The Relationship Between Air Pollution and Respiratory Infections: An Epidemiologic Perspective

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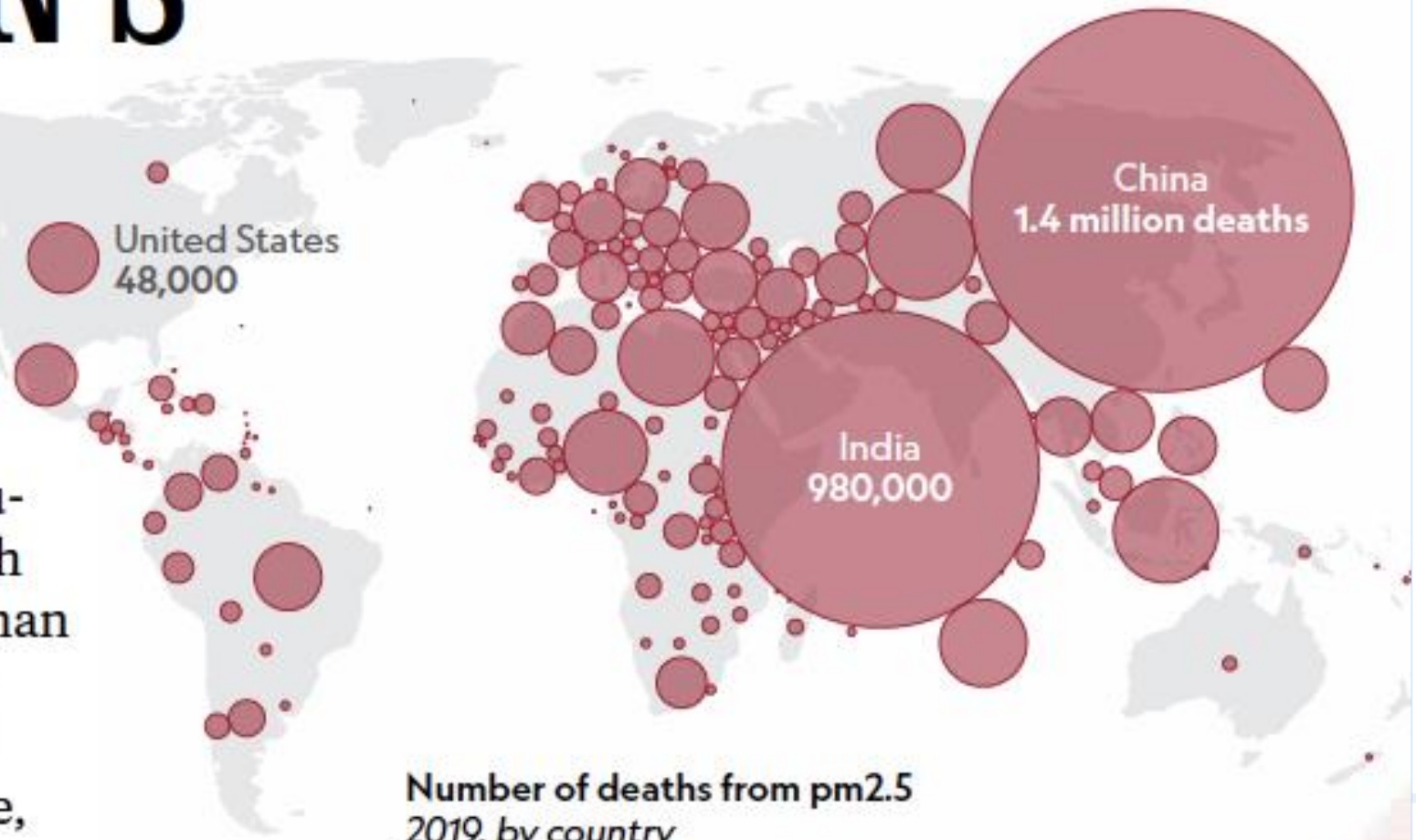
Overview

- Historical Perspective
- Ambient/Outdoor Air Pollution and Respiratory Infections
- Household/Indoor Air Pollution and Respiratory Infections
- Air Pollution and Respiratory Viral Pandemics
  - COVID-19

Overview and Historical Perspective

POLLUTION'S DEADLY TOLL

Air pollution is a complex mixture of gaseous and particulate components, each of which has detrimental effects on human health. In 2019, air pollution is estimated to have contributed to 6.7 million deaths worldwide, nearly 12 percent of the global total death toll.

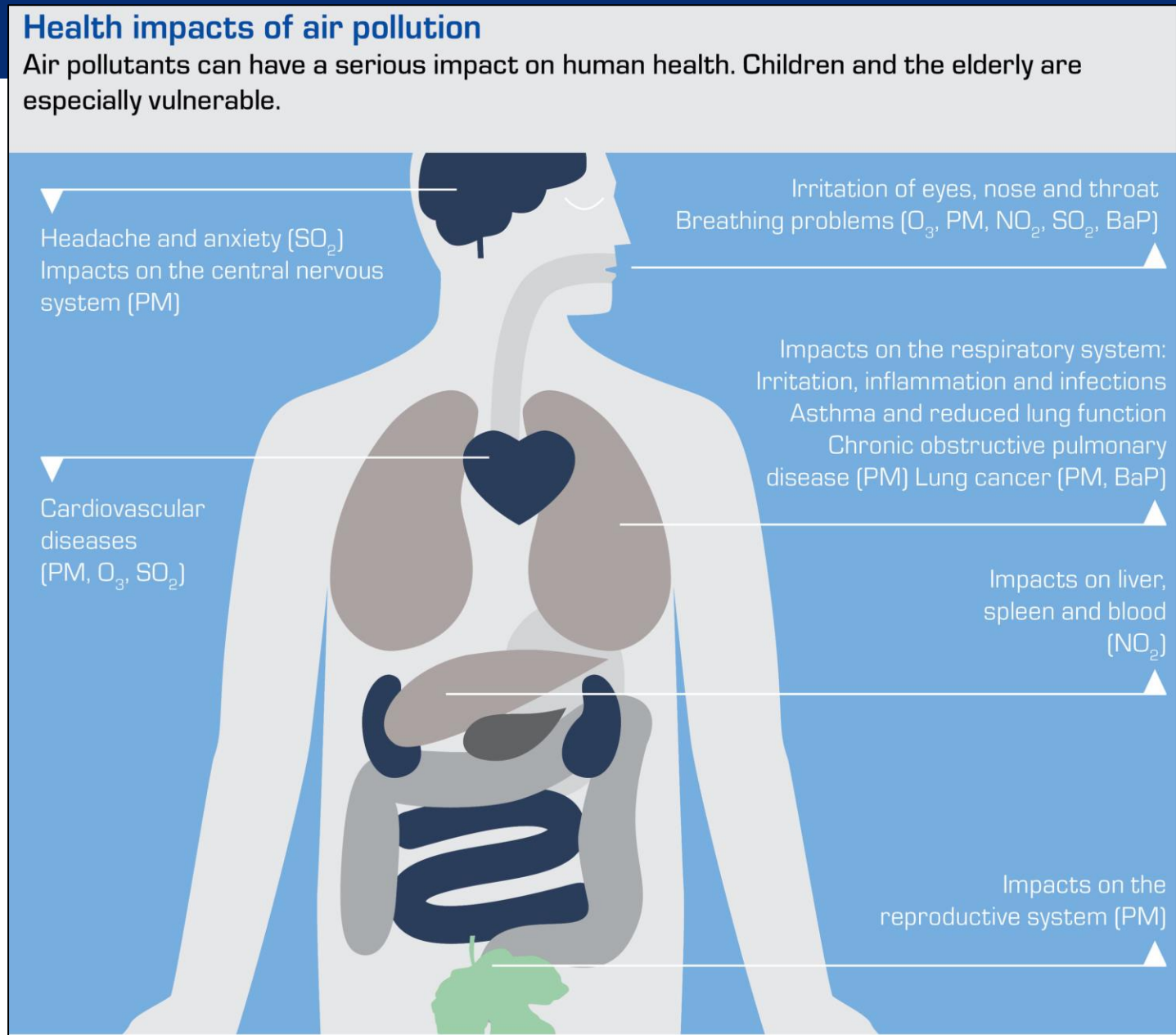


Number of deaths from pm2.5
2019, by country

Global Impact of Air Pollution

- Ambient Air Pollution:
  Contributes to 4.2 million deaths annually
- Household/Indoor Air Pollution:
  Contributes to 3.9 million deaths annually
- Significant burden related to non-communicable diseases: Cardiovascular Disease, COPD, Lung Cancer and Stroke
- There is also a strong association between air pollution exposure and respiratory infections in both children and adults

World Health Organization



Early Strong Evidence That Large Acute Air Pollution Events are Linked to Increased Risk for Respiratory Infections and Death

London Smog of 1952:

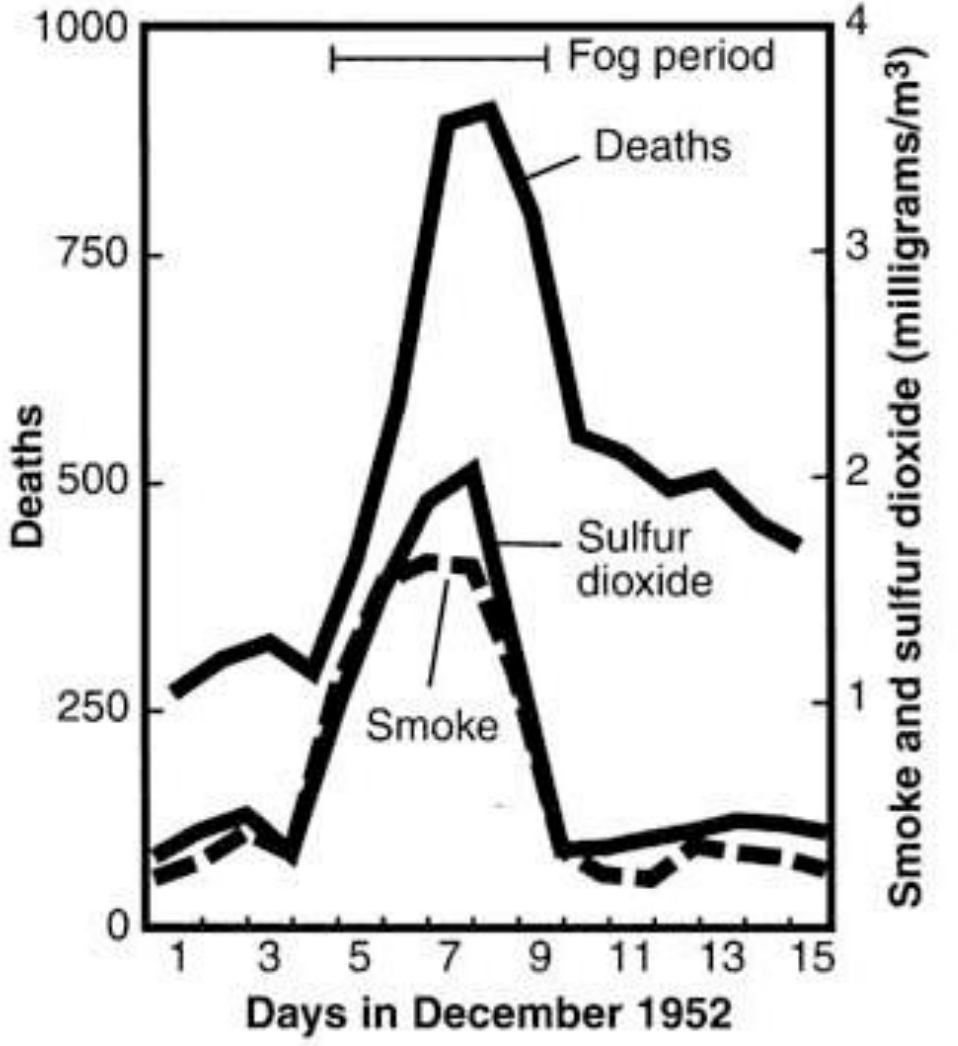
Stagnant air mass, heavy inversion
4000 excess deaths in 1 week

