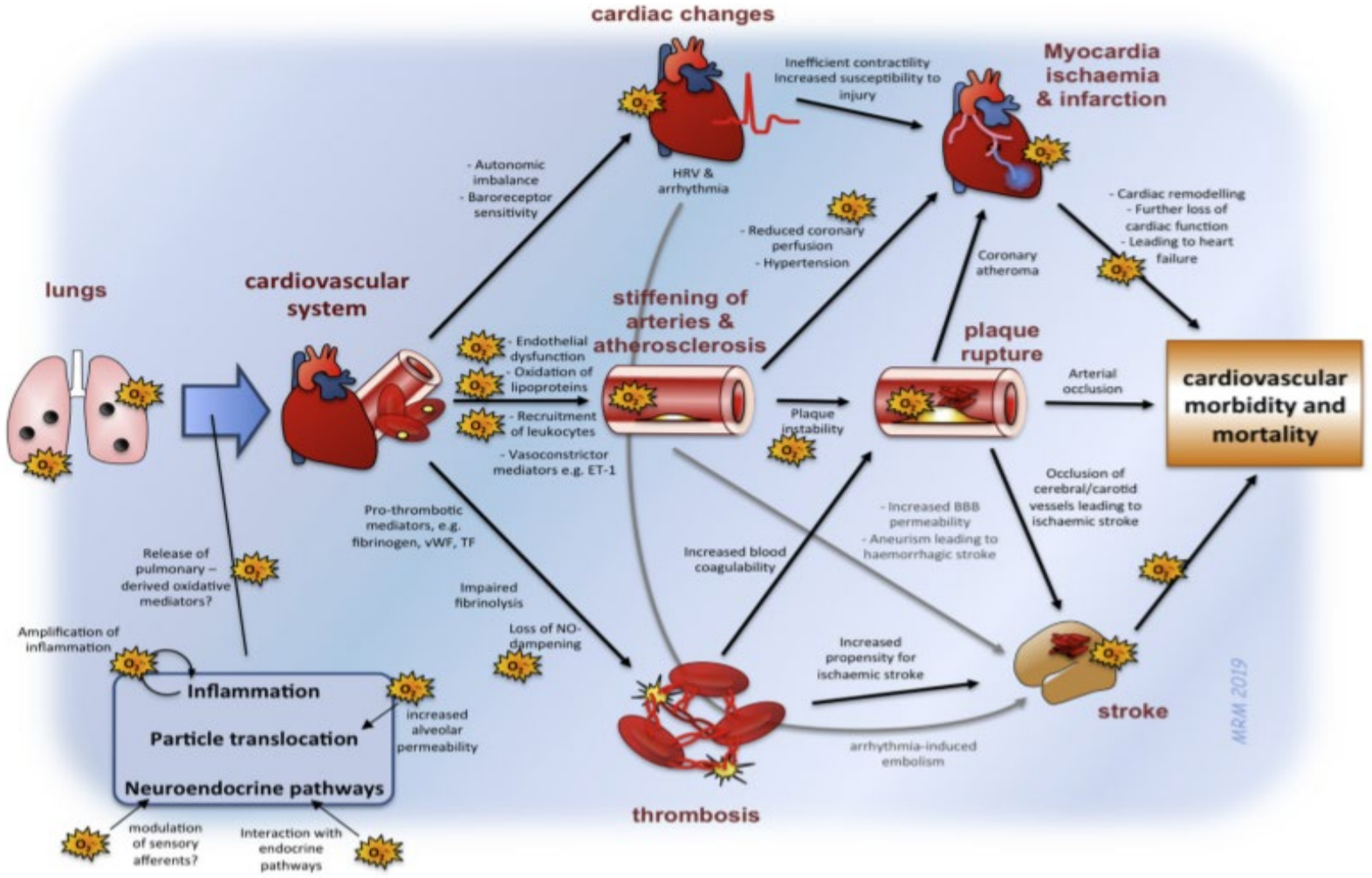


Fig. 8. Contribution of oxidative stress to the mechanisms by which inhaled PM induces cardiovascular dysfunction. A complex series of interconnecting mechanisms underlies the effects of inhaled PM on cardiovascular morbidity and mortality. $O_2^{\cdot-}$ is used to represent places where oxidative stress is likely to play a direct role in exacerbating the disease process. While a direct action of oxidative stress is not always immediately apparent, it is worth noting that oxidative stress has been associated with most of the cardiovascular impairments shown on the diagram, and may indirectly contribute to other pathways by which PM has cardiovascular actions. Abbreviations: BBB = blood brain barrier; ET-1 = endothelin-1; HRV = heart rate variability; NO = nitric oxide; TF = tissue factor; vWF = von Willebrand Factor.

Priorities for biologically-relevant mechanism research questions

Lorenzo Tomatis

- Outcomes? Exposure/outcome pairs “likely to be causal” or “Suggestive of, but not sufficient to infer, a causal relationship”. Priorities for “new outcomes” such as “aging” and its markers, child development, cognitive effects, etc

- Exposure? Effects of mixtures (particles of different sizes as wells as gaseous pollutants).

- Studies? Toxicological studies on the mechanisms of the effects that could explain the epidemiological findings (e.g. NO2 and Ozone)

- What? Understand the underlying pathophysiology due to interactions between pollutants and molecular or cellular structures (proteins, lipids, DNA and RNA, etc)

The NO_2 dilemma: per se… or not per se

