

Ambient Air Pollution - Respiratory Effects & Asthma in Children

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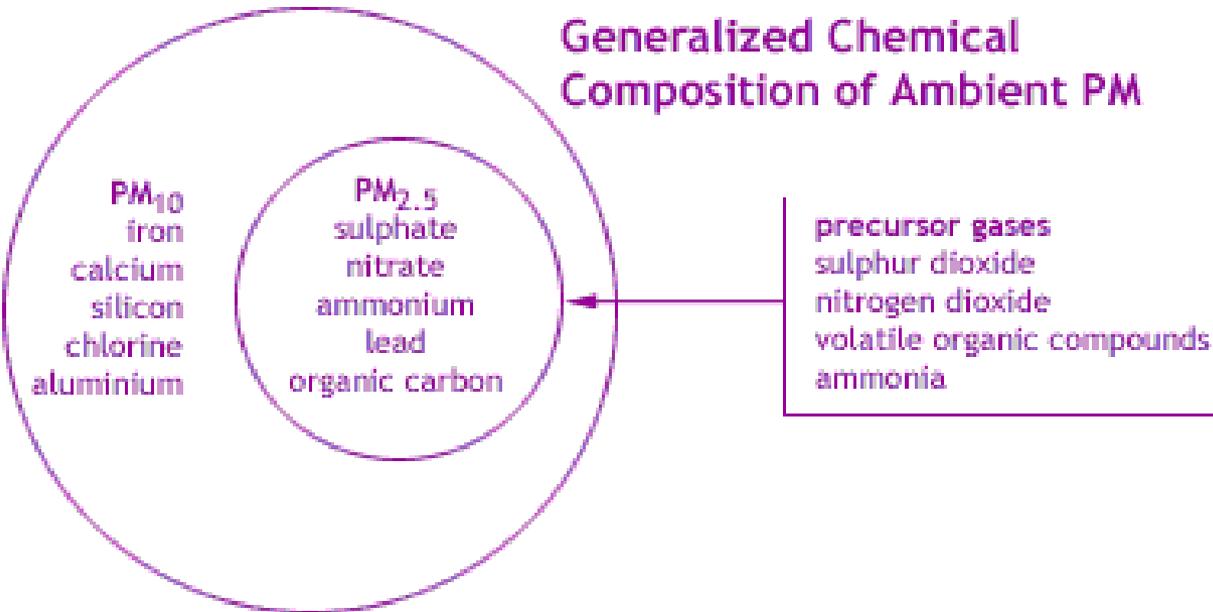
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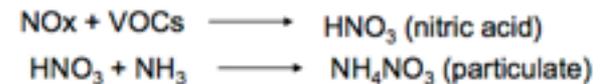
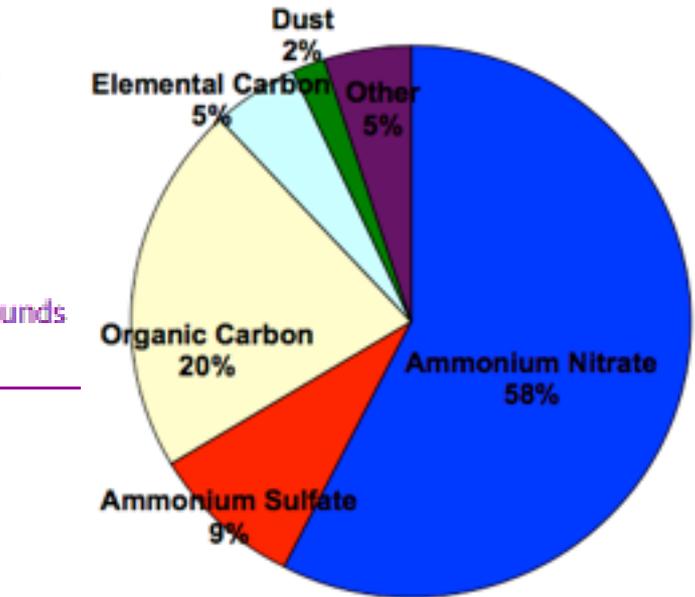
*Institute for
Exposomics Research*

Particulate air pollution – PM_{2.5} and nitrates

Generalized Chemical Composition of Ambient PM



PM_{2.5} Speciation



PM = particulate matter
 PM₁₀ = particulate matter < 10 µg/m³ in aerodynamic diameter
 PM_{2.5} = particulate matter < 2.5 µg/m³ in aerodynamic diameter
 NO_x = nitrogen oxides
 VOCs = volatile organic compounds



University of Utah,
 Atmospheric Sciences Dept

Criteria Pollutants

- ▶ Research on air pollution (AP) and early life respiratory outcomes has largely considered criteria pollutants
 - pollutants routinely monitored to assess air quality:
 - particulate matter with a diameter of 10 to 2.5 micrometers (μms) (PM_{10})
 - fine particles $\leq 2.5 \mu\text{ms}$ ($\text{PM}_{2.5}$)
 - ambient nitrogen dioxide (NO_2) or nitrates (NO_3)

Chronic Obstructive Pulmonary Disease (COPD) - When does this story begin?



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Chronic Obstructive Pulmonary Disease (COPD) - When does this story begin?



Human fetus is uniquely vulnerable

- ▶ Gestation is period of rapid lung growth and maturation, particularly sensitive to insult
- ▶ Prenatal pollutant exposures linked to early childhood wheeze, asthma, deficits in lung function



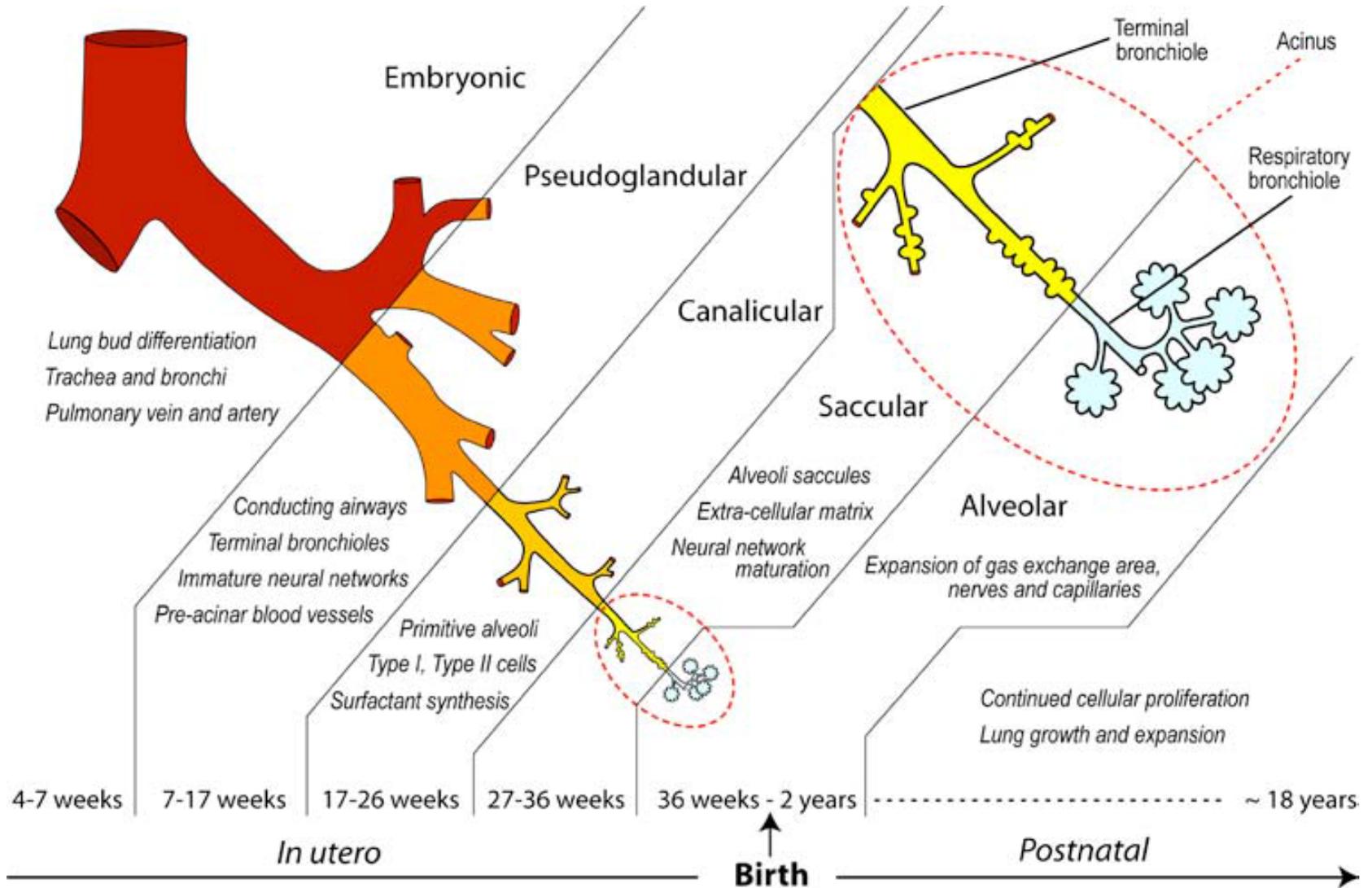
Who's most affected by **poor air quality?**

- ▶ People who have:
 - Asthma
 - Heart disease
 - COPD (a long-term lung disease)

The infographic features silhouettes of a family (a child, a woman, a man, and another man) and a pregnant woman, set against a city skyline. The pregnant woman is highlighted with a pink border.