WORSE THAN 1866 CHOLERA

Deaths After Fog

The rise in deaths in the week after London's great fog early in December was greater than that in the worst week of the cholera epidemic in 1866. This is disclosed in a report of the health

Effect of the ‘Killer Fog,’ London 1952

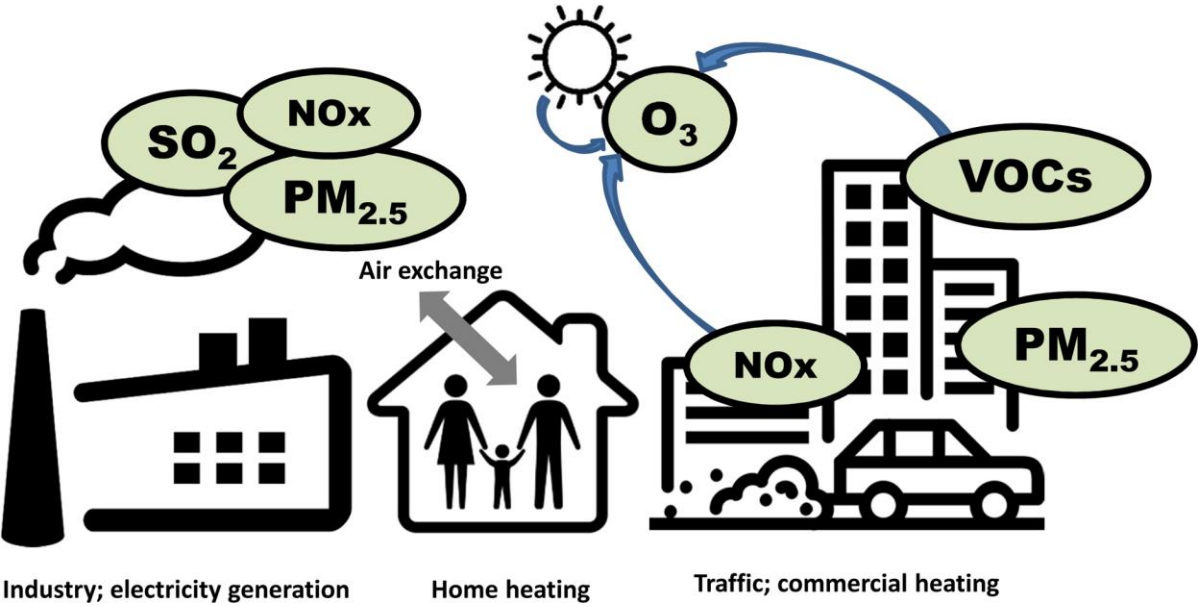


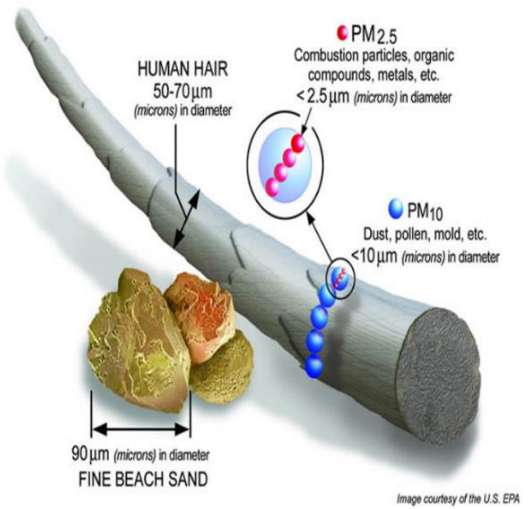
- Follow-up reports describe increased death from respiratory infections (bacterial pneumonia / bronchitis) related to the fog
- Risk for pneumonia increased 1.4-fold during the smog event, and 2.4- to 2.7-fold for 2 weeks after compared with the corresponding weekly average during 1947–1951.
- Estimated pneumonia was a significant cause of the 12,000 excess deaths resulting from acute and persisting effects of exposure

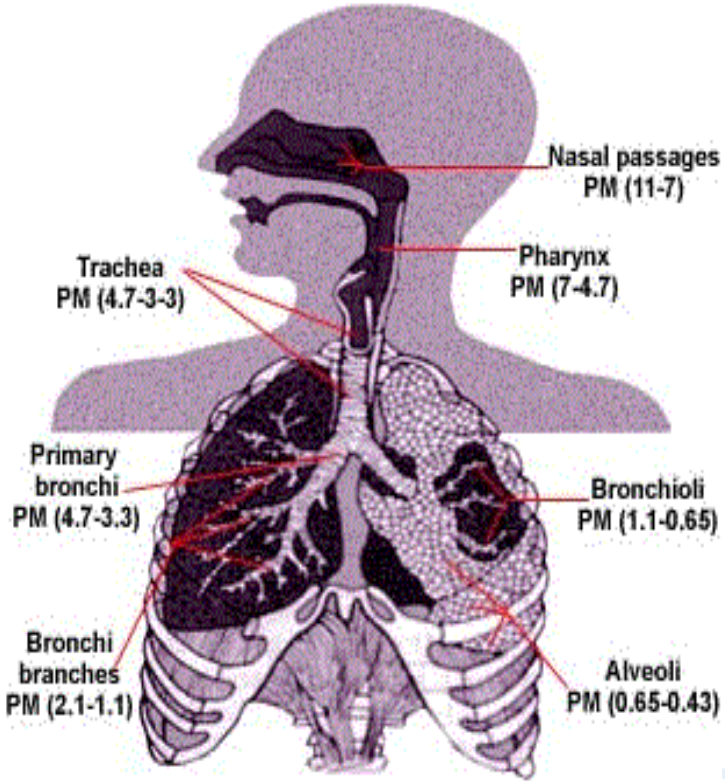
Bell ML, Davis DL. Reassessment of the lethal London fog of 1952: novel indicators of acute and chronic consequences of acute exposure to air pollution. *Environ Health Perspect* 2001;109:389–394.

Ambient/Outdoor Air Pollution and Respiratory Infections

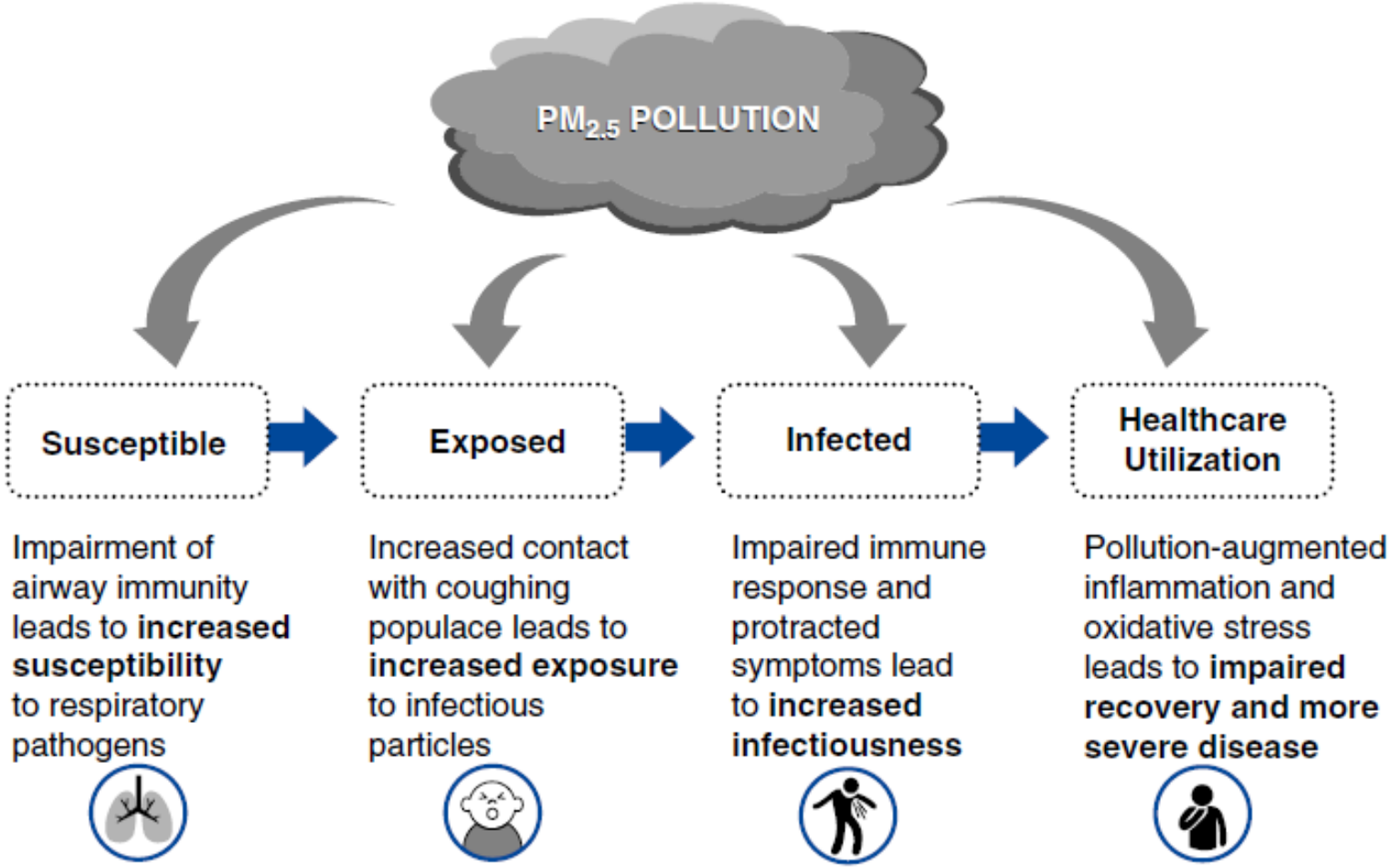
Sources: Considerations with Ambient/Outdoor Air Pollution







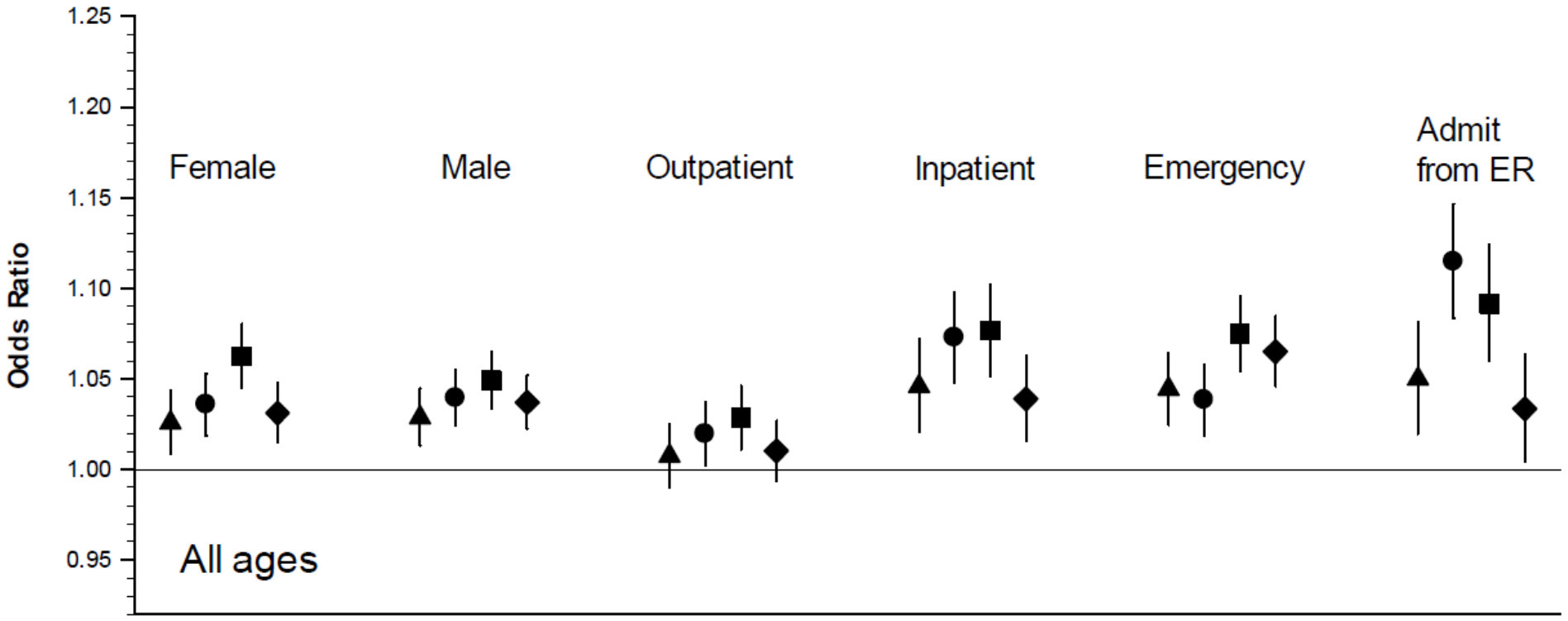
Impact on Respiratory Immunity



Horne et al, Short-Term Elevation of Fine Particulate Matter Air Pollution and Acute Lower Respiratory Infection, AJRCCM 2018

