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Air Pollution and Pediatric Health Effects

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Presentation main points

- Data overview – Focus on Meta-analyses
- Respiratory Outcomes
  - Cumulative / Chronic Effects
  - Short Term Effects
- CNS Outcomes
- Leukemia
- Congenital Heart Disease

Air Pollution and Respiratory Outcomes

- Children are particularly vulnerable to airborne pollution
  - narrower airways
  - breathe more air per pound of body weight than adults, increasing exposure to air pollutants.

- Cumulative / Chronic Effects on Risk/Prevalence/Incidence of
  - Asthma and or Wheeze
  - Allergic Sensitization
  - Allergic Rhinitis or Rhinoconjuctivitis and or Eczema
  - Lung Function

- Short Term Effects on Incidence of
  - Asthma exacerbations
  - Pneumonia
  - Otitis Media
  - Respiratory Mortality

Traffic Related Air Pollution (TRAP) Cumulative Effects on Asthma/Wheeze

- **42 studies** examined associations between TRAP and subsequent childhood asthma incidence or lifetime prevalence, published since 1999 (Khreis 2017, Int. J. Environ. Res. Public Health)

- Land-use regression modelling most commonly used method
- Nitrogen dioxide (NO2) most commonly used pollutant in exposure assessments
- Estimated TRAP exposure at the residential address - Mostly assessed at birth year - only a few studies considered different and/or multiple exposure time windows

- **Exposure to TRAP and risk of development of childhood asthma: A systematic review and meta-analysis (Khreis 2017, Environ Int)**

Notable variability in asthma definitions, TRAP exposure assessment methods and confounder adjustment

- Overall random-effects risk estimates (95% CI) were
  - **1.08** (1.03, 1.14) per 0.5 × 10−5 m−1 of **BC**,
  - **1.05** (1.02, 1.07) per 4 μg/m3 of **NO2**,
  - 1.48 (0.89, 2.45) per 30 μg/m3 of NOx,
  - **1.03** (1.01, 1.05) per 1 μg/m3 of **PM2.5**,
  - **1.05** (1.02, 1.08) per 2 μg/m3 of **PM10**.

Traffic Related Air Pollution (TRAP) Cumulative Effects on Asthma/Wheeze

TRAP and Development of Asthma Phenotypes in Children (Lau 2018, Int J Chronic Dis)

- Systematic review of studies on TRAP exposure and development of childhood asthma and wheezing phenotypes (transient, persistent, and late-onset asthma/wheezing).

- **7 articles** were included in the final review

- TRAP exposure appears to be associated with both **transient** and **persistent asthma**/wheezing phenotypes.
- Little evidence to suggest a relationship between TRAP exposure and late-onset asthma/wheezing

Traffic-related organic and inorganic air pollution and risk of development of childhood asthma: A meta-analysis (Han 2020, Environ Res)

- **27 studies** were included in the meta-analysis and the results showed that TRAP increased the risk of asthma among children:

PM2.5 (meta-OR = **1.07**, 95% CI:1.00–1.13),

NO2 (meta-OR = **1.11**, 95% CI:1.06–1.17),

Benzene (meta-OR: **1.21**, 95% CI:1.13–1.29) and

TVOC (meta-OR:**1.06**, 95% CI: 1.03–1.10)

- Regional analysis showed that **ORs of inorganic TRAP (PM2.5 and NO2)** on the risk of childhood asthma were **significantly higher in Asia** than those in Europe and North America

Traffic Related Air Pollution (TRAP) Cumulative Effects on Asthma/Wheeze

- **Global, national, and urban burdens of pediatric asthma incidence attributable to ambient NO_2 pollution (Achakulwisut 2019, Lancet Planet Health)**

- Estimated the **NO2-attributable burden** of asthma incidence in **children aged 1–18 years** in **194 countries** and 125 major cities.

- Globally, **4·0 million** (95% uncertainty interval [UI] 1·8–5·2) new paediatric asthma cases could be attributable to NO_2 pollution annually; 64% of these occur in **urban centres.** This burden accounts for **13%** (6–16) **of global incidence.**

- About 92% of paediatric asthma incidence attributable to NO2 exposure occurred in areas with annual average NO2 concentrations **lower than the WHO guideline** of 21 parts per billion.

Traffic Related Air Pollution (TRAP) Cumulative Effects on Asthma/Wheeze

- **TRAP and the burden of childhood asthma in the United States in 2000 and 2010 (Alotaibi 2019, Environment International)**

- **NO2, PM2.5** and **PM10** were used as **surrogates of TRAP** exposures

- Asthma incidence rate and a exposure for each pollutant were obtained from the literature

- **Asthma incident cases** due to TRAP represented **27%–42%** of all cases in **2000** and **18%–36%** in **2010**.