- Capacity of NO_2 to induce bronchial hyperresponsiveness and responses to inhaled allergen in patients with asthma
  - **Particle Depletion Does Not Remediate Acute Effects of Traffic-related Air Pollution and Allergen. A Randomized, Double-Blind Crossover Study. Wooding et al, AJRCCM 2019**
    - Controlled chamber exposure experiments in allergen-sensitized individuals
    - Nasal instillation of allergen and diesel exhaust exposure >> exhaust particles enhanced both sensitization to neoallergen and the allergen response
    - Filtering out the particles (NO2 increased) provided no protection
- This strongly implicates NO_2 associated with diesel exhaust as an important adjuvant factor enhancing allergen sensitization (Bosson et al, AJRCCM 2019)

Progress in Health Burden Assessment (Katy Walker)

- Burden assessments have played a key role in identifying the overall and relative importance of air pollution
- A foundation for identifying priorities and tracking the effectiveness of solutions
- ***Despite scientific differences in key assumptions***, multiple estimates point to ***substantial contributions of air pollution*** to adverse health outcomes
- Estimates that may continue to grow as the effects of additional air pollutants and health outcomes are more fully addressed
- Need to converge on a common exposure-response function for mortality (form at lower and upper end of the distribution) and give priority to air pollution studies (Burnett et al, 2018)
- Expand on exposure-response function for morbidity and differential source attribution (e.g. traffic in EU, desert dust)
- Need of regular updates; **need of HRAPIE-2 for Europe**