Short Term Increase in Ambient $PM_{2.5}$ Linked to Increased Odds of Severe Lower Respiratory Tract Infections

Increased odds of dx of acute lower respiratory tract infection - $10_{ug/m3}$ increase in $PM_{2.5}$



Presented with differing lag models from exposures

0-6 days

7-13 days

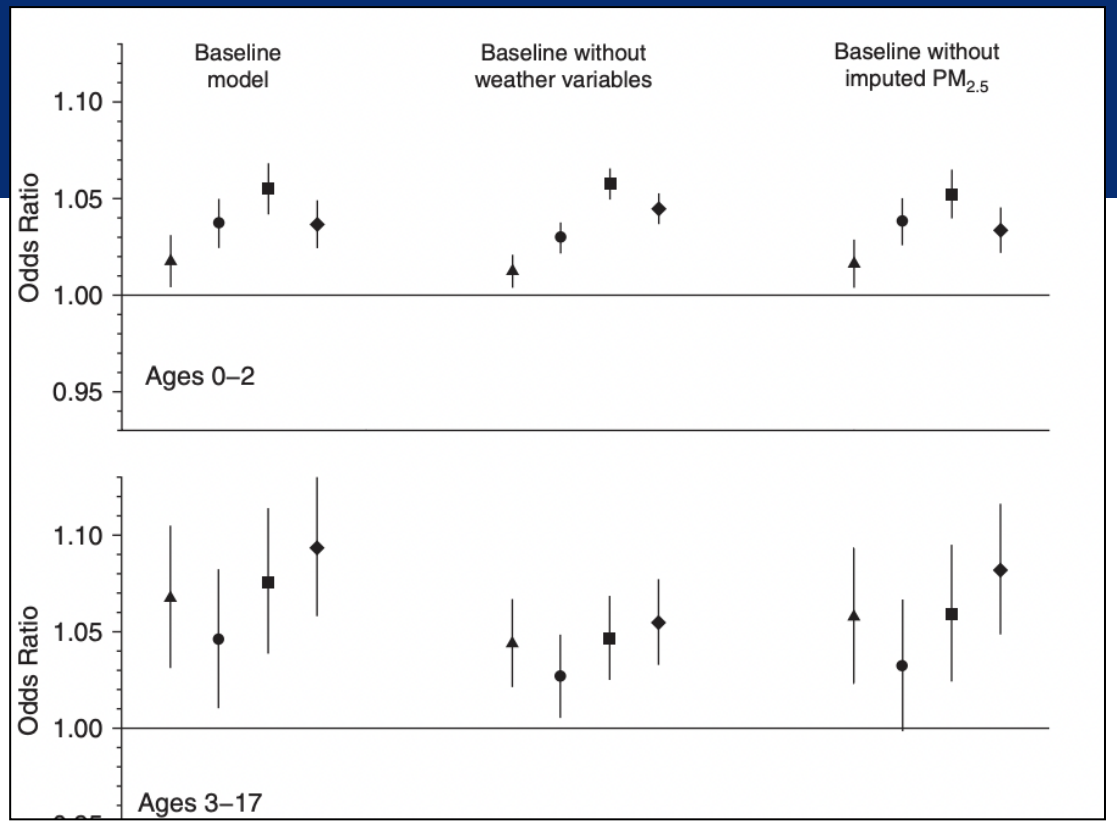
14-20 days

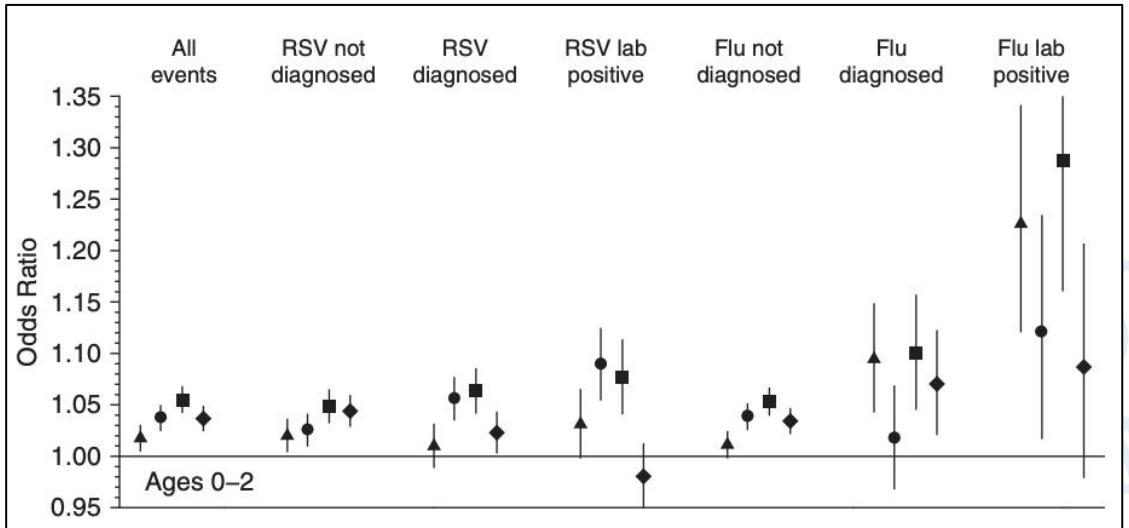
21-27 days

Horne et al, Short-Term Elevation of Fine Particulate Matter Air Pollution and Acute Lower Respiratory Infection, AJRCCM 2018

Strongest Association between Air Pollution and HealthCare Utilization for Infections in Young Children

- ALRI encounters for young children increased within 1 week of elevated $PM_{2.5}$ and peaked after 3 weeks
- Cumulative 28-day Odds Ratio of 1.15 per +10 $\mu g/m^3$ (95% CI: 1.12–1.19)
- Greater risk for Respiratory Syncytial Virus in 0-2 age group
- Potential association with Influenza in 0-2 group
- An association with specific viral infections not identified in older groups
- Findings are critical as ALRI is a leading cause of mortality in children < 5





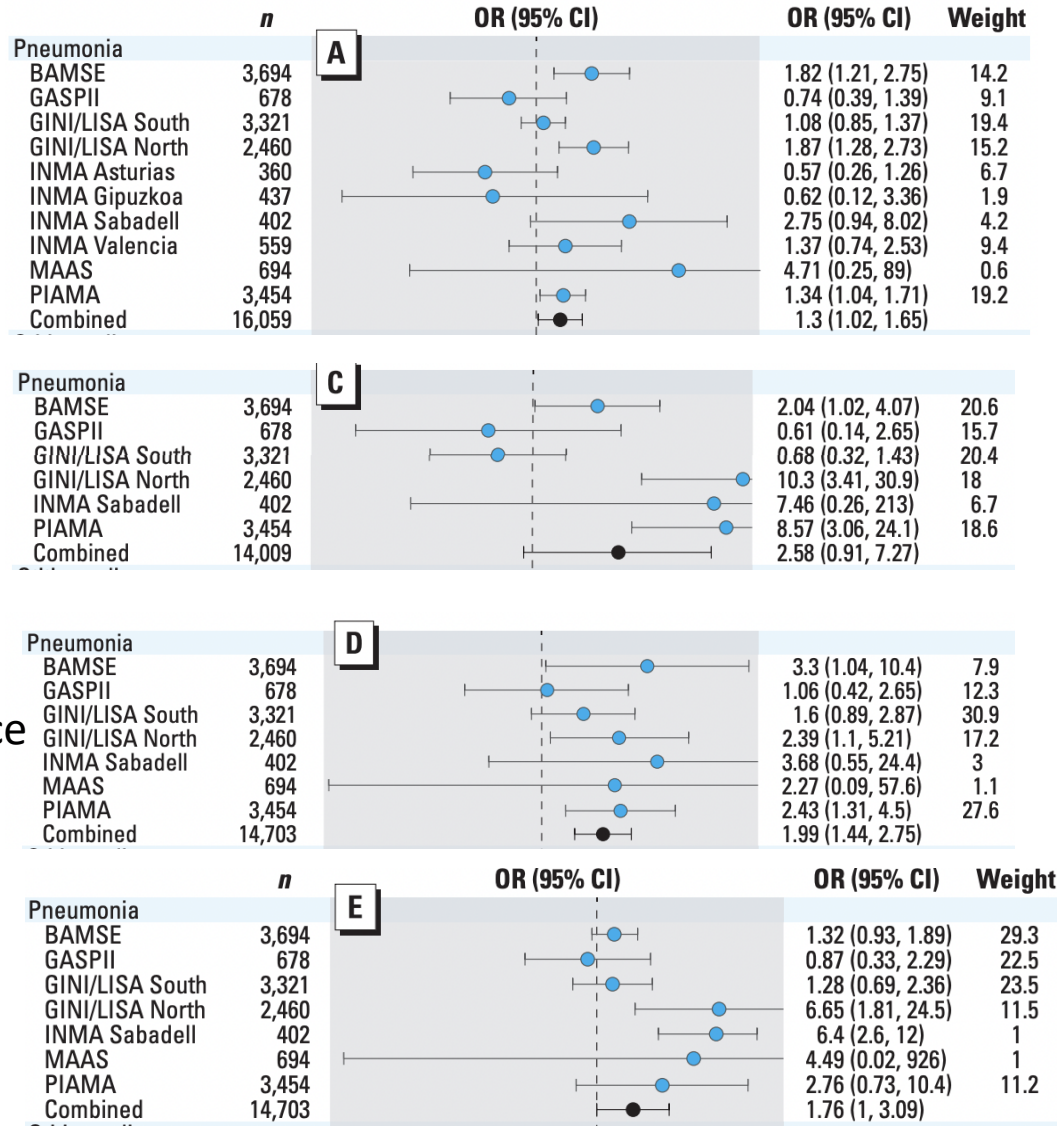
Impact of Multiple Pollutants in Children: Associations Noted Between Multiple Pollutants and Pediatric Pneumonia in European Birth Cohorts