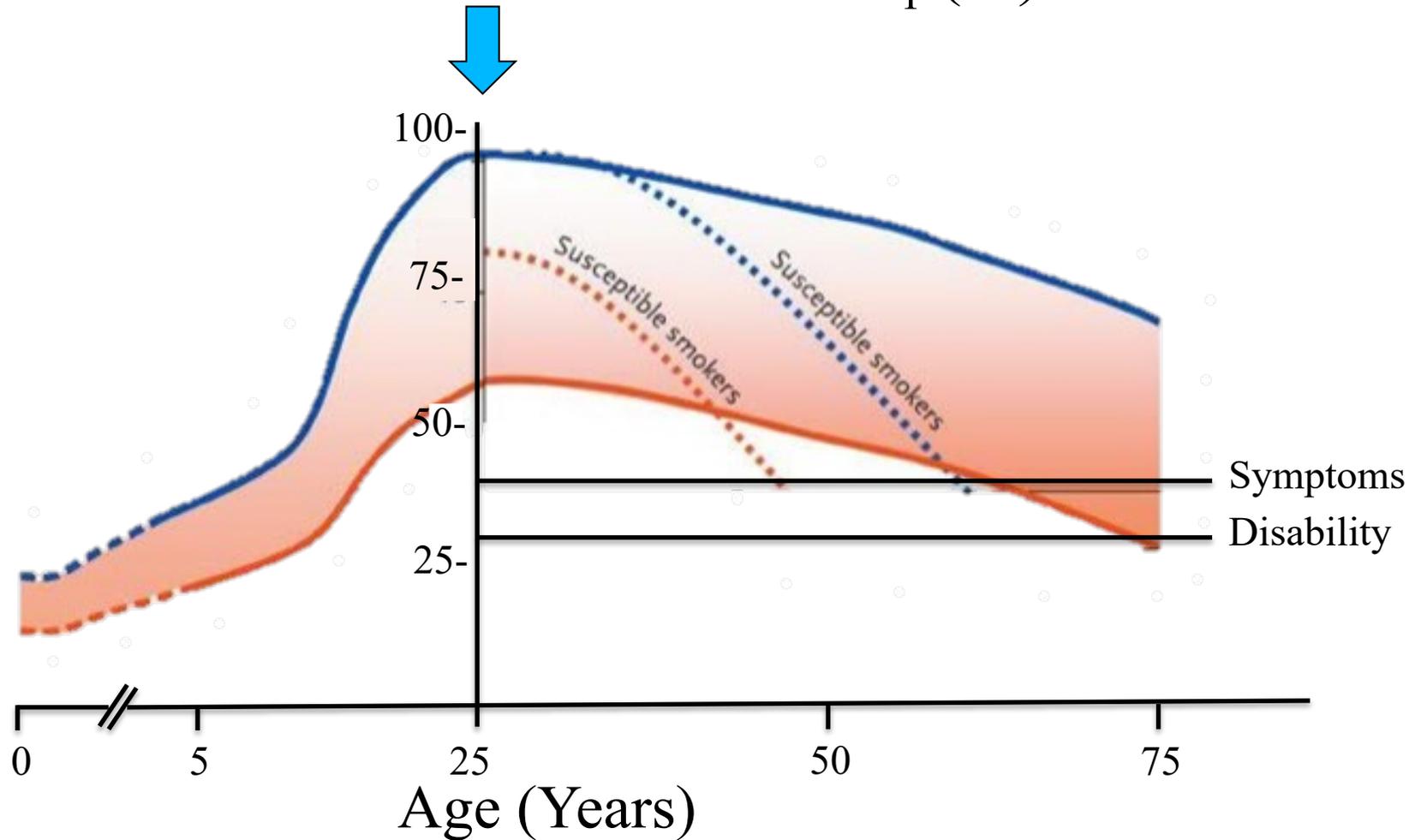
 Centers for Disease Control and Prevention
National Center for Environmental Health

Critical Windows – Pregnancy and Early Life



Kajekar R. Pharmacol Therapy 2007; 114:129-145

MAXIMAL LEVEL OF FEV₁ (%)



Lung function (FEV₁) over the life course

Lung function “tracks” throughout childhood, therefore impaired early life lung function results in reduced maximally attainable FEV₁, a strong risk factor for the development of subsequent respiratory disease such as COPD, early mortality, etc.

Life Course Epidemiology – Key Concepts

- ▶ Study of long term effects on later health/disease risk of physical, chemical, or social exposures during gestation, childhood, adolescence, young adulthood, and later adult life

- ▶ Premise that various biological and social factors throughout life independently, cumulatively, and interactively influence health and disease in later life

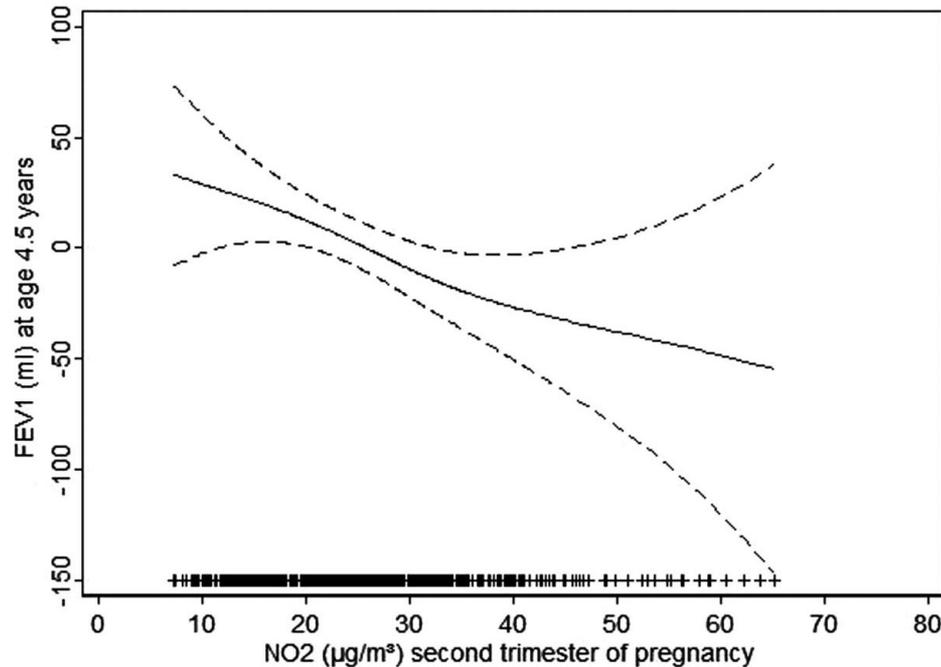
- ▶ Critical/sensitive periods
 - Focus on importance of timing of exposure(s)

Kuh D, Ben-Shlomo Y, et al., *JECH* 2003

Ben-Shlomo Y, Kuh D. *Int J Epidemiol* 2002

Blane D, Netuveil G, Stone J. *Rev Epidemiol Sante Publique* 2007

Traffic pollution during pregnancy and child lung function (INMA)