Accountability research

Environment International 135 (2020) 105400

Contents lists available at ScienceDirect

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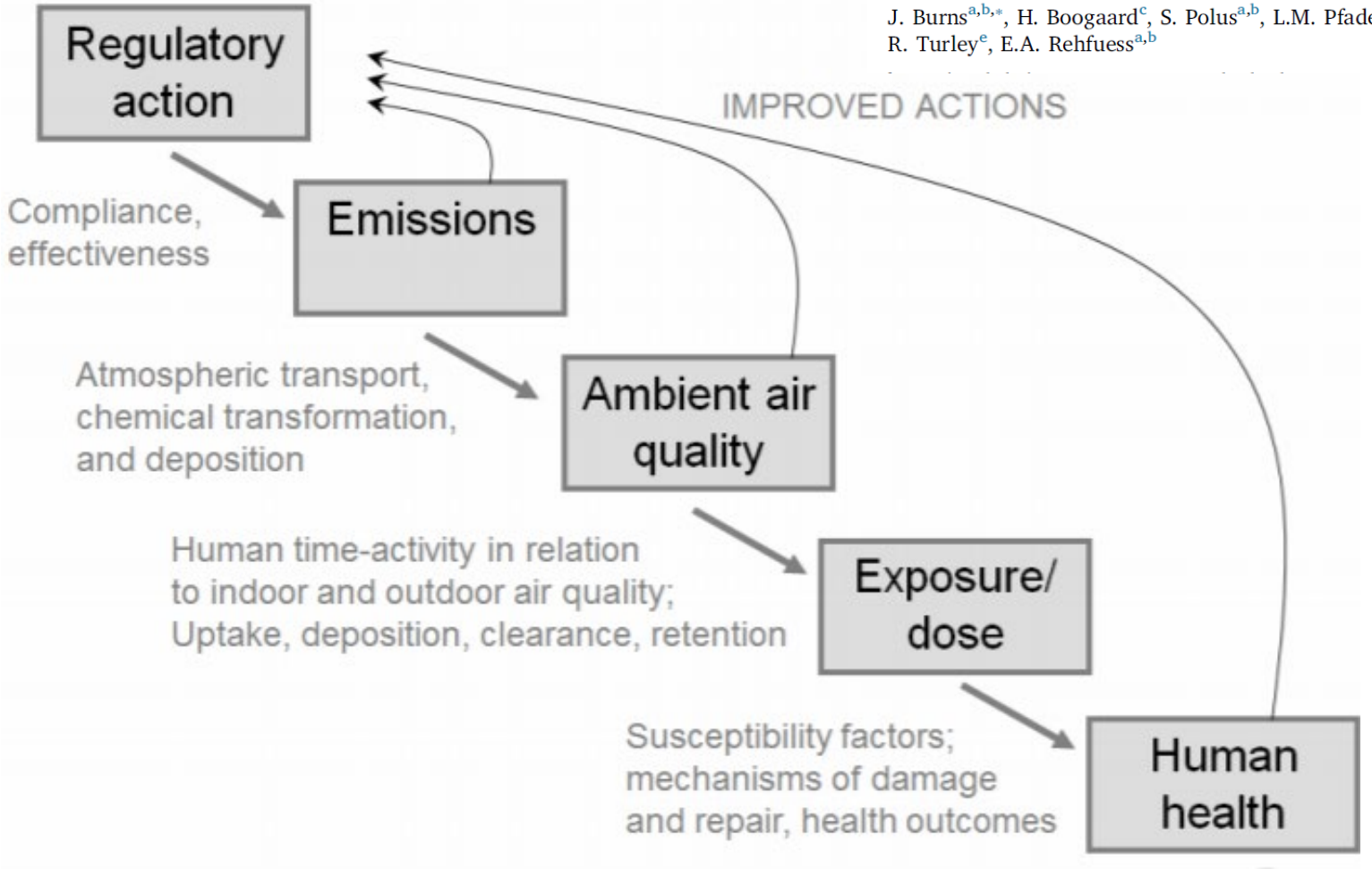
journal homepage: www.elsevier.com/locate/envint

Interventions to reduce ambient air pollution and their effects on health: An abridged Cochrane systematic review

J. Burns[a,b,*], H. Boogaard[c], S. Polus[a,b], L.M. Pfadenhauer[a,b], A.C. Rohwer[d], A.M. van Erp[c], R. Turley[e], E.A. Rehfuess[a,b]



Accountability research

'Randomistas' win economics Nobel

Abhijit Banerjee, Esther Duflo and Michael Kremer have been awarded this year's Nobel Prize in Economic Sciences. The three economists are at the vanguard of the influential 'randomista' movement, which applies the methods of rigorous randomized medical trials to social interventions such as improving education.

- Evaluate key long-term interventions in the EU, e.g. local traffic interventions, interventions to reduce emissions from industrial sources; changes in energy use (gas vs electricity), efforts to reduce exposure for at-risk communities
- Evaluate key short-term community (e.g. school closure) and individual interventions (e.g. face masks) during acute episodes, incl. population exposure, health effects, societal and economic implications
- Develop methods for accountability studies that would enhance the attribution of changes in air quality and health directly to an air quality action
- Integrate (climate) related co-benefits and dis-benefits in future studies
- Apply novel study design, use natural experiments, and randomized trial