NO_2

$PM_{2.5}$

$PM_{2.5}$ Absorbance

PM_{10}

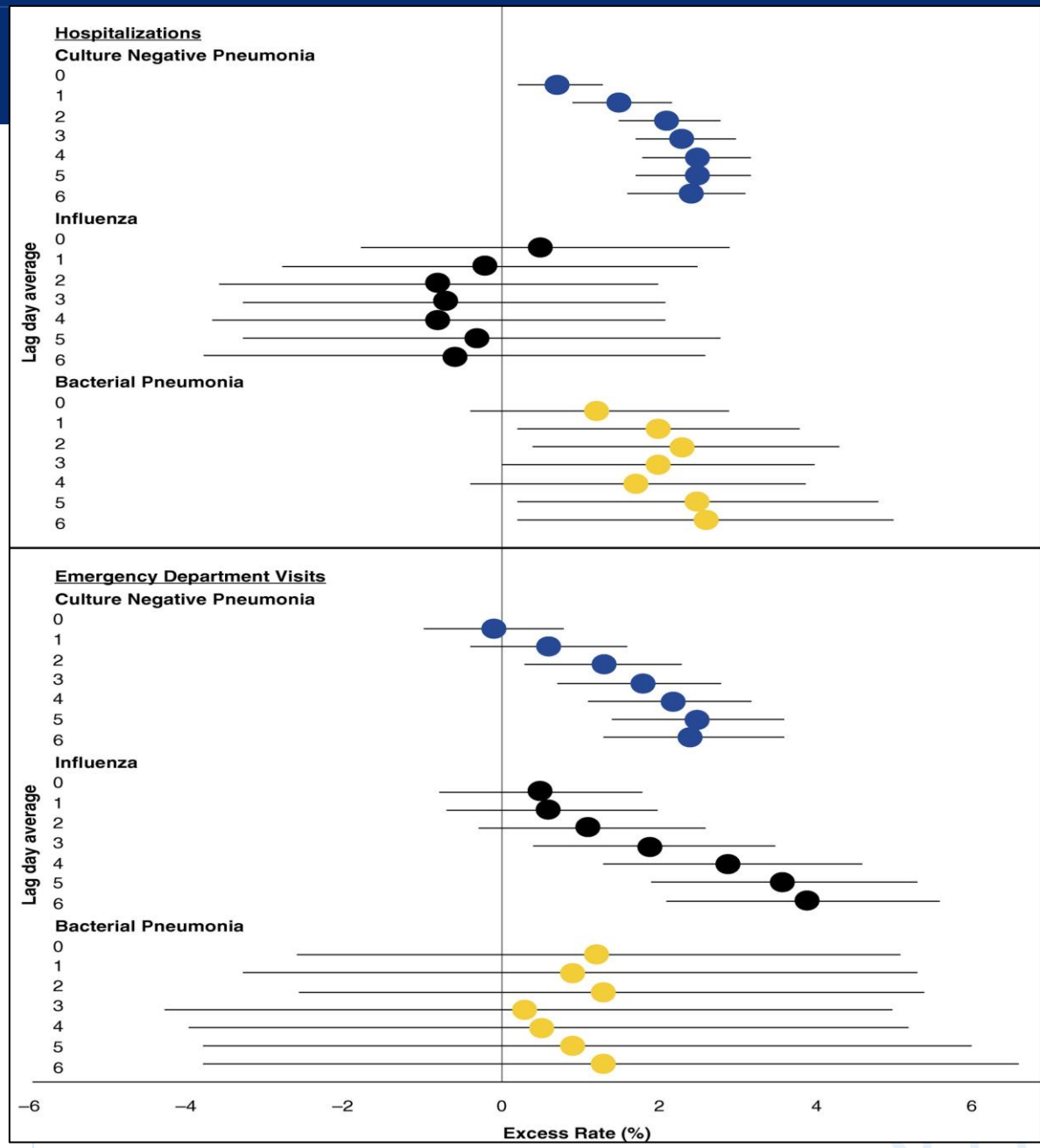


- Association between air pollution and pneumonia studied in 10 European birth cohorts
- Examined association with annual NO_2, NO_X, $PM_{2.5}$, PM_{10}, PM_{coarse}
- Increased odds with PM_{10} (1.76) and NO_2 (OR 1.3), not clearly established with $PM_{2.5}$ in this study
- These frequent respiratory infections in early childhood may impact lung development later in life in addition to mortality

MacIntyre EA, et al. Air pollution and respiratory infections during early childhood: an analysis of 10 European birth cohorts within the ESCAPE Project. Environ Health Perspect. 2014 Jan;122(1):107-13. doi: 10.1289/ehp.1306755. Epub 2013 Oct 22. Erratum in: Environ Health Perspect. 2014 Jan;122(1):112. PMID: 24149084; PMCID: PMC3888562.

Associations Persist In Older US Adult Populations

- Large population-based study of primarily older US adults (mean 65yo) with healthcare use for respiratory infections (Croft et al.)
- Studied Relative Rate of Health Encounters (ED Visits and Hospitalization) for pneumonia in New York State, 2005-2016 associated with increases in ambient $PM_{2.5}$
- IQR increases in $PM_{2.5}$ in 7 days prior associated with :
  - Culture negative pneumonia hospitalizations (ER 2.5%) and ED Visits (ER 2.5%)
  - ED Visits for Influenza (ER 3.9%)
- Showed a persistent impact of air pollution on respiratory infection policies to improve indoor air quality (from 2008-2013)



Long-Term Air Pollution Exposure in Older Adults Associated with Risk Related to Respiratory Infections

- Studies have additionally demonstrated risk from long-term air pollution in older adults
- Studied 859 aged >65 from Ontario, Canada with hospitalization for community acquired pneumonia (or matched controls) from 2003-2005
- Examined risk from multiple pollutants ($PM_{2.5}$, SO_2, NO_2) estimated over 1-year
- Pneumonia associated with increased $PM_{2.5}$ (OR 2.26: 95% CI 1.20-4.24) and NO_2 (OR 2.30: 1.25-4.21) (no association with SO_2)

TABLE 3. ADJUSTED ESTIMATES OF ASSOCIATIONS OF AIR POLLUTION VARIABLES* WITH HOSPITALIZATION WITH COMMUNITY-ACQUIRED PNEUMONIA

Air Pollution Variables†	OR‡	95% CI‡	*P* Value
NO_2, ppb (IDW)	2.30	1.25, 4.21	0.007
NO_2, ppb (SPL)	2.19	1.25, 3.83	0.006
NO_2, ppb (LUR)	1.70	1.00 - 2.89	0.049
SO_2, ppb (IDW)	0.97	0.59, 1.61	0.918
SO_2, ppb (SPL)	1.09	0.63, 1.89	0.766
$PM_{2.5}$, ppb (IDW)	2.26	1.20, 4.24	0.012
$PM_{2.5}$, ppb (SPL)	1.70	0.99, 2.92	0.053

* Air pollution ambient levels were estimated on the basis of the Ontario Ministry of Environment's pollution measurements in 2001 and 2002, using inverse distance weighting and bicubic splined methods, and in 2002 by the land use regression method.

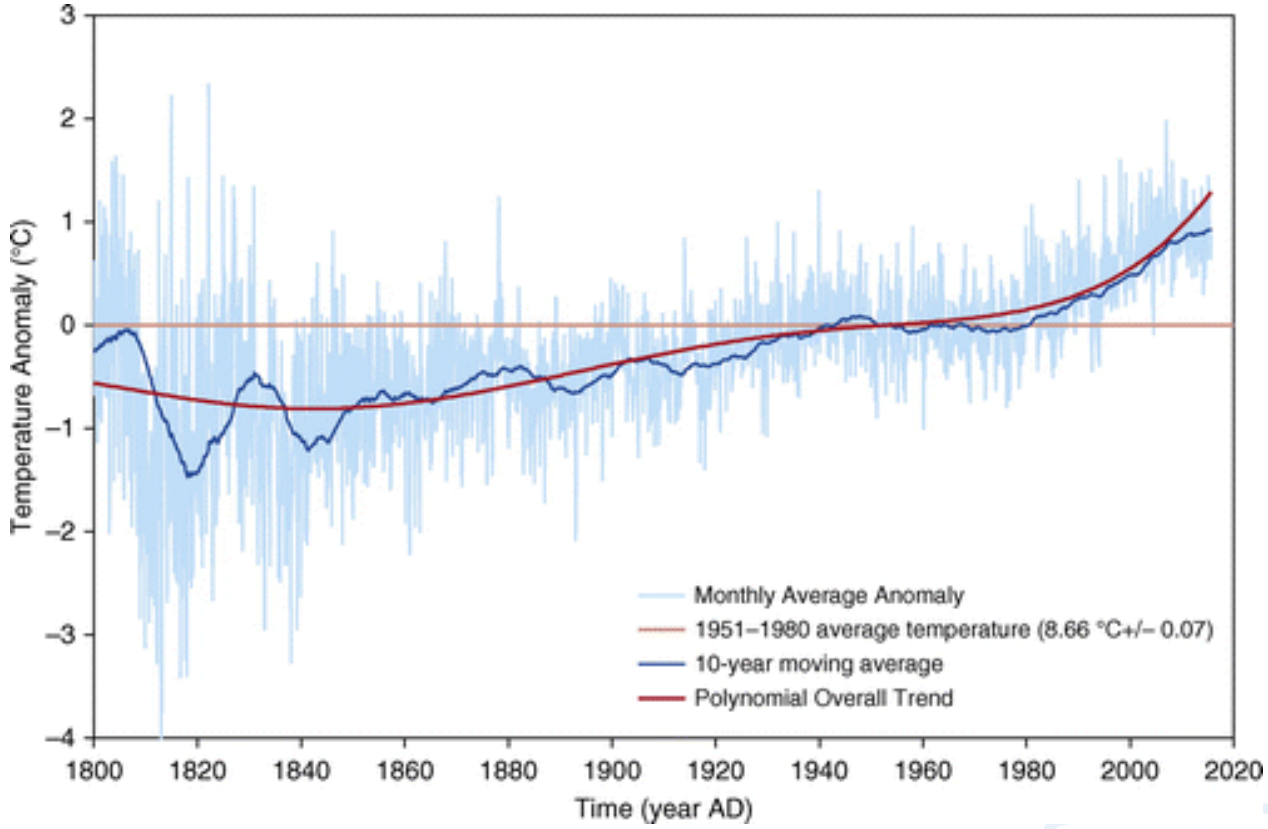
† SPL, IDW, and LUR stand for air pollution levels estimated by bicubic splined regression, inverse distance weighting function, and land use regression methods, respectively.

‡ OR and 95% CI are calculated for the 5th−95th percentile range increment of the pollution.

Neupane B, Jerrett M, Burnett RT, Marrie T, Arain A, Loeb M. Long-term exposure to ambient air pollution and risk of hospitalization with community-acquired pneumonia in older adults. Am J Respir Crit Care Med. 2010 Jan 1;181(1):47-53.

Climate Factors Influence Risk From Pollution

- The effect of air pollution may be modified by other climate factors including rising temperatures
- Studies suggest at both extremes of temperatures (very high and low) air pollution may be have a greater impact on risk for resp infections
- Concern weather patterns may influence viral transmission
- Humidity can influence pathogen risk as well



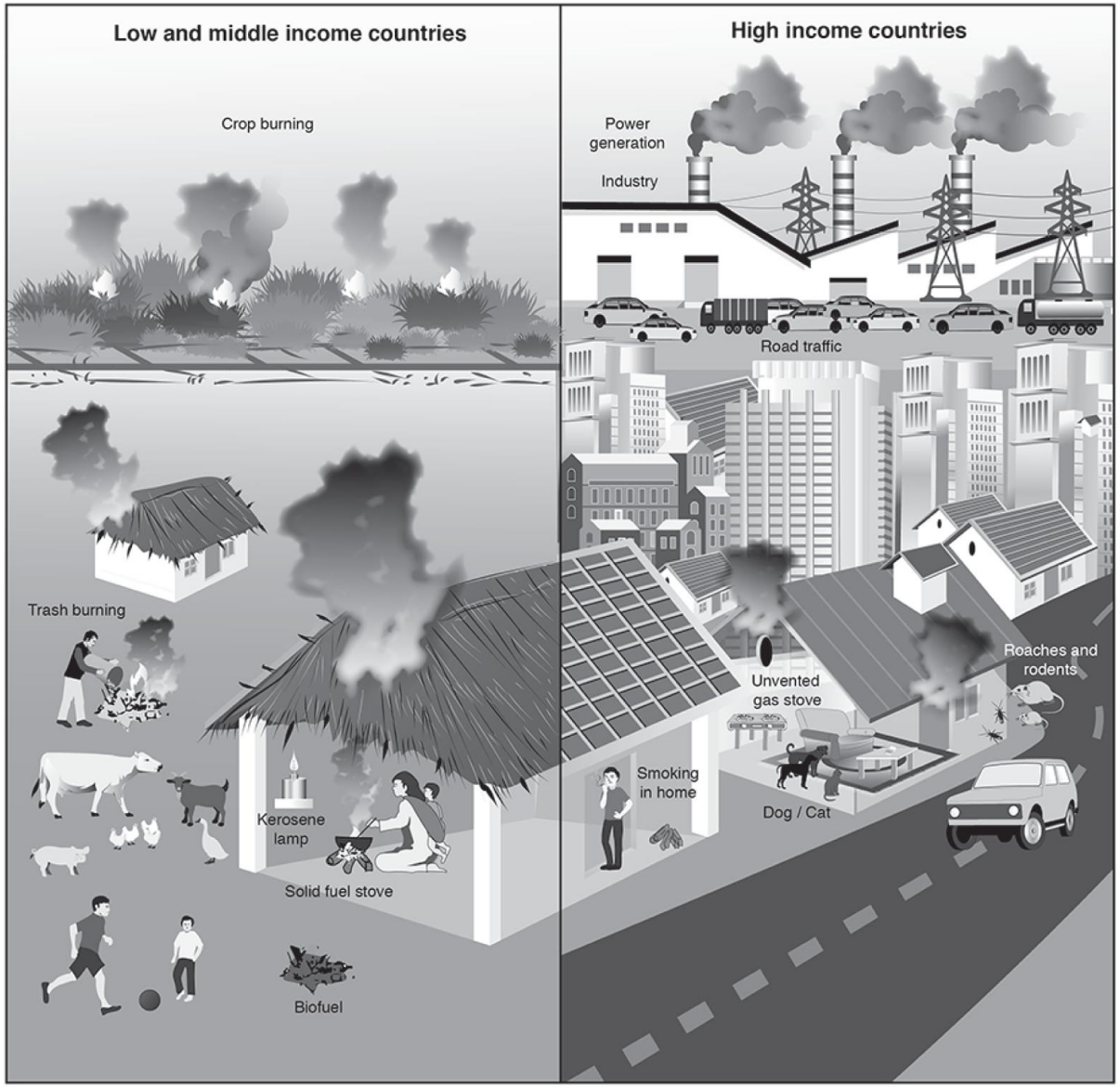
Zhang, R., Meng, Y., Song, H. *et al.* The modification effect of temperature on the relationship between air pollutants and daily incidence of influenza in Ningbo, China.*Respir Res* **22,** 153 (2021). https://doi.org/10.1186/s12931-021-01744-6