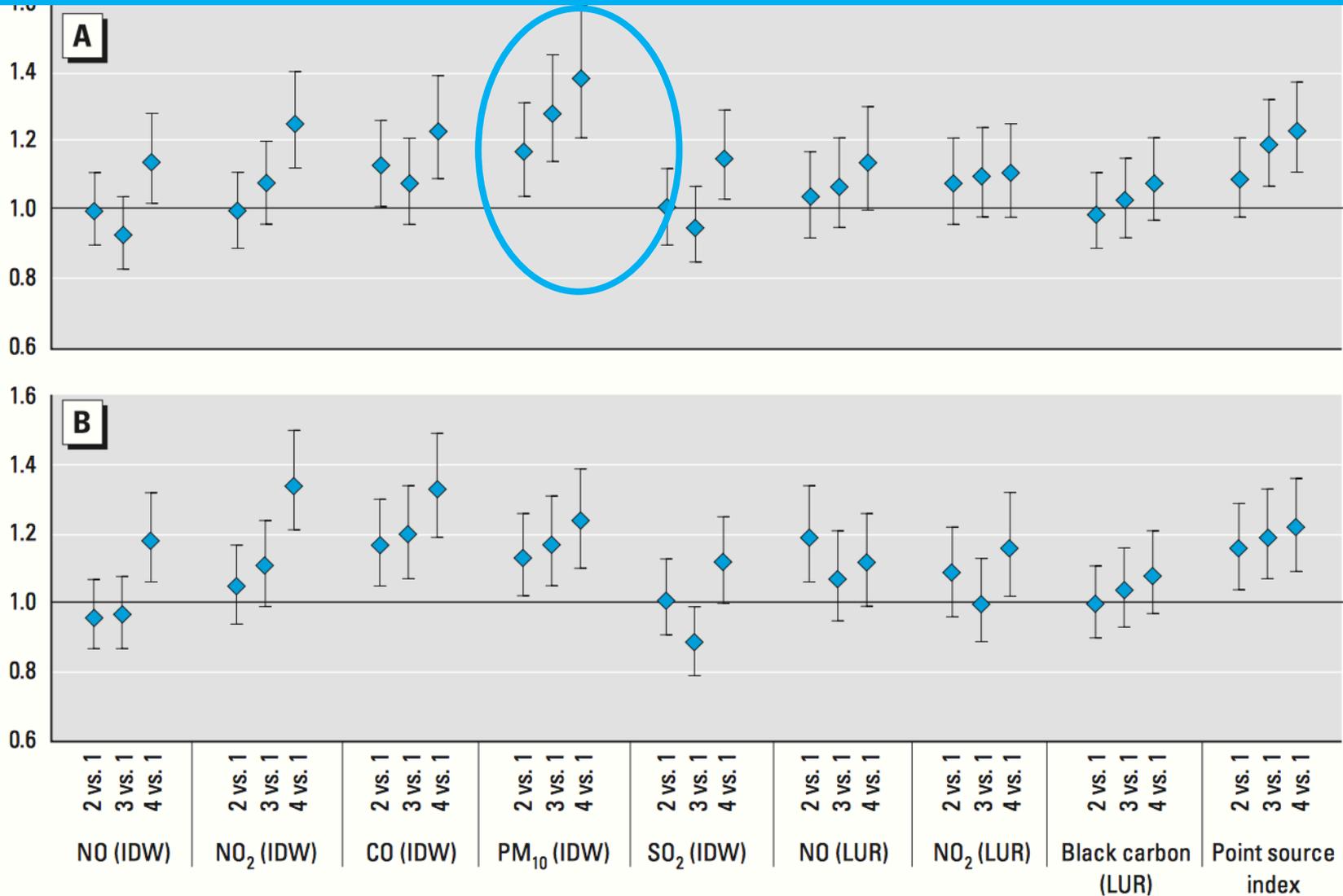


NO₂

Relative risk (RR) of low lung function (<80% of predicted FEV₁) for an IQR increase during second trimester: 1.30 (0.97 to 1.76)

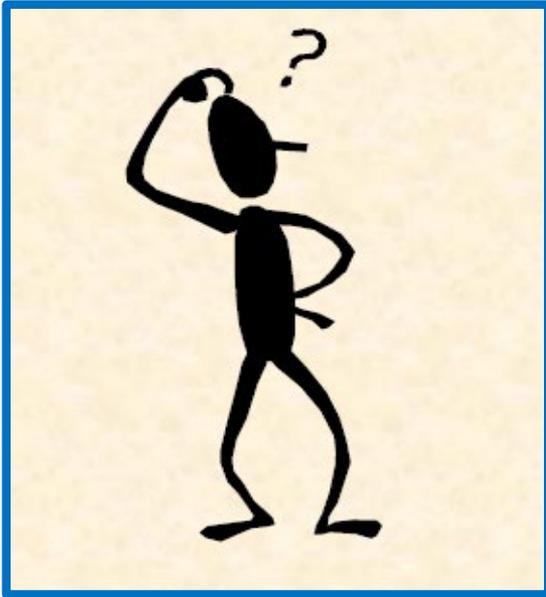
Perinatal air pollution exposures and asthma in preschoolers

Clark et al. *EHP* 2010



Important

Ambient Pollutant



Timing?



Asthma Coalition on Community, Environment & Social Stress (ACCESS)

**Air
Pollution**

Stress

Allergens

**Tobacco
Smoke**



Diet

NIEHS, NHLBI, NIMH, NIMHD,
Leaves of Grass Foundation

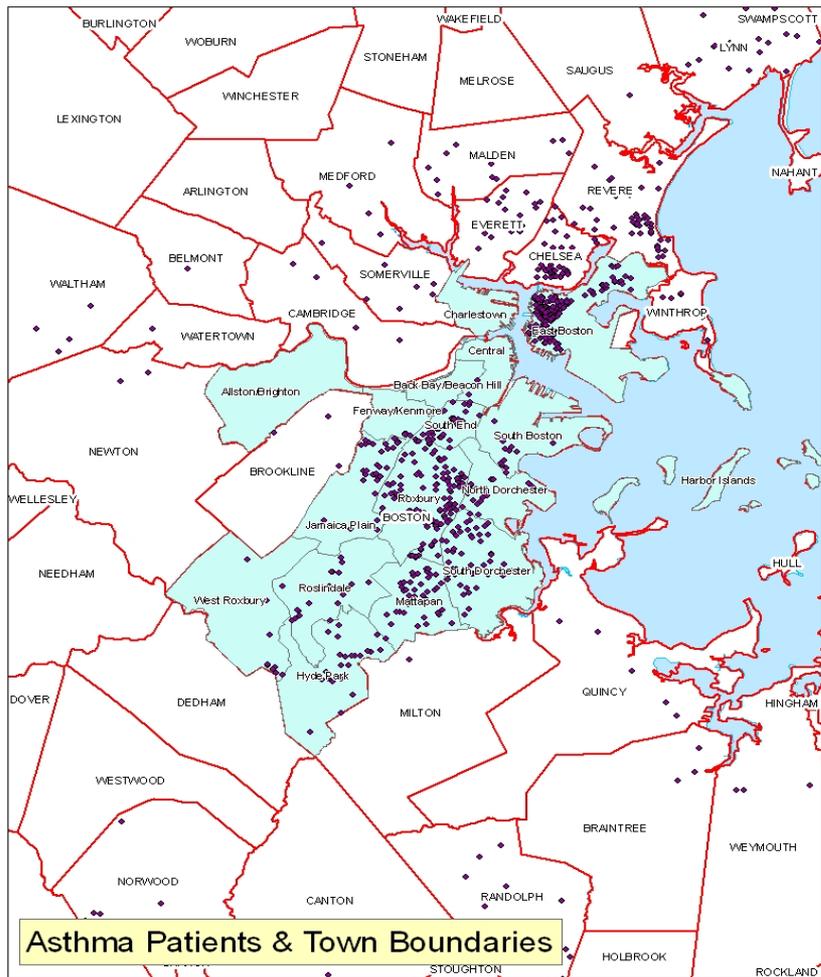
Lung Function Development
Childhood Asthma Risk



Asthma Coalition on Community, Environment and Social Stress (ACCESS)

Pregnant women ≥ 18 years recruited from Brigham and Women's Hospital, Boston Medical Center, and affiliated community health centers

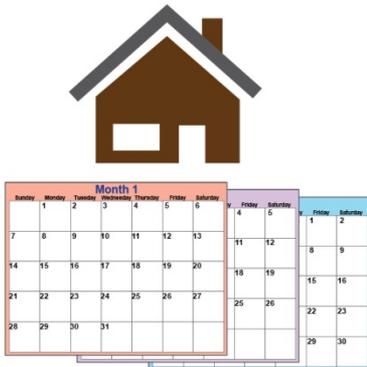
- 989 women enrolled
- Average 28.4 (7.9) weeks gestation
- 955 live singleton births
- N= 752 entered analysis with complete environmental and health data



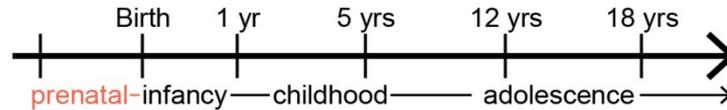
'Place-based' Exposures: Geomarker Data



1) Collect Addresses and Dates



2) Construct Individual Residential Timelines



3) Geocode Addresses (lat/lon coordinates)