Policy implications: working across silos is harder than it looks

Climate

Air Quality

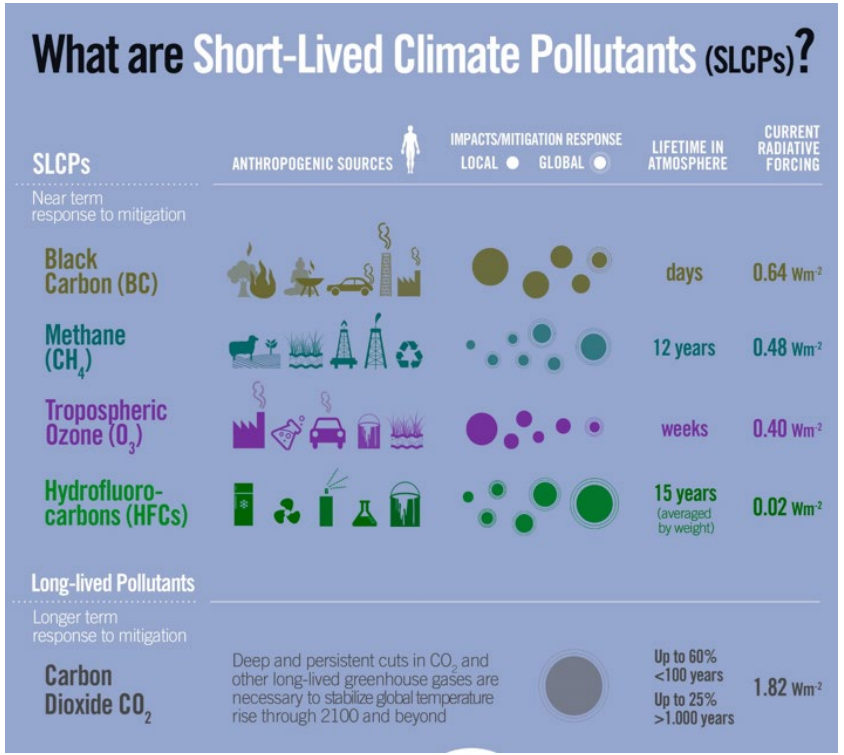
Science

Policy

Climate change and air quality

- The majority of air pollutants impact the climate (directly or indirectly)
- The majority of greenhouse sources co-emit air pollutants

"Climate change is now the lived experience in Australia"



Climate change and air quality benefits

- Air quality & climate are intricately interlinked
- Need for policies to address both together
- Major challenge to identify policies that provide “win-win” solutions
- Also, need to identify and quantify trade-offs