Ambient Air Pollution and Respiratory Infections

- Increased ambient $PM_{2.5}$ associated with healthcare utilization related to respiratory infections
- Greatest risk noted in young children facing risk from respiratory viruses (RSV and influenza), though older adults still face risk (extremes of age most affected)
- Epidemiologic studies commonly focus on healthcare utilization for respiratory infections and less about transmissibility
- Most studies are focused on short-term pollution exposure but there is also data on long term exposures and respiratory infections
- Additional factors like temperature and humidity may impact transmissibility (*observed with H1N1 pandemic)*
- Limited data from multi-pollutant models that examine risk

Indoor Air Pollution and Respiratory Infections

Sources of Indoor Air Pollution: Differ from Low Income to High Income Countries

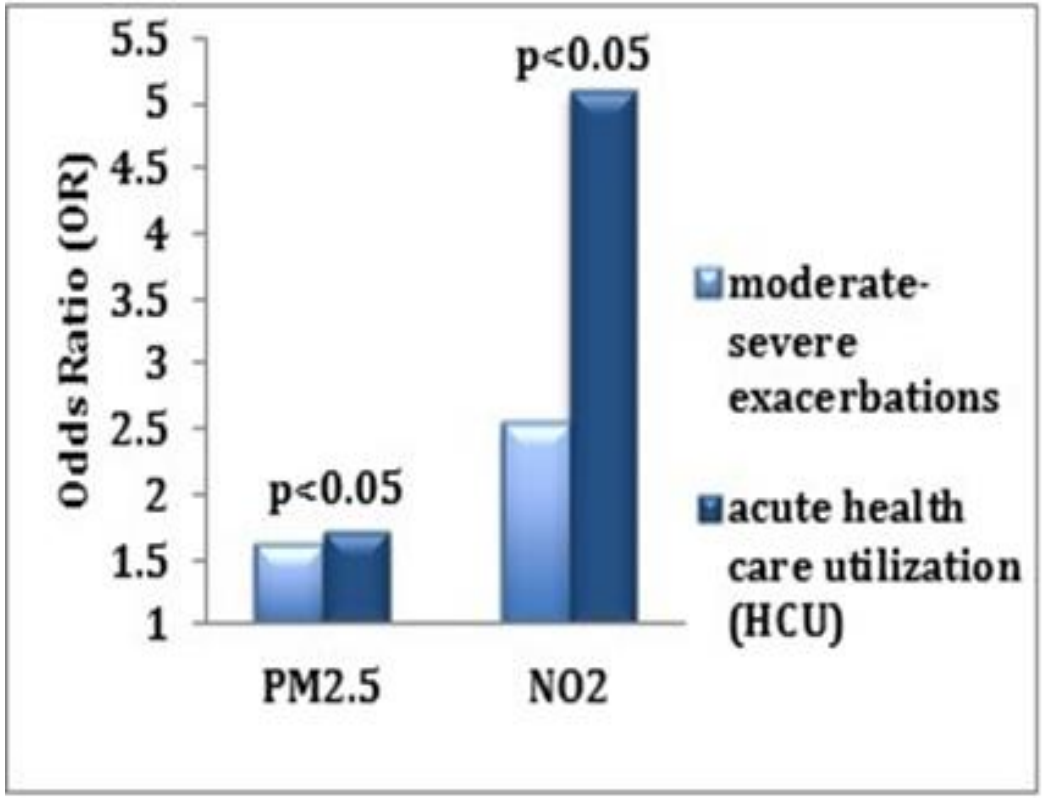


Small Increase in Indoor Pollution Associated with Significant Respiratory Health Effects in COPD and Asthma Patients

Asthma Study

	$PM_{2.5}$ (per 10 µg/m^3 increase)	
	IRR	**P-value**
Cough, wheeze, chest tightness	1.03	0.18
Slow down	1.04	0.06
Symptoms with running	**1.07**	**<0.01**
Nocturnal symptoms	**1.06**	**0.01**
Limited speech	**1.07**	**0.04**
Rescue medication use	**1.04**	**0.04**

COPD Study



[1]*McCormack et al, In-Home Particle Concentrations and Childhood Asthma Morbidity, EHP 2009*
[2]*Hansel et al, In-Home Air Pollution is Linked to Respiratory Morbidity in Former Smokers with COPD, AJRCCM 2011*

Environmental Tobacco Smoke and Pediatric Pneumonia

- Large Cross-Sectional Survey of 353,525 children in central Vietnam
- Described the association between household environmental tobacco smoke (ETS) and hospitalization for pediatric pneumonia
- ETS independently associated with hospitalization for pediatric pneumonia. (aOR 1.55; 95% CI 1.25 to 1.92)
- Estimated that 28.7 % of childhood pneumonia in this community attributable to ETS
- Notably a high smoking population (71%)

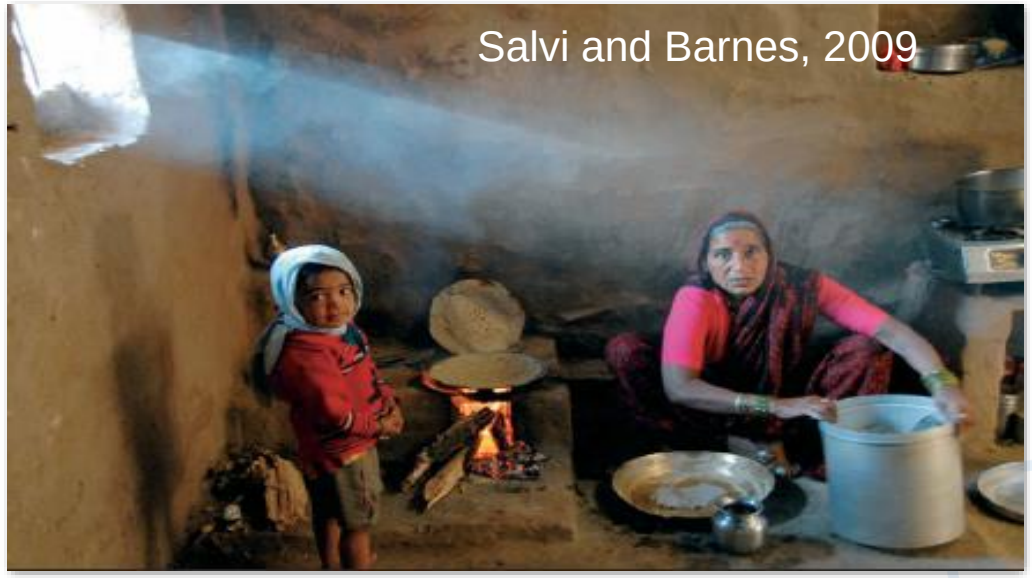
Table 4 Adjusted odds ratios (ORs) and population attributable fractions (PAFs) of exposure to environmental tobacco smoke (ETS) for hospital admissions with pneumonia among children aged <5 years

	Unadjusted OR		Adjusted OR*		PAF (%)
	(95% CI)	p Value	(95% CI)	p Value	(95% CI)
ETS exposure					
Yes	1.81 (1.48 to 2.21)	<0.001	1.55 (1.25 to 1.92)	<0.001	28.7 (15.2 to 40.0)
No	1		1		
Number of smokers in household					
⩾2	1.64 (1.27 to 2.11)	<0.001	1.43 (1.08 to 1.89)	0.012	15.2 (2.8 to 26.0)
1	1.87 (1.52 to 2.30)	<0.001	1.59 (1.27 to 1.98)	<0.001	28.2 (17.5 to 37.5)
0	1		1		
Type of smoker					
Parental smoking	1.88 (1.53 to 2.31)	<0.001	1.53 (1.21 to 1.93)	<0.001	26.5 (12.6 to 38.1)
Other than parental smoking	1.61 (1.25 to 2.07)	<0.001	1.58 (1.21 to 2.08)	0.001	18.5 (7.0 to 28.6)
No	1		1		

*Adjusted for sex, age (months), have siblings, wealth level, water source, father's educational level and area, which was selected by backward stepwise selection.

Household Air Pollution from Solid Fuel and Pediatric Pneumonia in LMICs

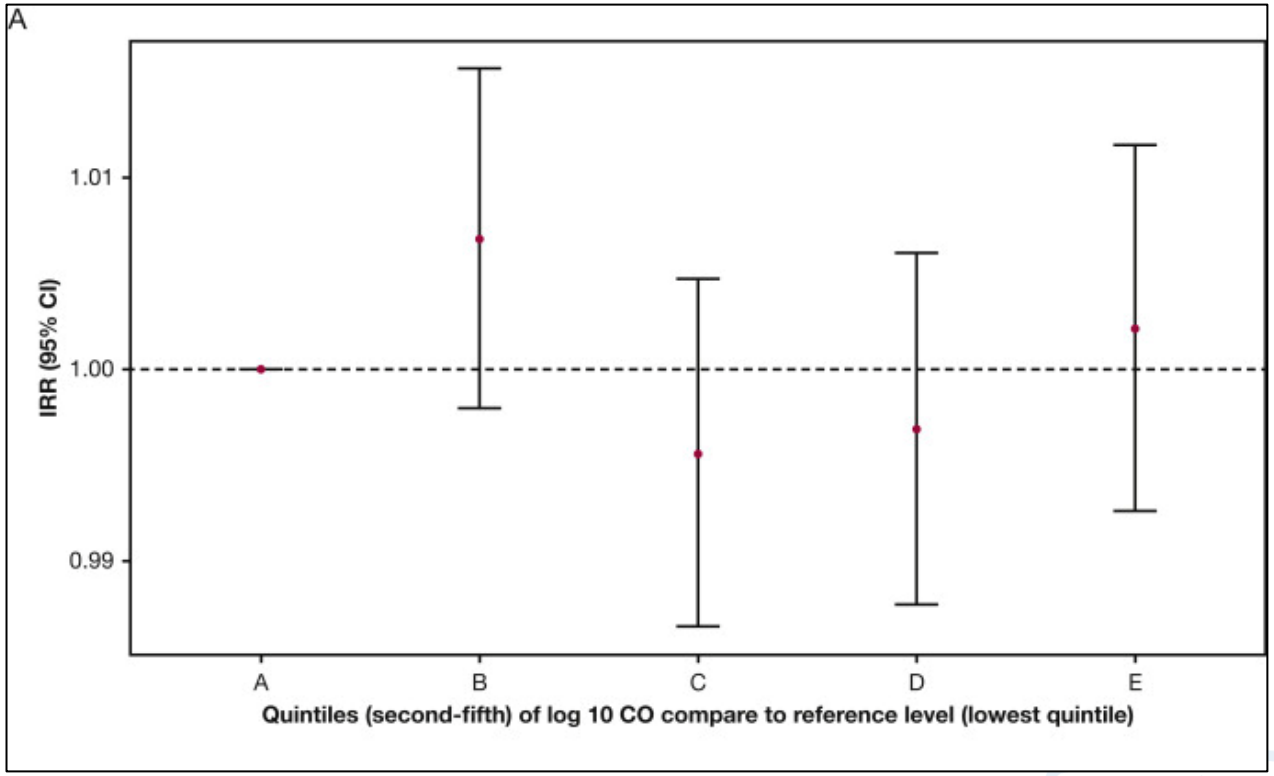
- Multiple Studies in LMICs showing the association between solid fuel use and pediatric pneumonia
- Solid fuel use increases pediatric pneumonia risk by 78% (pooled odds ratio = 1.78 (95% CI 1.45 to 2.18) in meta-analysis of 28 studies
- Multiple Cookstove Interventions for Household Air Pollution in LMICs powered to address pediatric pneumonia
- Limited evidence to suggest association in adults



Dherani M, Pope D, Mascarenhas M, Smith KR, Weber M, Bruce N. Indoor air pollution from unprocessed solid fuel use and pneumonia risk in children aged under five years: a systematic review and meta-analysis. *Bull World Health Organ*. 2008;86(5):390–398C.