4) Assign Exposures

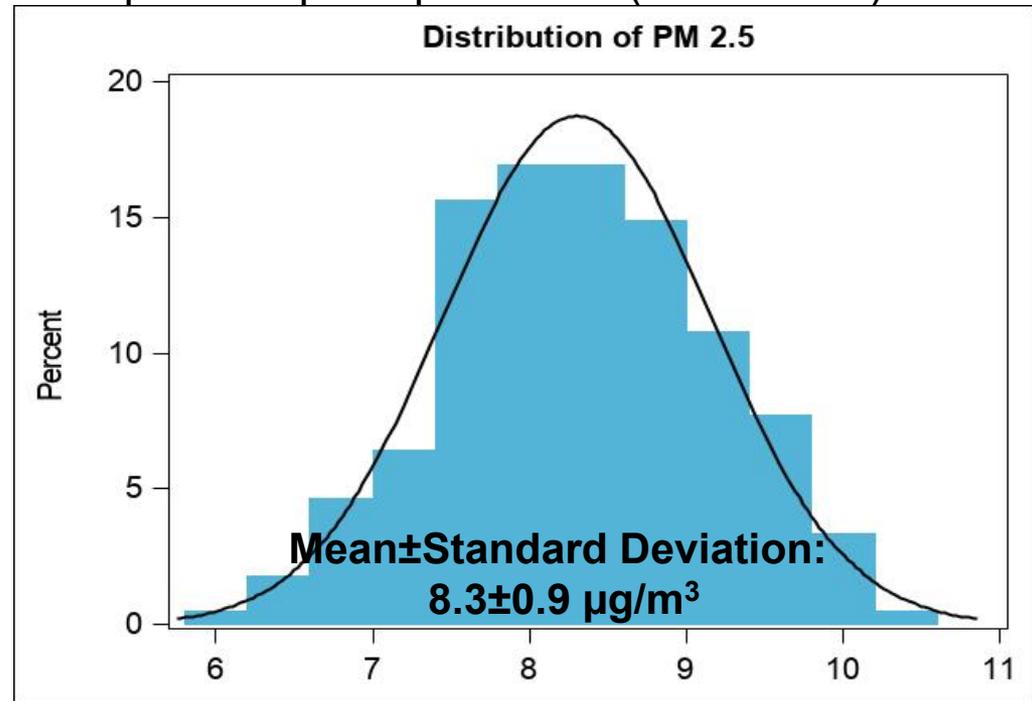
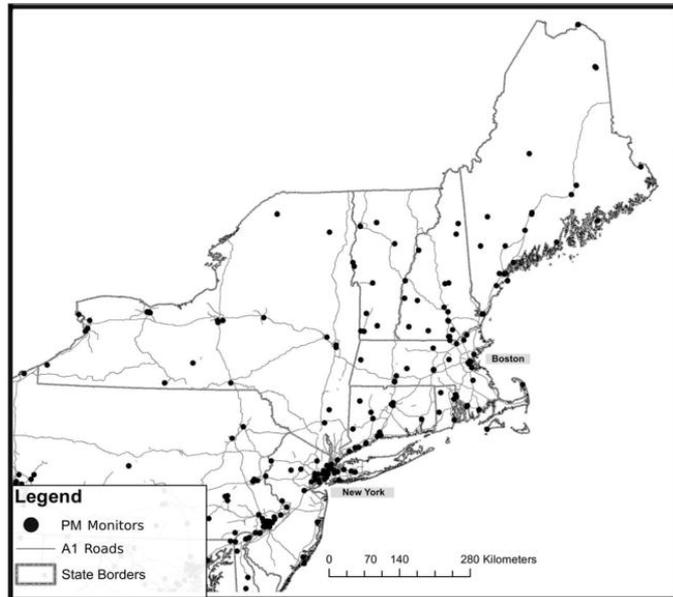
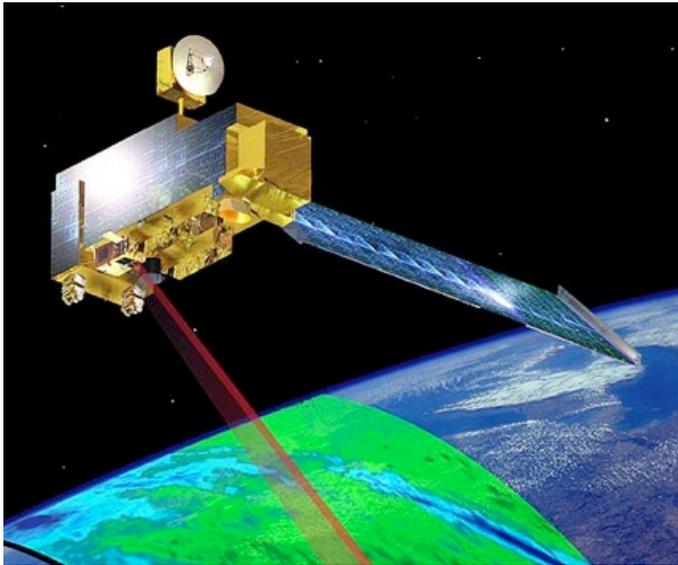


J Gregory ©2019 Mount Sinai Health System

Exposure Assessment

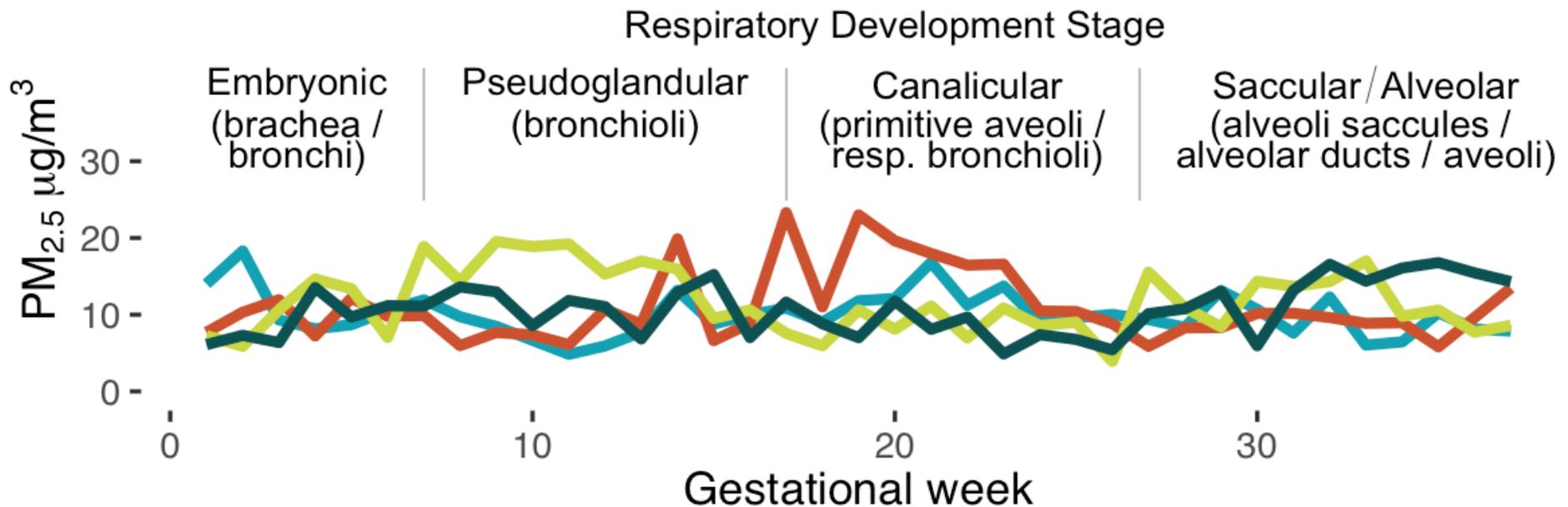
Daily PM_{2.5} exposure estimated for each study participant using a high-resolution satellite based hybrid model:

- Aerosol optical depth (AOD) from Moderate Resolution Imaging Spectroradiometer (MODIS) satellite sensor (1x1 km)
- PM_{2.5} monitoring data (EPA & IMPROVE)
- Spatiotemporal predictors (200x200 m)



Critical/Sensitive Windows

Wilson A, et al., Potential for bias when estimating critical windows for air pollution in children's health. *A J Epidemiol* 2017

