Particulate air pollution – PM$_{2.5}$ and nitrates

PM = particulate matter
PM$_{10}$ = particulate matter < 10 $\mu$g/m$^3$ in aerodynamic diameter
PM$_{2.5}$ = particulate matter < 2.5 $\mu$g/m$^3$ in aerodynamic diameter
NO$_x$ = nitrogen oxides
VOCs = volatile organic compounds
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 \(\leq 2.5 \text{ μms} \) \((PM_{2.5})\)
- ambient nitrogen dioxide \((NO_2)\) or nitrates \((NO_3)\)
Chronic Obstructive Pulmonary Disease (COPD) - When does this story begin?
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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)
Critical Windows – Pregnancy and Early Life

Lung function (FEV$_1$) over the life course

Lung function “tracks” throughout childhood, therefore impaired early life lung function results in reduced maximally attainable FEV$_1$, 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 Epidem* 2002
Traffic pollution during pregnancy and child lung function (INMA)

Relative risk (RR) of low lung function (<80% of predicted FEV$_1$) for an IQR increase during second trimester: 1.30 (0.97 to 1.76)

INMA = INfancia y Medio Ambiente Project

Morales, Thorax 2015
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)

Stress

Air Pollution

Allergens

Tobacco Smoke

Diet

Lung Function Development
Childhood Asthma Risk

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

- Crime/violence
- Green space
- Traffic related air pollution
- Industrial air pollution

GIS = geographic information system
EHR = electronic health record
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)

$\text{Mean±Standard Deviation: } 8.3±0.9 \mu g/m^3$

IMPROVE = Interagency Monitoring of Protected Visual Environments (an air quality monitoring network)
Critical/Sensitive Windows


![Graph showing PM$_{2.5}$ levels across different respiratory development stages and gestational weeks.](image-url)
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

Timing?

Sex/Gender?
Prenatal PM$_{2.5}$ and Asthma Onset by Age 6

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

OR = odds ratio
Critical Windows – Pregnancy and Early Life

Pregnancy or trimester-averaged exposure estimates may miss significant relationships

Wilson A, et al., AJE 2017

mtDNA = mitochondrial DNA
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 $\text{NO}_3^-$

- 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 (25$^{th}$-75$^{th}$) prenatal $\text{NO}_3^-$ $\mu\text{g/m}^3$: 23.1 (20.8-24.5)

$\text{NO}_3^-$ = nitrate

Di et al. *J Air Waste Manag Assoc* 2017
Lung development occurs in stages

Kajekar et al. *Pharmacology & Therapeutics* 2007
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
While air quality regulations currently do not address UFPs $\leq 0.1 \mu m$, 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


- 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 2$_{nd}$ trimester remained positively associated with asthma incidence adjusted for other components
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