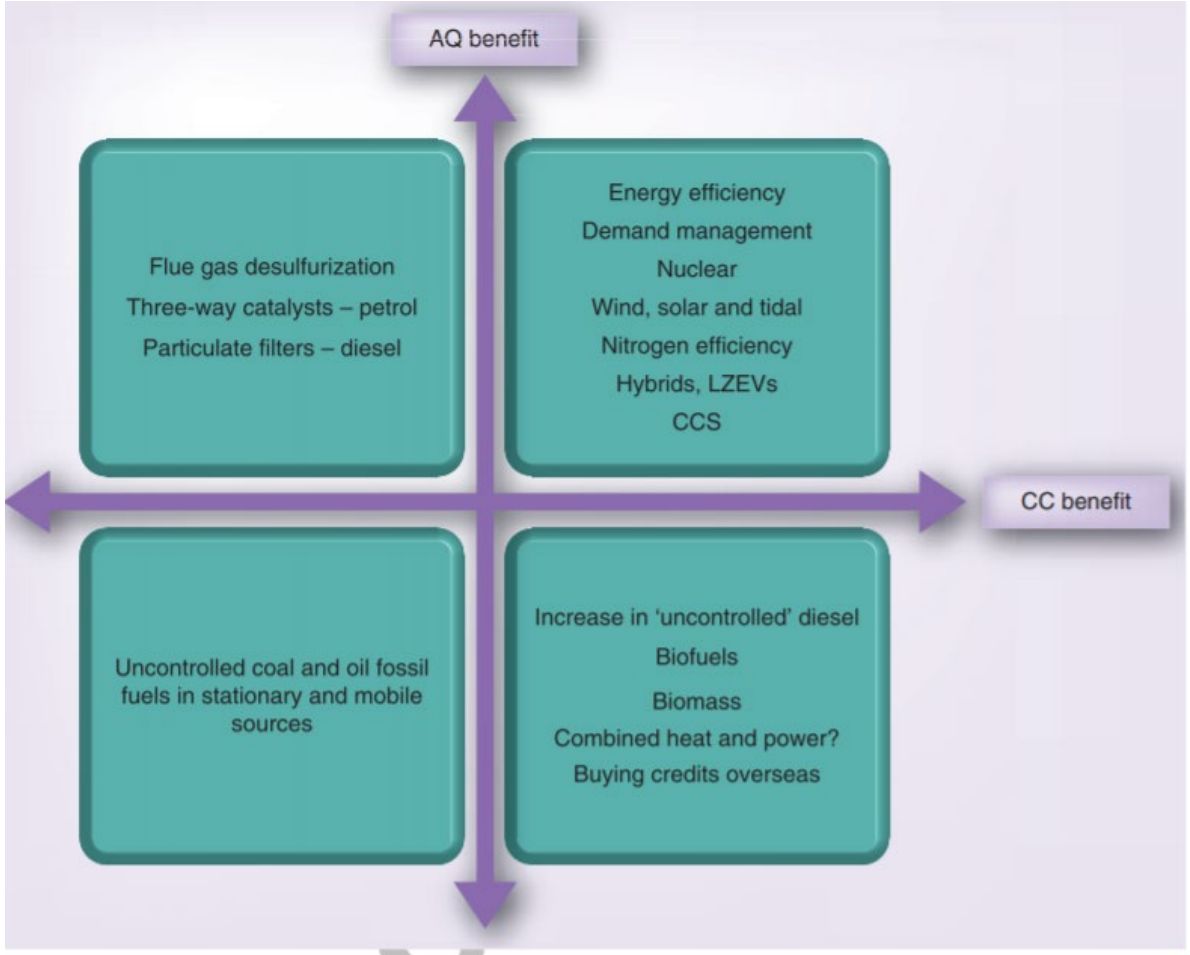


Figure 1. Synergies and trade-offs from policies and technologies to address climate change and air pollution.

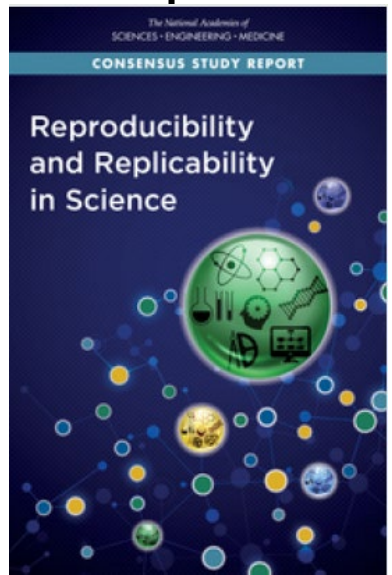
M. Williams, Carbon Management, 2012

Policy implications

- Evaluate co-benefits in other policy areas (climate change, green-deal, health effects through changed urban structure, etc.)
- Filling the gaps of air quality monitoring (current focus on limit values, little attention to population exposure)
- Need for regular evidence synthesis and revision of the air quality standards in the EU and comprehensive HIA

Core principles and assumptions of scientific inquiry

1. Nature is not capricious
2. Knowledge grows through exploration of the limits of existing rules and mutually reinforcing evidence
3. Science is a communal enterprise
4. Science aims for refined degrees of confidence, rather than complete certainty
5. **Scientific knowledge is durable and mutable**



REPRODUCIBILITY AND REPLICABILITY IN SCIENCE, Natl Academy of Science, 2019

Key messages: broad research areas

European Commission

- Effects at low air pollution levels, multipollutant exposures and interactions
- Major PM sizes, components and sources
- Methodology, health impact assessment, and accountability studies
- Co-benefits of air quality, climate policies, and green deal

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