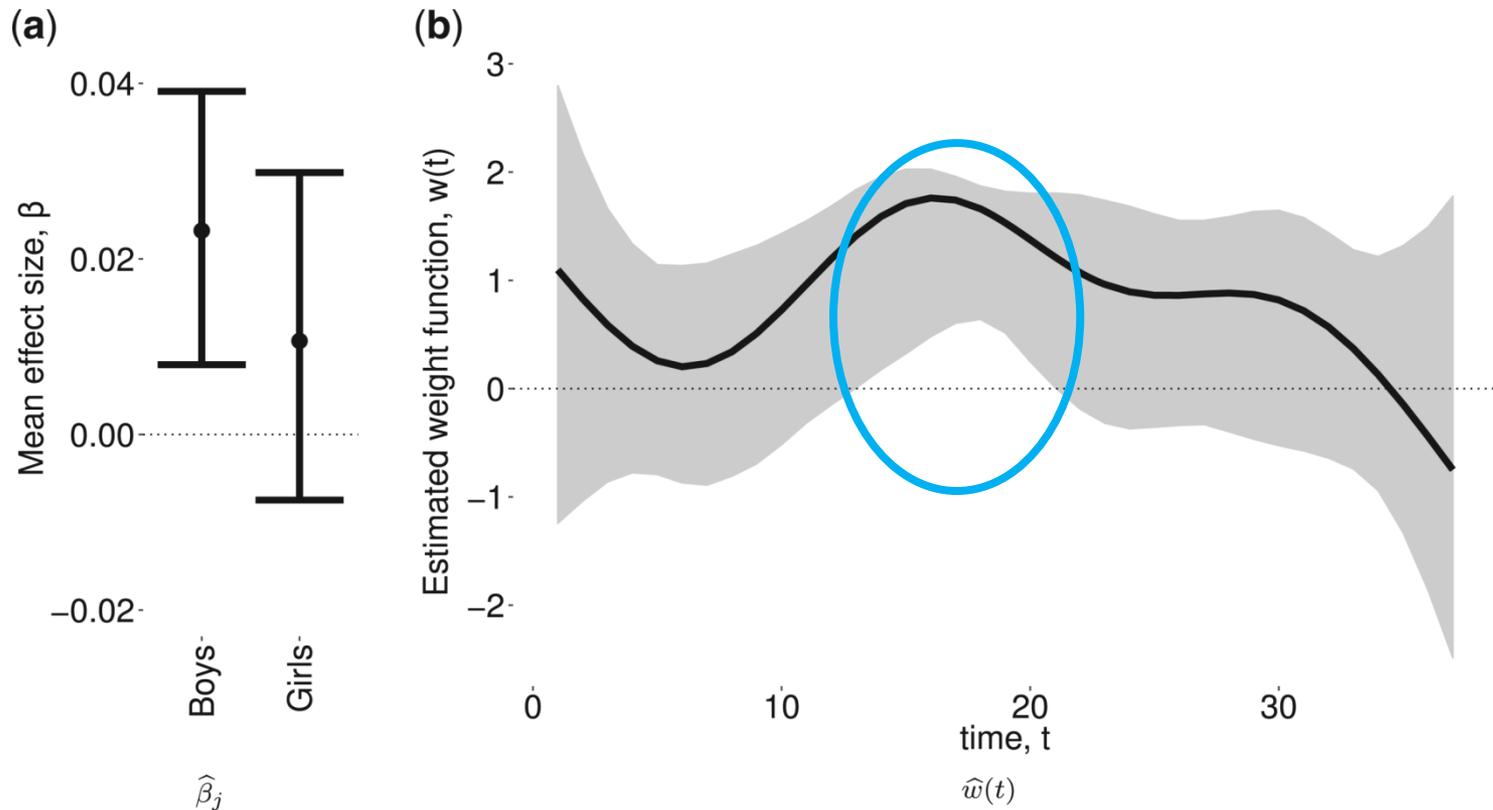


DLMs and BDLIMs and Sensitive Windows

Wilson A, et al., *Biostatistics* 2017

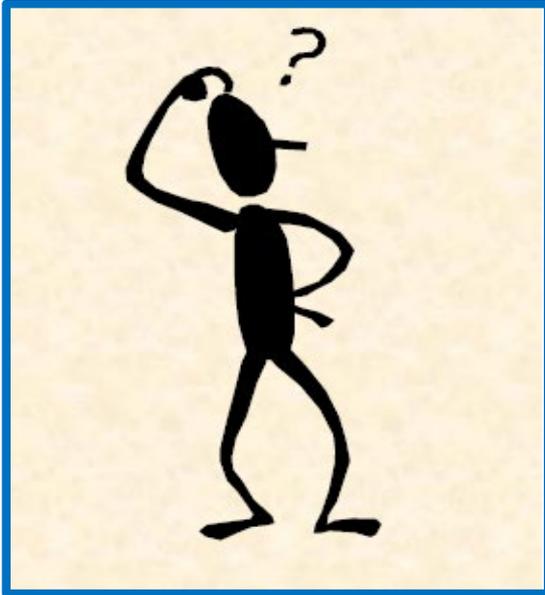
- ▶ Air pollution – can be highly temporally resolved (daily, weekly)
 - Distributed lag model (DLM) - like doing a regression for each day then plotting the change in the betas over time
 - Accounts for correlation between measures close in time
 - Data driven approach rather than using arbitrarily defined trimesters, etc
 - Bayesian distributed lag interaction models (BDLIMs)
 - » Additionally accounts for effect modification

Identifying perinatal windows of vulnerability to $PM_{2.5}$ in children's asthma risk

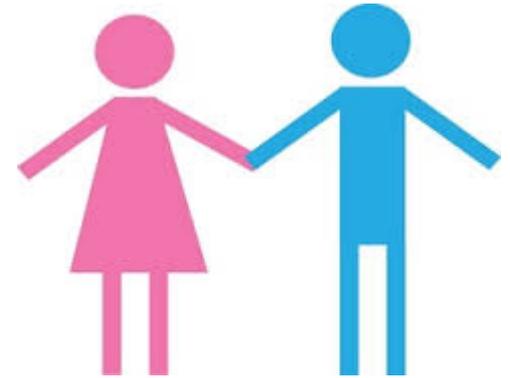


Important

Ambient Pollutant



Sex/Gender?

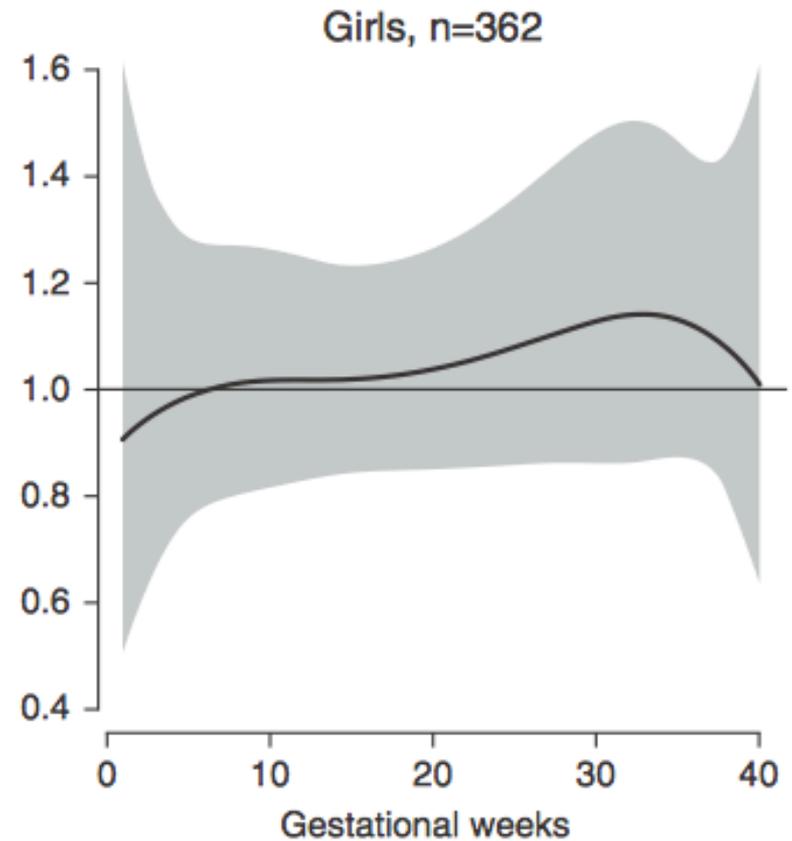
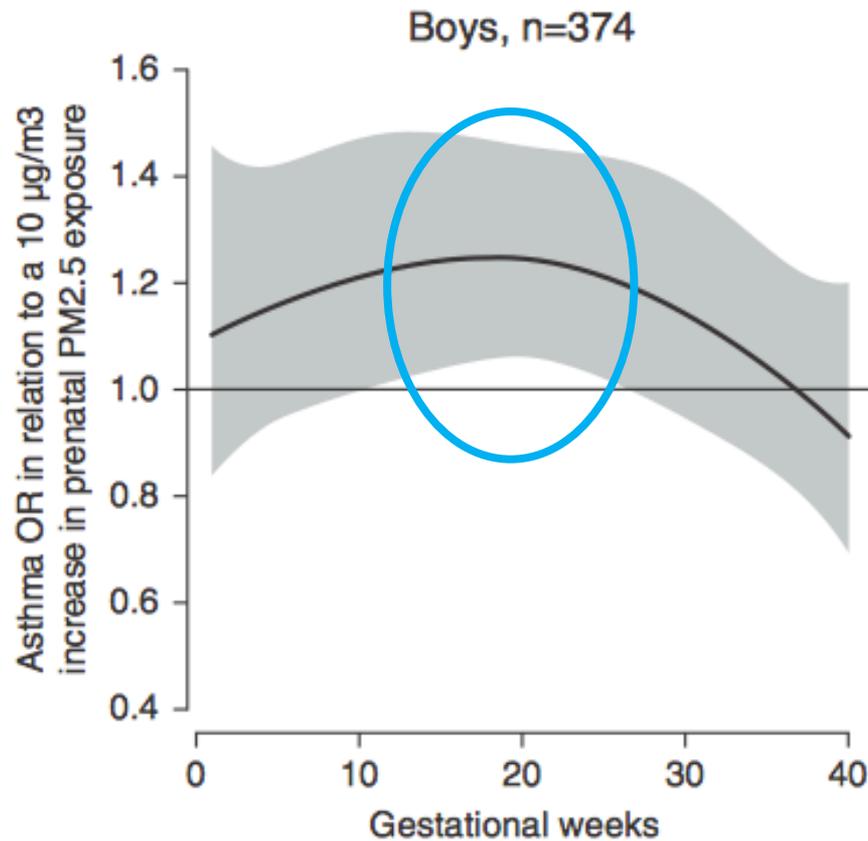
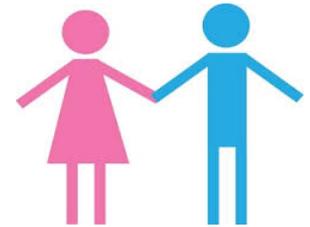


Timing?