Personal Exposures and Pediatric Pneumonia

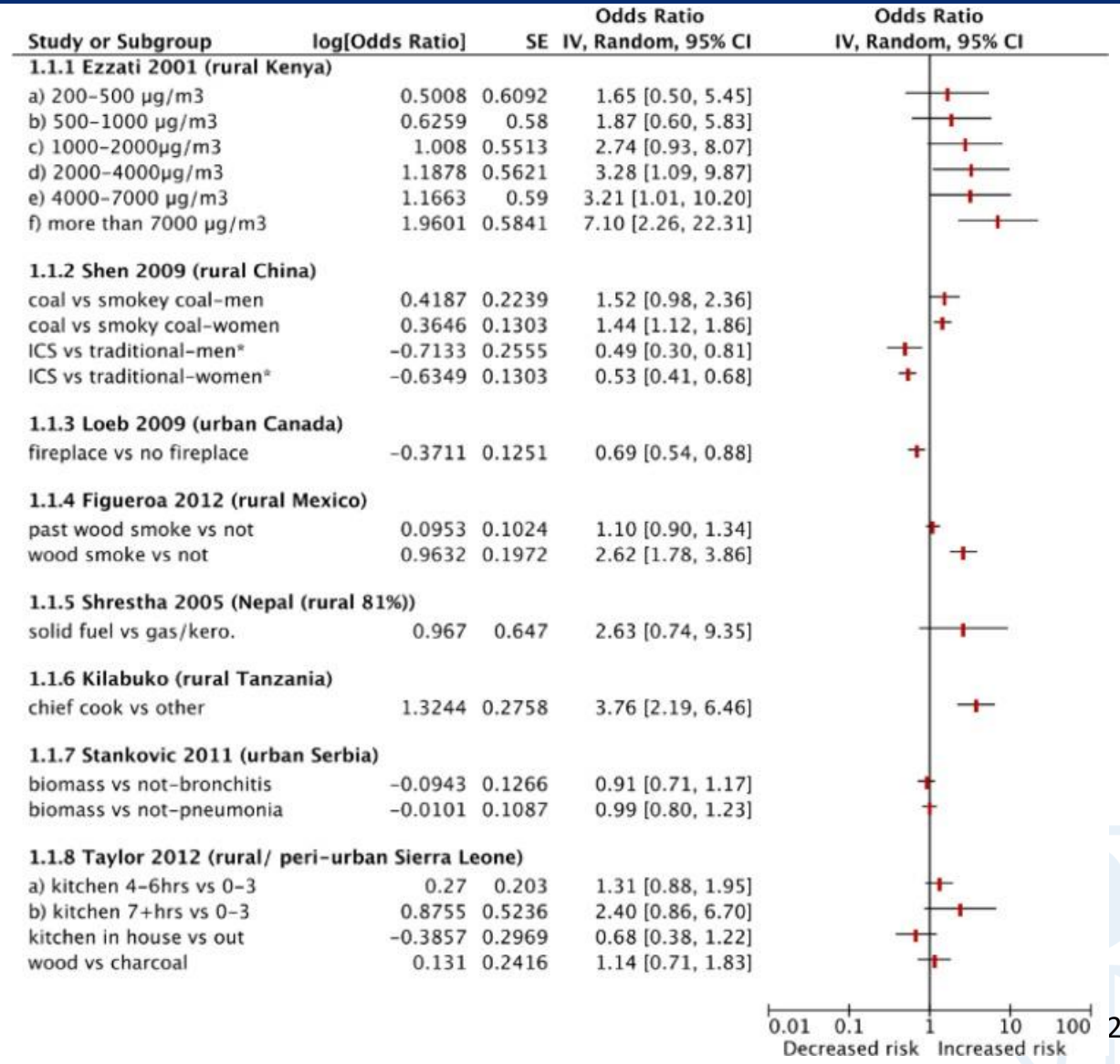
- Association between personal exposure to pollutants from cookstoves and pediatric pneumonia in rural Malawi (CAPS study)
- Participants living in biomass homes underwent repeat measures of personal CO exposure (personal monitor for 48 hours)
- After recruiting 1805 children no association between exposure to CO or carboxyhemoglobin and pneumonia was observed
- Suggest other exposures should be considered – CO exposure notably low



Mortimer K, Lesosky M, Semple S, et al. Pneumonia and Exposure to Household Air Pollution in Children Under the Age of 5 Years in Rural Malawi: Findings From the Cooking and Pneumonia Study. *Chest*. 2020;158(2):501-511.

Limited Data on the Association between HAP and Pneumonia in Adults and in High Income Countries

- Systemic review analyzed literature for association between HAP and adult lower respiratory tract infection (LRTI)
- Studies with significant heterogeneity in methods in exposure collection to date
- Found no conclusive association between HAP and LRTI in adults
- Limited studies in high income countries to date



Jary H, Simpson H, Havens D, et al. Household Air Pollution and Acute Lower Respiratory Infections in Adults: A Systematic Review. *PLoS One*. 2016;11(12):e0167656. Published 2016 Dec 1. doi:10.1371/journal.pone.0167656

Effect of Interventions to Reduce Household Air Pollution: Cookstove Interventions

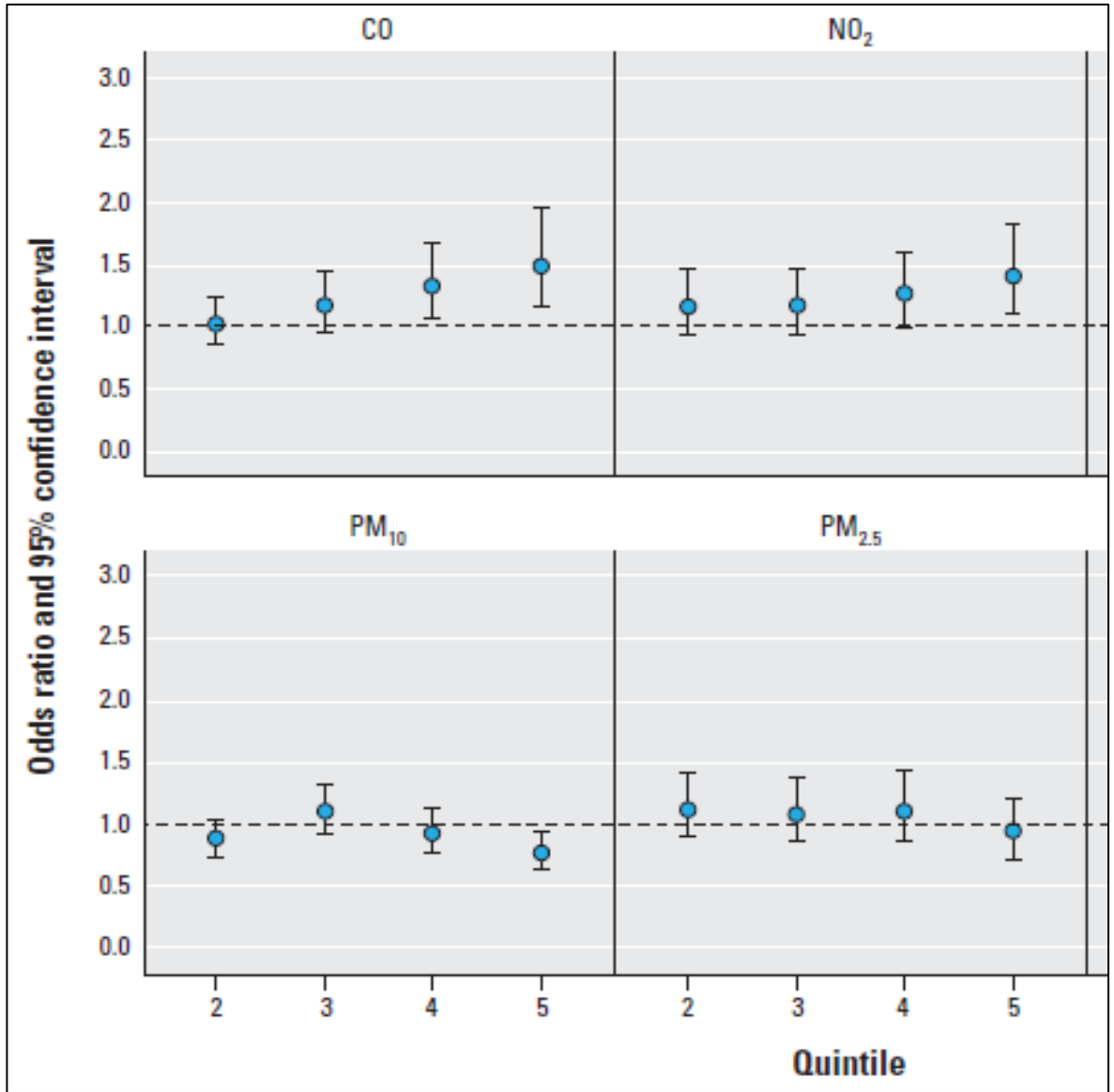
- Pediatric Pneumonia has been the focus of multiple cookstove interventions in LMICs
- Repeated trials to date have not shown a clinically meaningful benefit
- Studies have been heterogenous and often have failed to achieve meaningful exposure reductions
- Ongoing studies are examining interventions with participants across a lifespan and with longer follow-up to determine effective strategies to reduce exposure and pneumonia risk

Mortimer K, Balmes JR. Cookstove Trials and Tribulations: What Is Needed to Decrease the Burden of Household Air Pollution? *Ann Am Thorac Soc*. 2018;15(5):539–541. 10.1513/AnnalsATS.201710-831GH
Raju S, Siddharthan T, McCormack MC. Indoor Air Pollution and Respiratory Health. *Clin Chest Med*. 2020;41(4):825-843. doi:10.1016/j.ccm.2020.08.014

Household/Indoor Air Pollution and Respiratory Infections

- Indoor air pollution remains a significant source of respiratory morbidity
- Household pollution from the burning of solids fuels, and environmental tobacco smoke, is a major contributor to pediatric pneumonia in LMICs
- The impact of indoor air pollution on respiratory infections has not yet been established for adults or in high-income countries
- Ongoing studies are measuring total personal (both indoor and outdoor) exposures – via personal monitoring - and examining risk for respiratory infections
- Efforts are ongoing to develop interventions for sustained improvements in indoor pollutants that can reduce risk from respiratory infections

Special Cases: Air Pollution and TB?