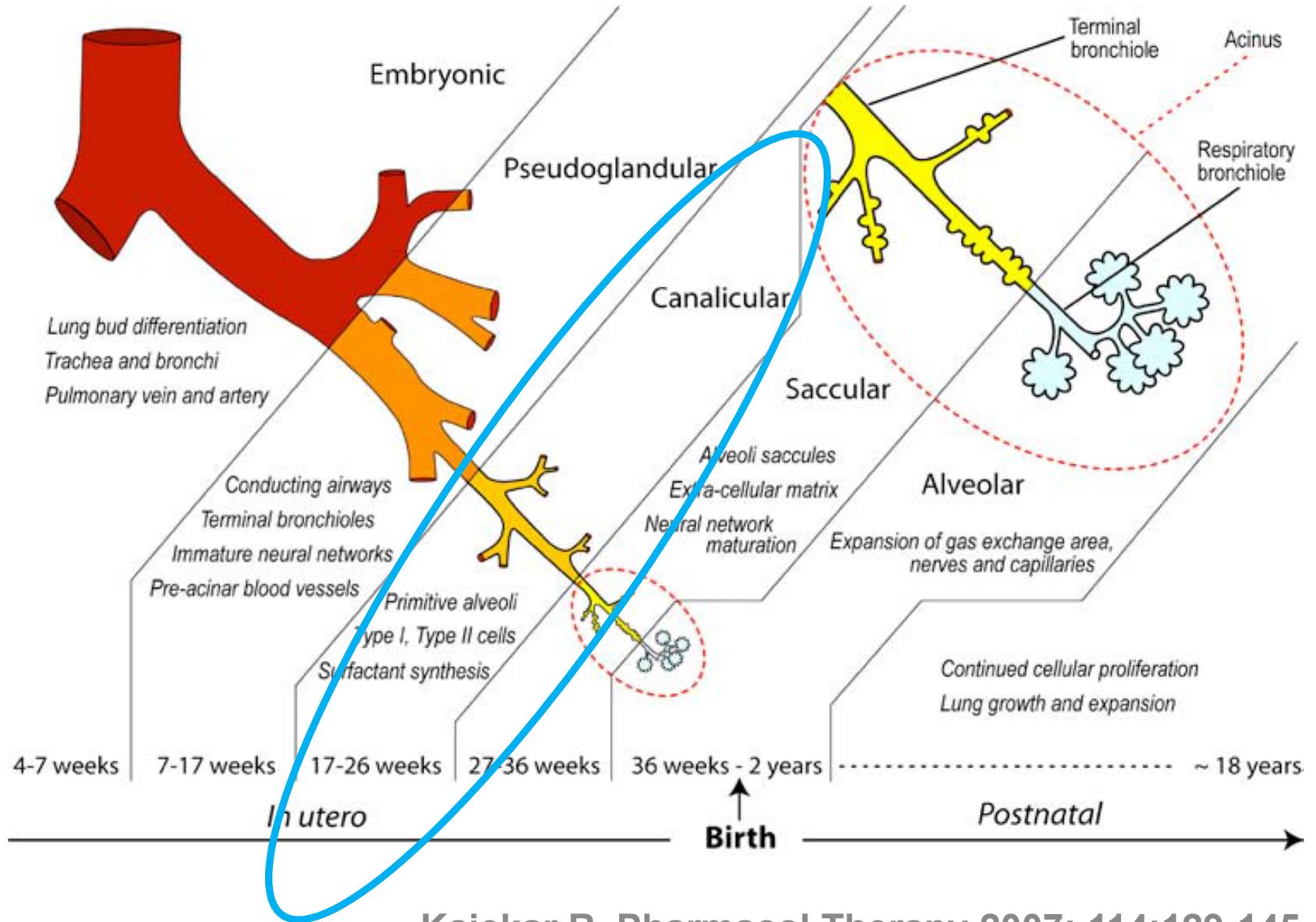


Prenatal PM_{2.5} and Asthma Onset by Age 6

Hsu et al. *AJRCCM* 2015; 192(9): 1052-1059

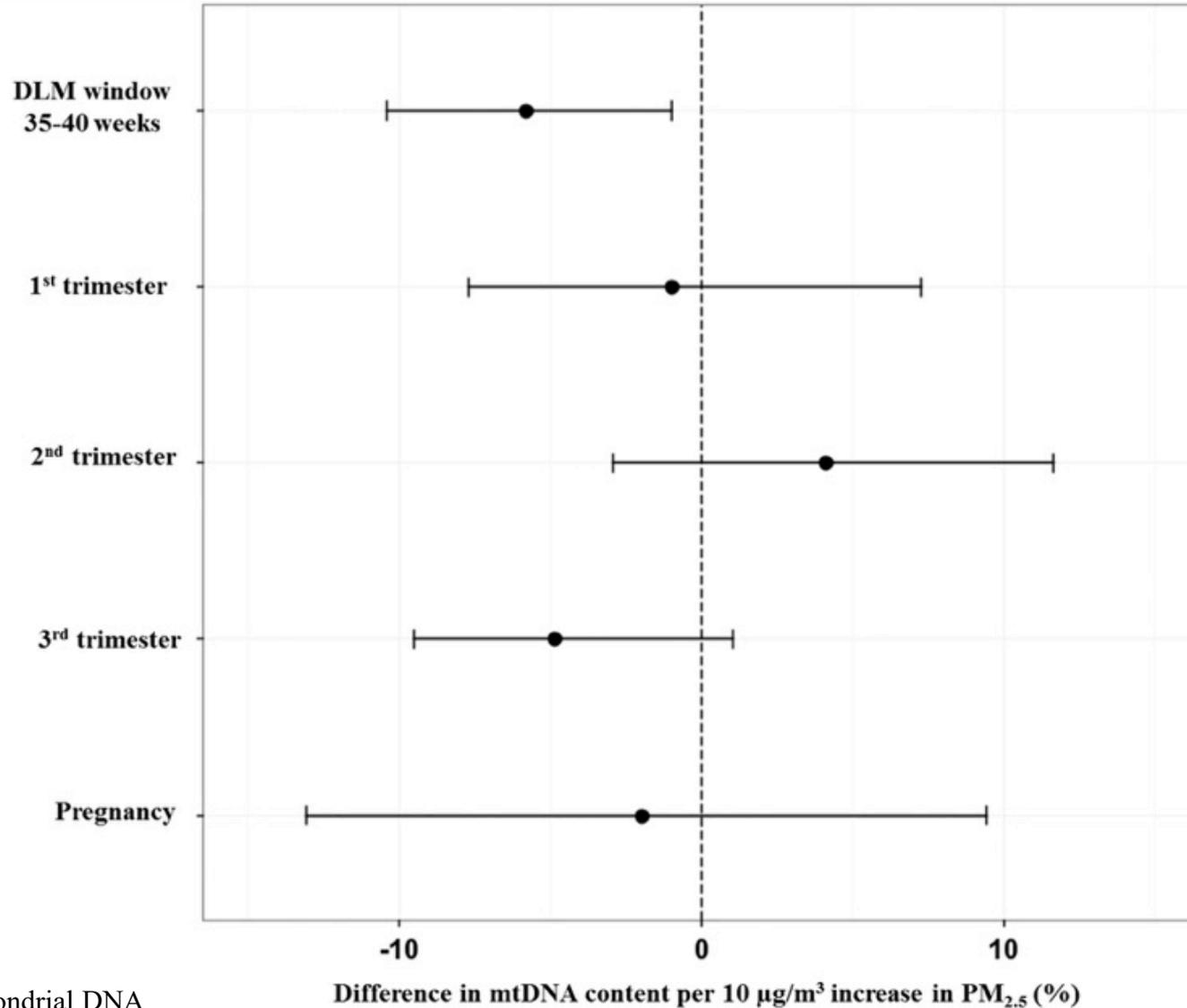


Critical Windows – Pregnancy and Early Life



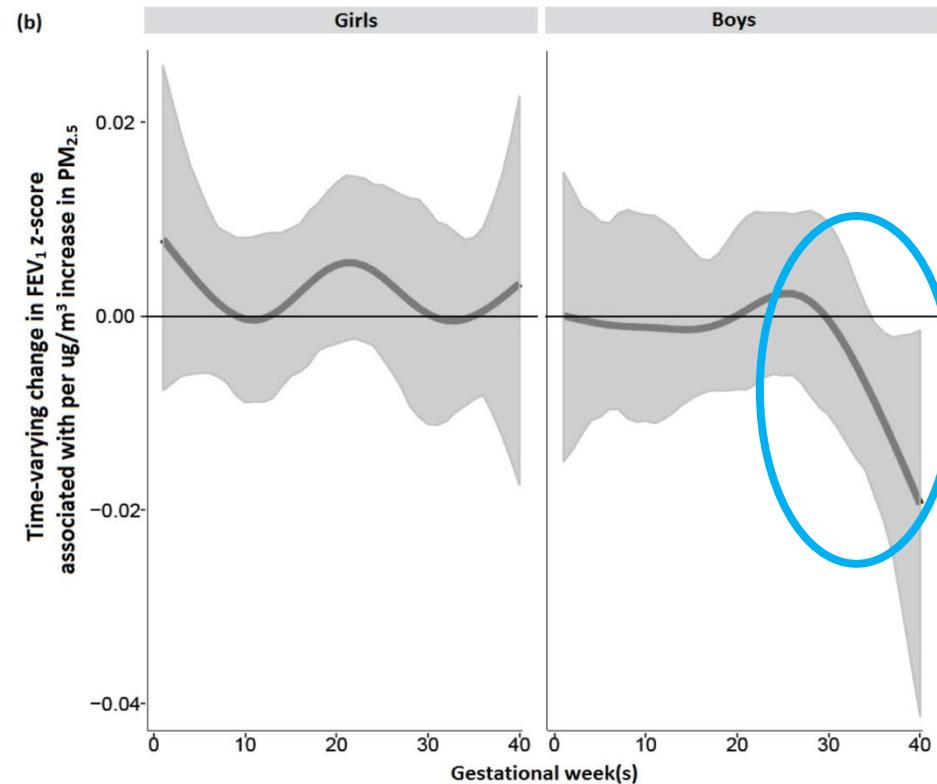
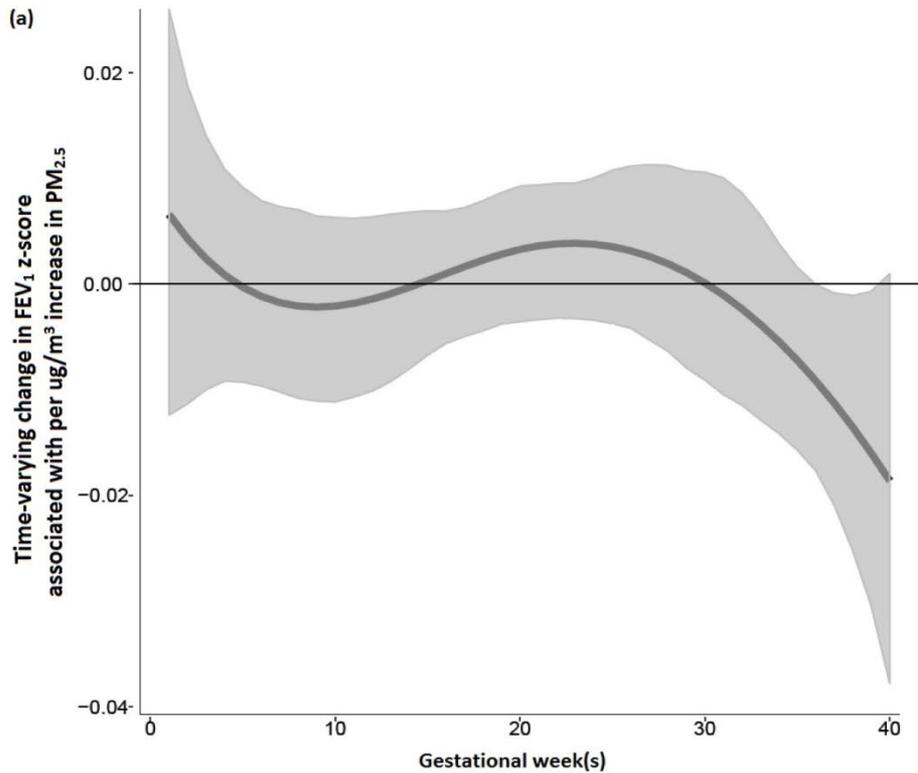
Pregnancy or trimester-averaged exposure estimates may miss significant relationships

Wilson A, et al., *AJE* 2017

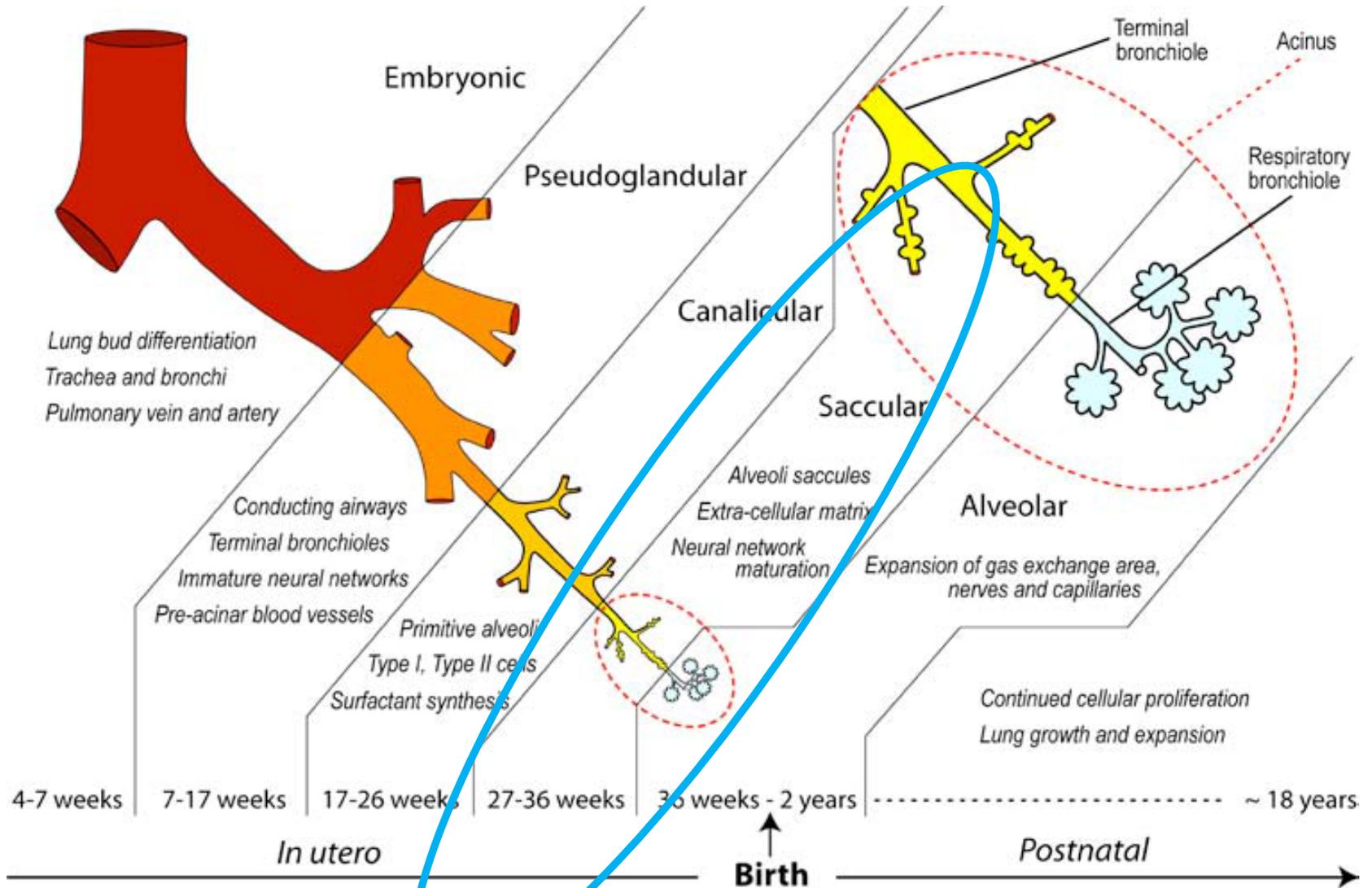


Prenatal PM_{2.5} and lung function age 7 yrs

Lee AG, et al., *Respir Res* 2018

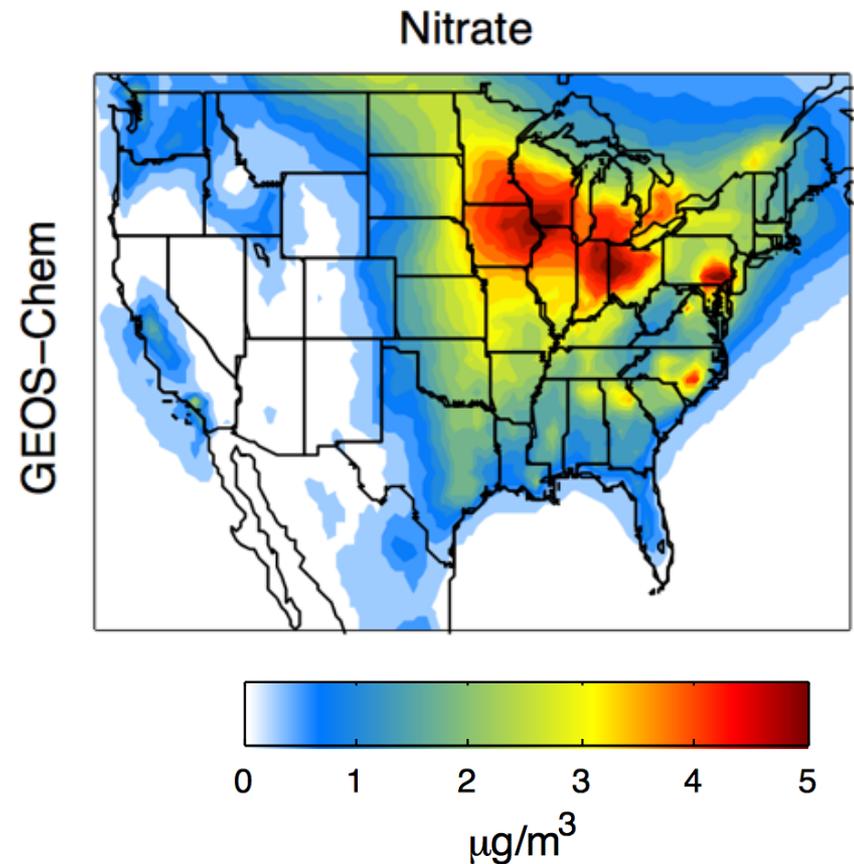


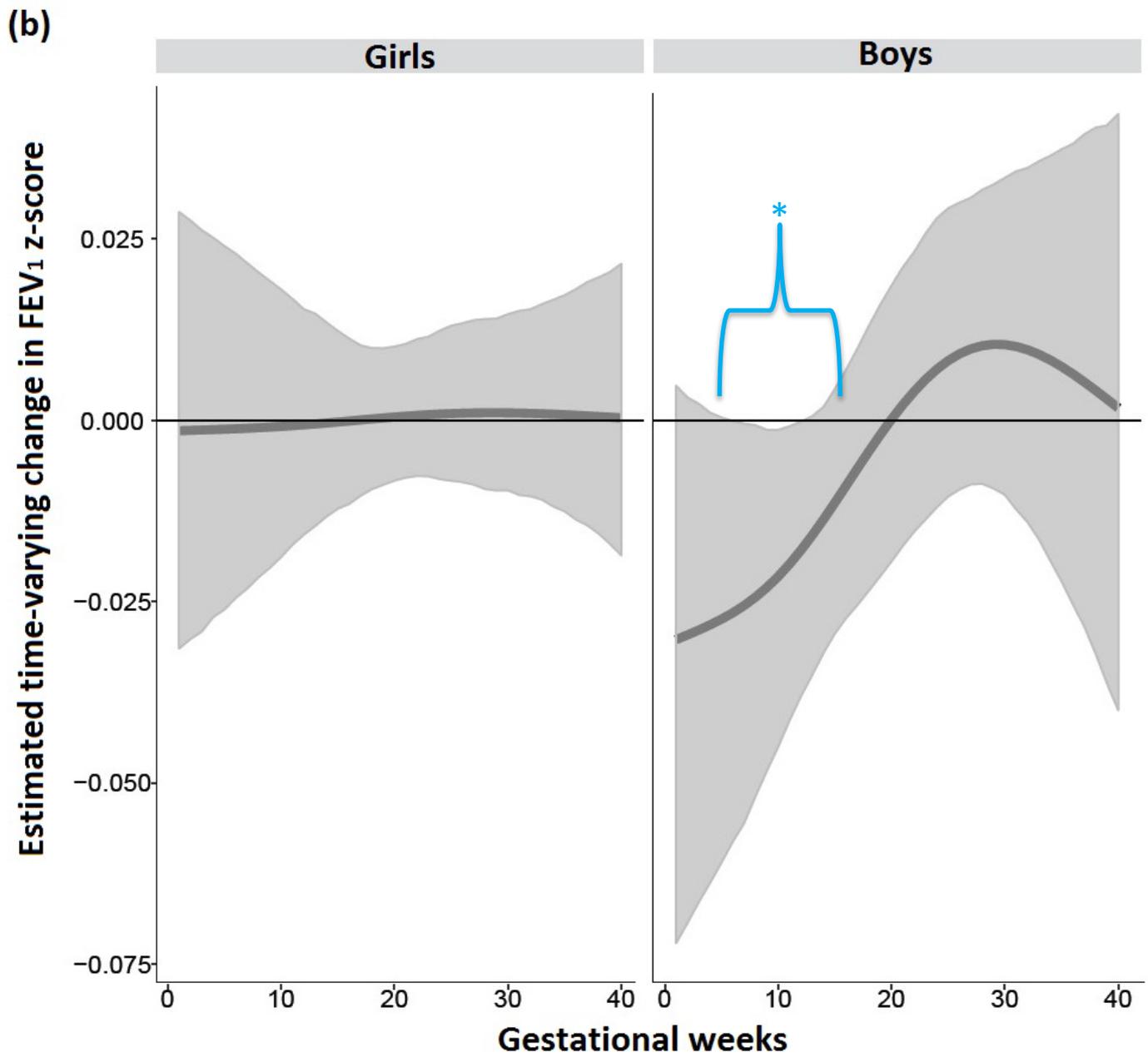
Critical Windows – Pregnancy and Early Life



Modeling of daily NO_3^-

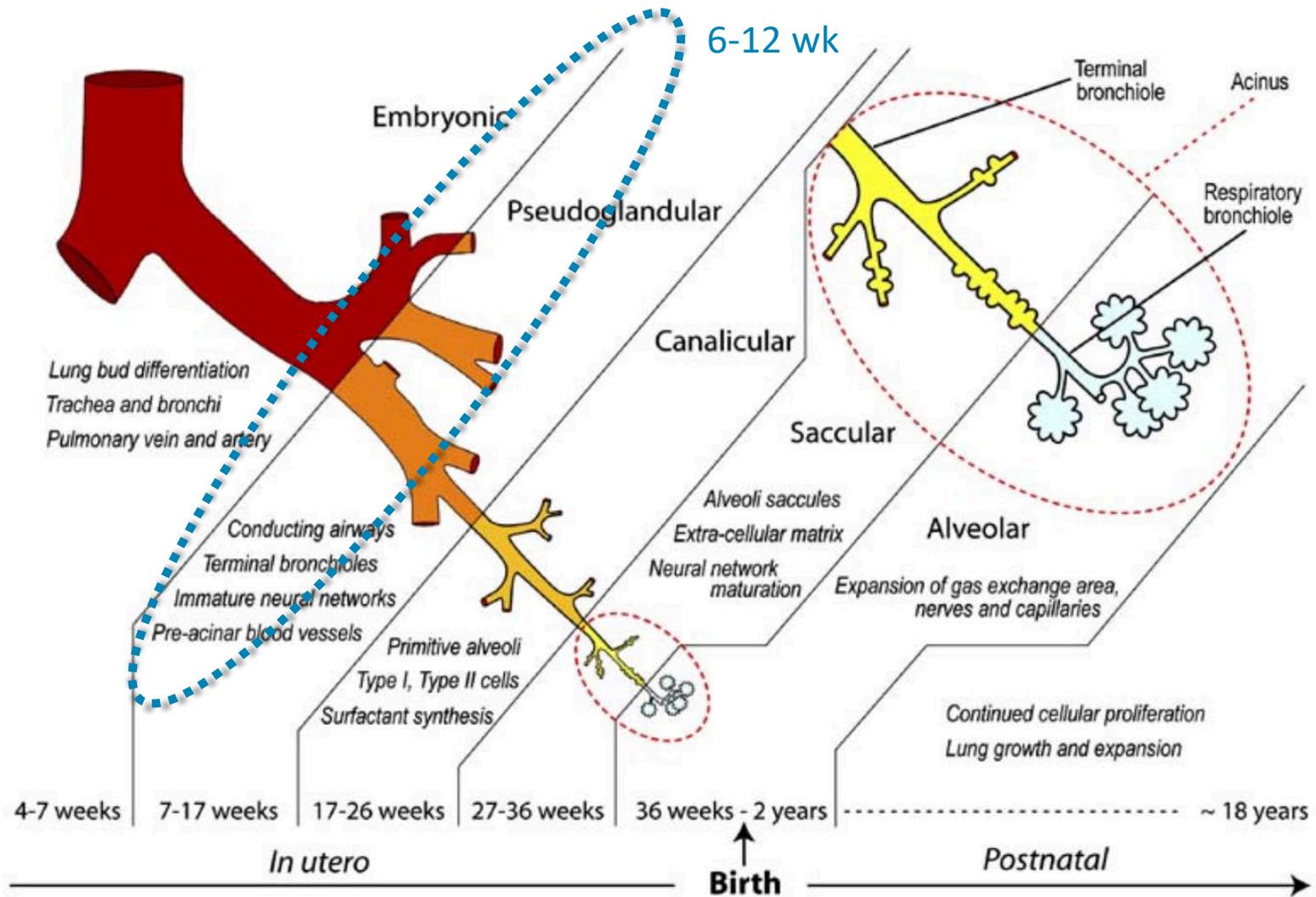
- ▶ Hybrid model consisted of:
 - Chemical transport model (GEOS-Chem) and
 - Land-use regression term
- ▶ 1 km x 1 km grid cell predictions
- ▶ Weekly averages used in analysis
- ▶ Median (25th-75th) prenatal NO_3^- $\mu\text{g}/\text{m}^3$: 23.1 (20.8-24.5)





Bose S et al. *Environ Res* 2018

Lung development occurs in stages



Sensitive windows

- ▶ Sensitive exposure windows can tell us something about biology
 - i.e. what is happening biologically in the critical/developmental window can inform us on the mechanism if we narrow in on the exposure window

Prenatal Ultra Fine Particles (UFPs) and asthma by age 6 yrs

Lavigne E, et al., *Am J Resp Crit Care Med* 2019

- ▶ While air quality regulations currently do not address UFPs ≤ 0.1 μms , sub-micron sized particles may exert greater toxic effects as compared with larger molecules due to their larger surface area/mass ratio, chemical composition, deeper lung penetration, and enhanced oxidative capacity and ability to translocate to the systemic circulation

- ▶ Workshop identified the lack of studies differentiating the effects associated with UFP exposures from effects related to other particle size fractions and gaseous co-pollutants as a significant gap in the evidence needed to move toward regulation of UFPs (Bauldauf RW, et al., *IJERPH* 2016)

Prenatal UFPs and asthma by age 6 yrs

Lavigne E, et al., *Am J Resp Crit Care Med* 2019

- ▶ First large-scale epidemiology study to demonstrate independent risk associated with *in utero* UFP exposure and asthma in children aged 6 yrs
- ▶ Retrospective analysis combined data from province-wide birth registry in Toronto & health administrative data identifying incident asthma in children
 - 160,641 singleton live births 2006-2012
 - 27,062 incident asthma diagnosis by age 6 yrs
- ▶ Assigned pollution exposure during each week gestation and each month of childhood at centroid of postal code (~city block)
- ▶ Land use regression (LUR) model explained 67% variation in UFPs
- ▶ Able to adjust for other components (PM_{2.5}, nitrogen dioxide)
- ▶ Used distributed lag function in a multi-level Cox proportional hazards framework to identify sensitive windows
- ▶ Higher UFP exposure in 2nd trimester remained positively associated with asthma incidence adjusted for other components



Funding

Co-investigators

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ECHO