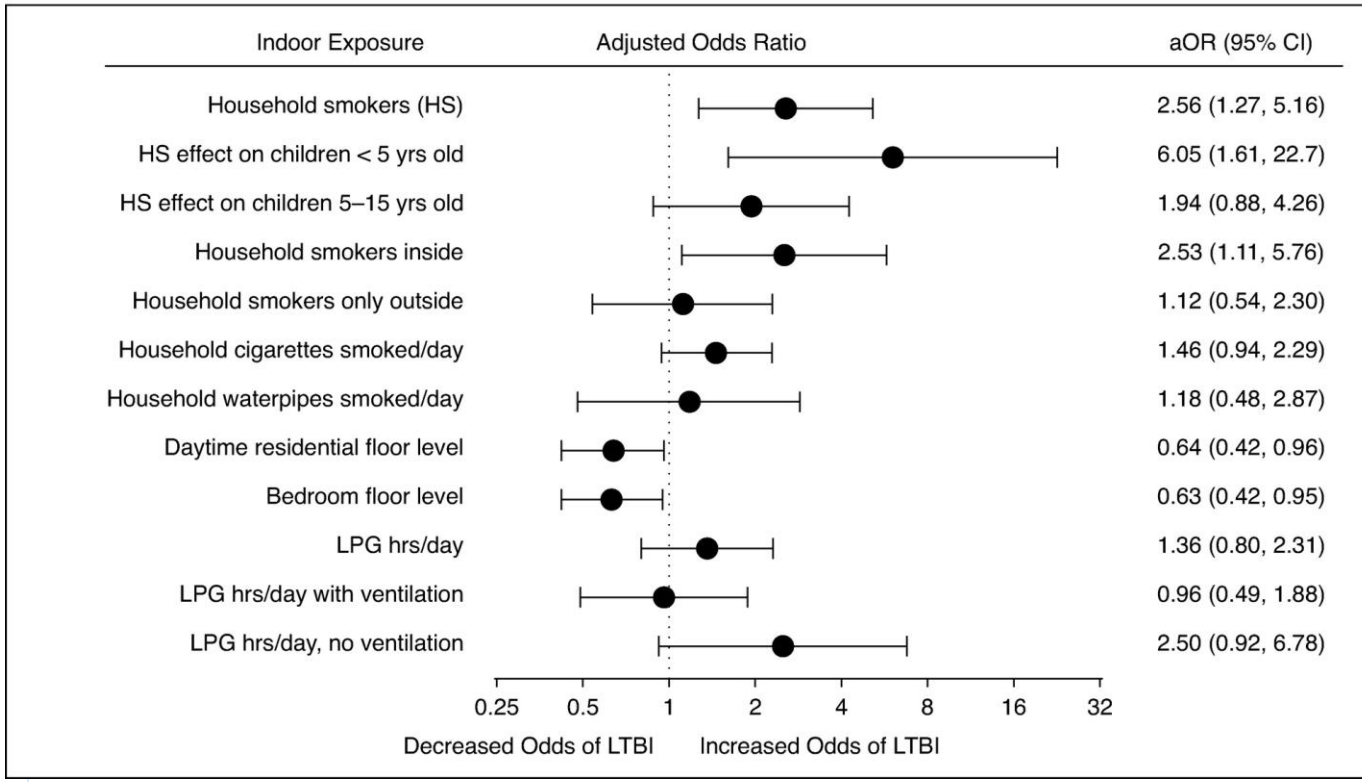


- Some concern that air pollution may increase risk for TB
- Odds of TB higher in areas with higher ambient NO_2 and CO
- Results not consistent for this association across studies

Smith et al, EHP 2016

Special Cases: Air Pollution Increases Transmission of TB?

- 109 child household contacts of patients with confirmed active tuberculosis in Vietnam enrolled
- Tested for associations between latent TB (LTBI) and both household environmental tobacco smoke (ETS) and personal $PM_{2.5}$ exposure
- 2.56x increased odds of latent TB associated with ETS (95% CI, 1.27–5.16)
- Gas stoves and traffic sources also increased odds of latent TB
- Did not detect clear association between personal $PM_{2.5}$ exposure and LTBI
  - Other pollutants (NO_2) not measured



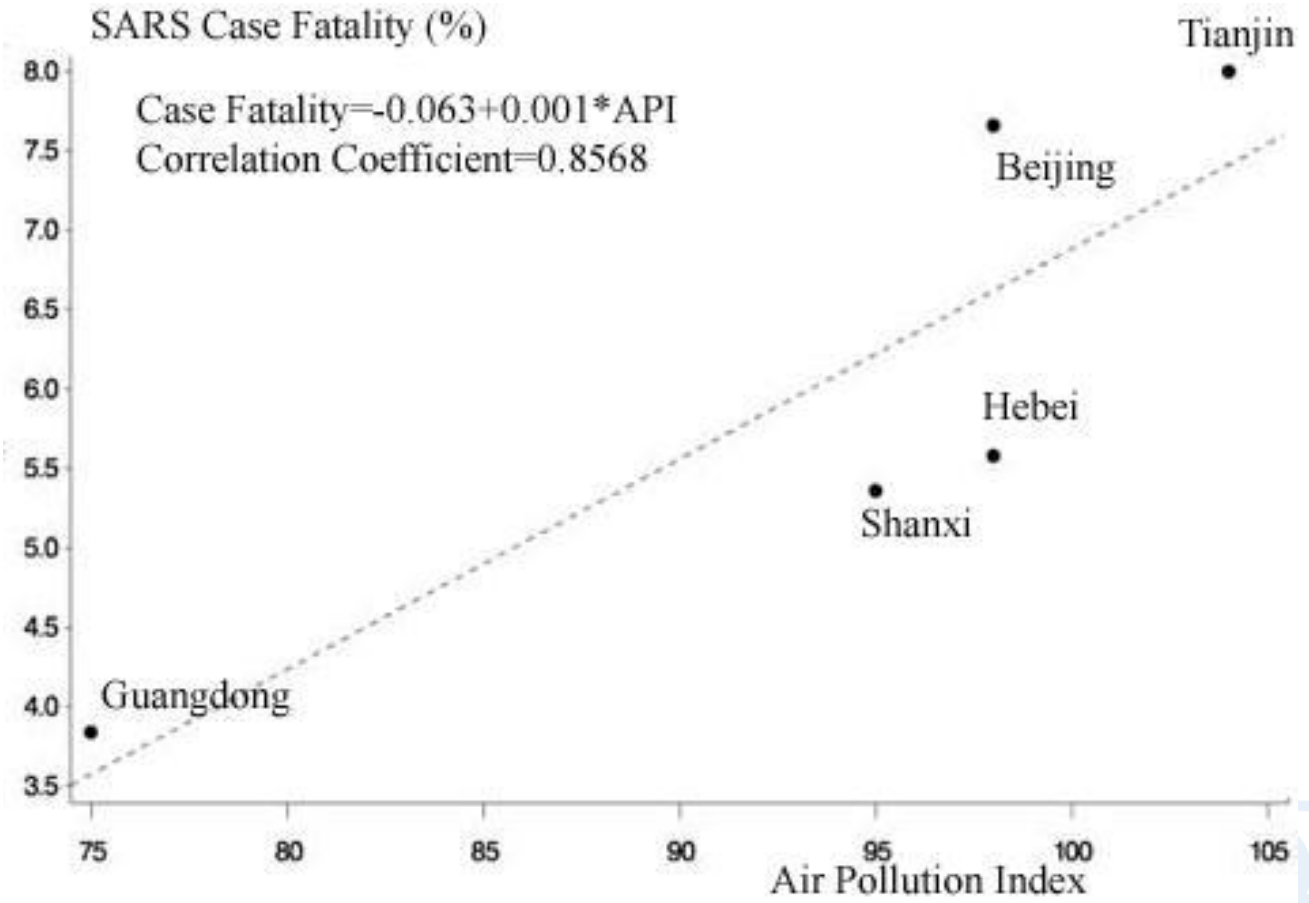
*Biggest effect in children < 5

Davis JL, Checkley W. Characterization of Air Pollution Exposures as Risk Factors for Tuberculosis Infection. Am J Respir Crit Care Med. 2021 Nov 15;204(10):1130-1131.

Air Pollution and Respiratory Viral Pandemics

SARS and Air Pollution Exposure

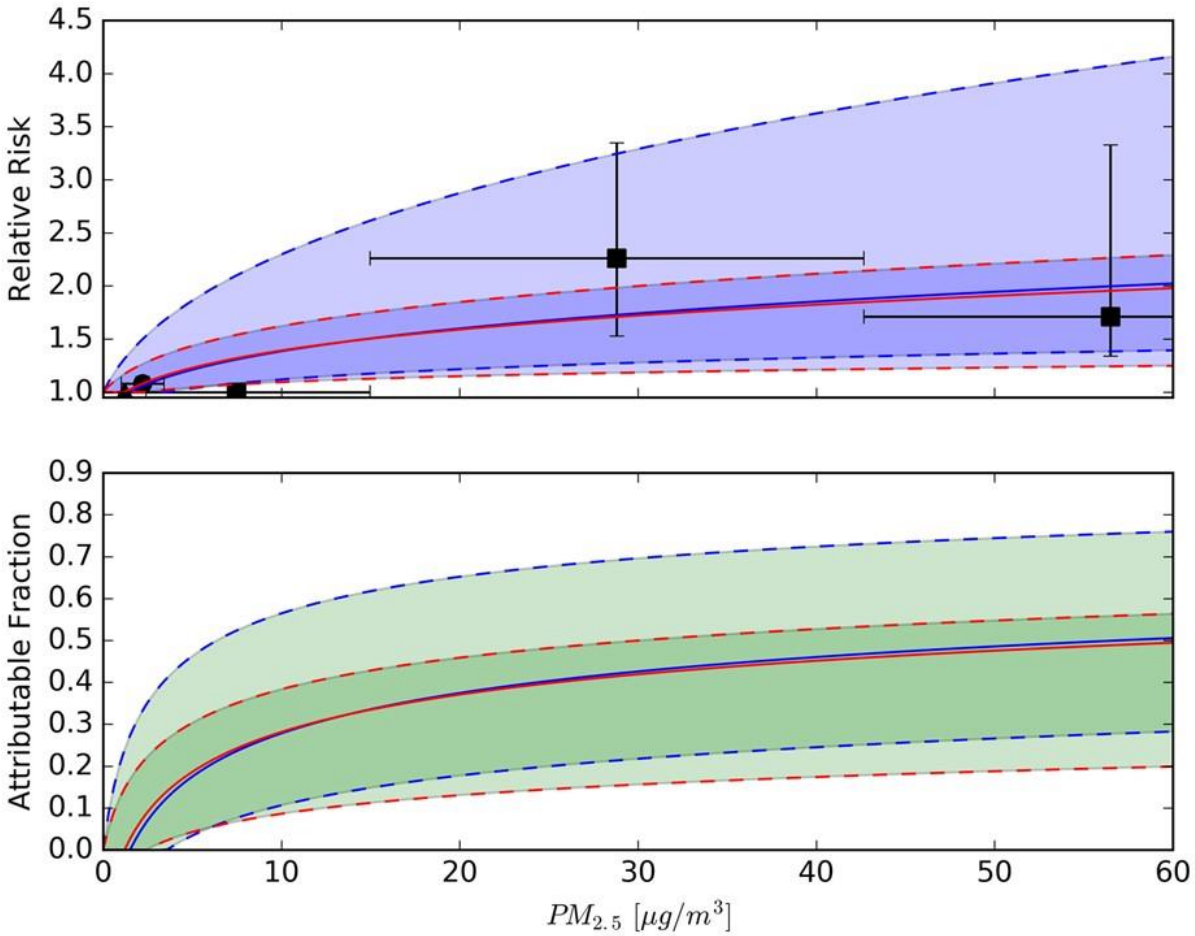
- Studies from original SARS pandemic (2003) in China looking at the impact of air quality on mortality
- Examined association between short and long-term Air Pollution Index – composite from PM_{10}, SO_2, NO_2, Ozone(O_3) and CO
- SARS patient with higher short-term APIs were twice as likely to die from SARS (RR 2.18)
- The trend as association with long-term pollution was less clear



Cui Y, Zhang ZF, Froines J, et al. Air pollution and case fatality of SARS in the People's Republic of China: an ecologic study. *Environ Health*. 2003;2(1):15. Published 2003 Nov 20. doi:10.1186/1476-069X-2-15

Early Studies of COVID-19 and Air Pollution

- Associations between Air Pollution and COVID-19 still being established (most studies from 2020 pre-vaccine availability)
- Nationwide US study showed 11% (95% CI: 6% to 17%) increase in COVID-19 mortality with 1 µg/m^3 in long term air pollution (Wu et al)
  - Racial disparities may have had a bigger impact
- In second US study increases in $PM_{2.5}$ (7% increase), O_3 (2%), and Hazard Pollutant Index (9%) associated with increased COVID-19 mortality
- Similar Associations noted worldwide (Pozzer)



How Can Climate Change Impact Your Health?

Mental Health

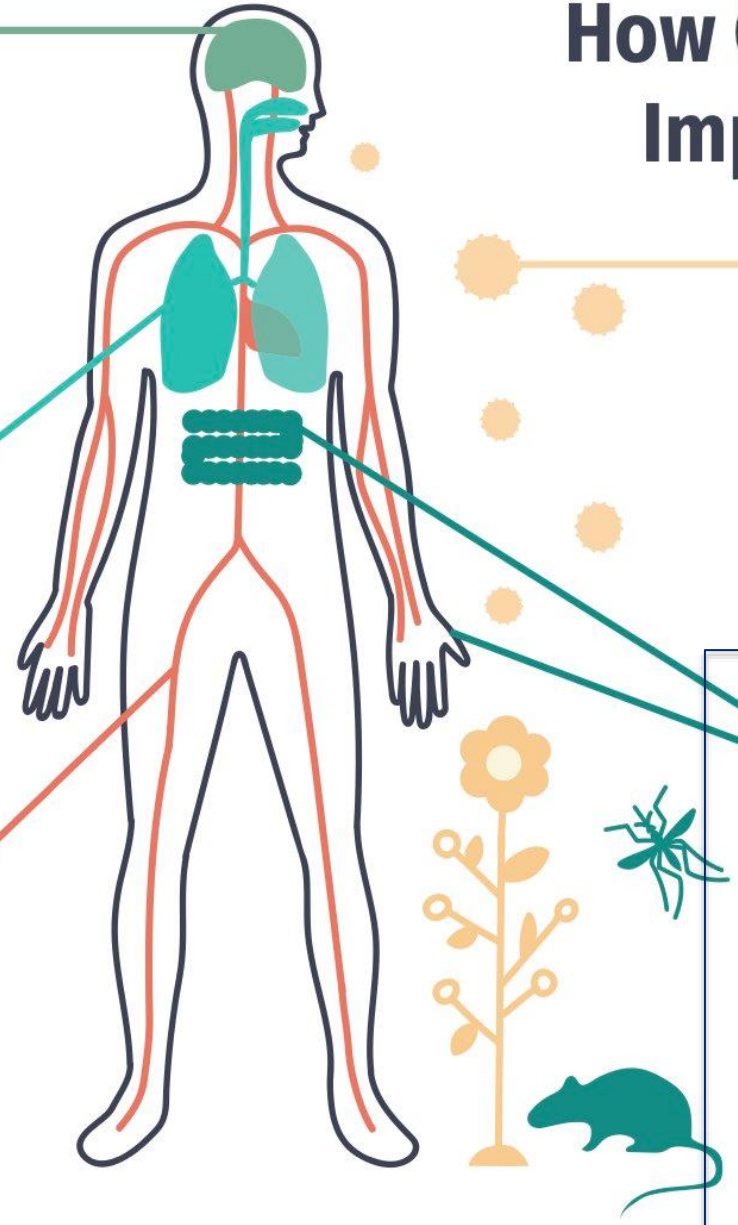
- Extreme heat can increase mood and behavioral disorders in people with mental illnesses and in elderly people.
- Major weather events (ex., floods, wildland fires) are linked with depression, anxiety, post-traumatic stress disorder (PTSD), and substance abuse.

Lungs

- Dust storms and wildfire smoke can increase inflammatory responses and exacerbate asthma.
- Air pollution can contribute to onset and exacerbation of asthma, allergic rhinitis, atopic dermatitis, and contact dermatitis.

Heart and Blood

- Air pollution exposure is linked to heart and blood vessel problems such as high blood pressure, heart attacks, cardiac arrhythmias, and ischemic stroke.
- Air pollution exposure early in life can increase risk for harmful cardiopulmonary effects in childhood.



Immunity and Allergy

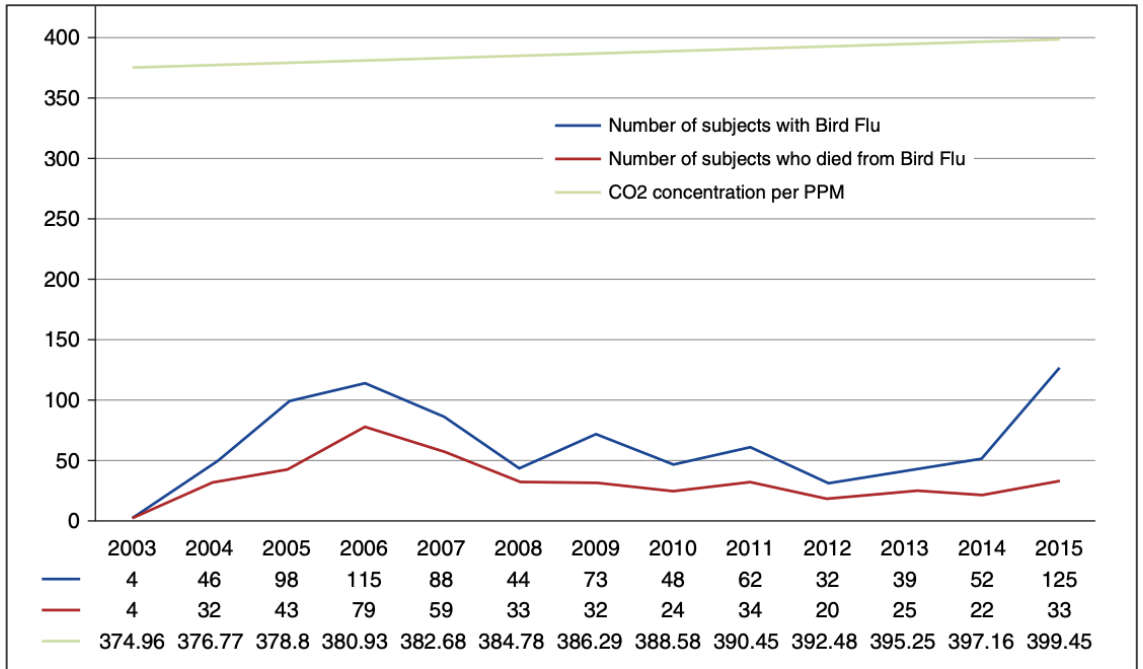
- Greenhouse gases increase pollen levels and spread.
- Inhaling air pollutants may allow for allergen particles to get into your airways more easily.
- Poor air quality can increase your susceptibility to respiratory infections.

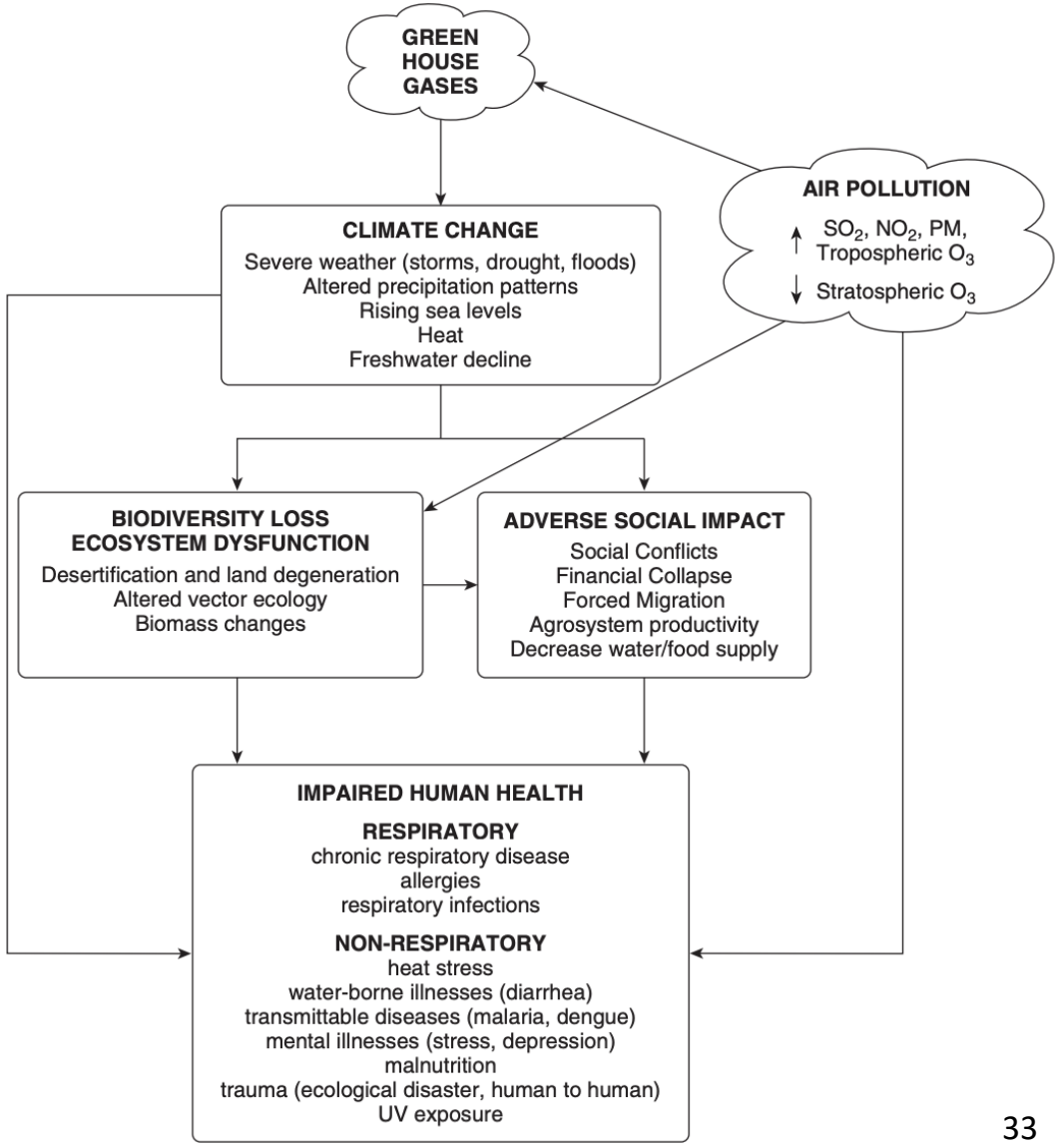
Germs and Spread of Infection

- Longer warm seasons allow for more disease from infections spread by insects (ex., West Nile virus) and rodents (ex., leptospirosis).
- Heavy rains and storm runoff increase the spread of waterborne pathogens (ex. Cholera, Cryptosporidium), which can contaminate water and lead to intestinal problems such as diarrhea.

Climate Change May Impact Future Risk

- Changes in Temperature, Precipitation, Humidity, and Air Pollution influence viral activity and transmission
- Modeling Studies Suggest Changes in Temperature and Humidity Increase Risk for Influenza and Other Viral Pandemic Outbreaks
- Changes in temperature may increase risk from other pathogens (i.e fungal) due to inhalational exposure and changing ecosystem





Take Home Points

- Both Household and Ambient Air Pollution Associated with Increased Risk from Respiratory Infections
- Air pollution contributes to a significant burden of infection and mortality in younger children worldwide
- Many studies thus far have focused on $PM_{2.5}$. Future studies should consider multi-pollutant models
- More data needed on the risk of indoor air pollution in adults and in high income countries
- Strategies are needed for sustained improvements in both household and ambient air pollution in order to reduce risk from infectious pathogens.
- Ongoing work is being done to understand the link between air pollution, viral pandemics, and climate change