- Percentage of cases due to TRAP were higher (1) in **urban areas** than rural areas, and (2) in block groups with **lowest median household income**

Air Pollution Cumulative Effects on Asthma/Wheeze

The impact of prenatal exposure to air pollution on childhood wheezing and asthma: A systematic review/meta-analysis (Hehua 2017, Environ Res)

- **18 studies**: notable variability in exposure assessment
- Overall random effects risk estimates of different pollutants for **childhood wheeze** were
  - 1.04 (0.94–1.15) for PAH,
  - **1.04** (1.01–1.07) for **NO2**,
  - 1.4 (0.97–2.03) for PM2.5 and
- for **childhood asthma**
  - **1.07** for (1.01–1.14) for **NO2**,
  - 1 (0.97–1..03) for PM2.5,
  - 1.02 (0.98–1.07) for SO2,
  - **1.08** (1.05–1.12) for **PM10**

The impact of prenatal exposure to PM2.5 on childhood asthma and wheezing: a meta-analysis (Yan 2020, Environ Sci Pollut Res)

- **9 studies** were included
- Prenatal exposure to **PM2.5** significantly increased risk of childhood asthma and wheezing (OR = **1.06**, 95% CI 1.02–1.11; per 5 μg/m3).
- Maternal exposure was more strongly related to **childhood asthma and wheezing before age 3** (OR =**1.15**, 95% CI 1.00–1.31; per 5 μg/m3) than after (OR = 1.04, 95% CI 1.00–1.09; per 5 μg/m3).
- Children in **developed countries** showed more severe effects (OR = 1.14, 95% CI 1.02–1.27; per 5 μg/m3).

Air Pollution Cumulative Effects on Allergic Sensitization

Influence of childhood TRAP exposure on allergic sensitization: systematic review & meta-analysis of birth cohort studies (Bowatte 2015, Allergy)

- **19 articles** from 11 birth cohorts (**7 European/4 American**)
- Defined TRAP as NOx and PM, or as proximity to roads. All studies assessed sensitization using serum IgE levels.
- **No associations** of sensitization to **indoor aeroallergens** with early childhood exposure to NO2 or PM2.5.
- Increased risk of sensitization to **outdoor aeroallergens** with increased exposure to **PM2.5** but not with NO2
- Early childhood exposure to **NO2** significantly increased the risk for sensitization to **food allergens at the age of 4 years.** These associations were modest at the **age of 8 years** for both **NO2 and PM2.5**

Meta-analysis of air pollution exposure association with allergic sensitization in European birth cohorts (Gruzieva 2014, JACI)

- **5 European birth cohorts**
- Blood samples drawn at 4 to 6 years of age, 8 to 10 years
- Analyzed for allergen-specific serum IgE against common allergens
- Overall, air pollution exposure was **not associated with sensitization** to any common allergen
  - odds ratios ranging from 0.94 (95% CI, 0.63-1.40) for a $1x10^{-5}.m^{-1}$ increase in measurement of the blackness of PM2.5 filters
  - 1.26 (95% CI, 0.90-1.77) for a 5 mg/m3 increase in PM2.5 exposure at birth address.

Air Pollution Cumulative Effects on Rhinitis/Rhinoconjuctivitis and Eczema

Exposure to air pollution and risk of prevalence of childhood allergic rhinitis: A meta-analysis (Zou 2018, Int J Pediatr Otorhinolaryngol)

- **13 studies** included in the meta-analysis (**8 cross-sectional studies, 5 cohort studies**).
- Exposure to **NO2**: OR= **1.138**, 95%CI [1.052,1.231], P = 0.001;
- Exposure to **SO2**: OR= **1.085**, 95%CI [1.013,1.163],P = 0.020;
- Exposure to **PM10**: OR= **1.125**, 95%CI [1.062,1.191], P = 0.000;
- Exposure to **PM2.5**: OR= **1.172**, 95%CI [1.095,1.254], P = 0.000.

Associations between air pollution and pediatric eczema and rhinoconjunctivitis: A meta-analysis of European birth cohorts (Fuertes 2020, Environ Int)

- Examined associations of long-term air pollution levels at the home address with pediatric eczema, rhinoconjunctivitis and asthma prevalences in **5 European birth cohorts.**
- **No increase** in the prevalence of these outcomes at 4 or 8 years with increasing air pollution exposure.
- Meta-analysis adjusted odds ratios (95% confidence intervals) for Eczema and Rhinoconjunctivitis at four years were
  - 0.94 (0.81, 1.09), and 0.90 (0.75, 1.09) respectively, per 10 μg/m3 increase in NO2 at the birth address,
  - 1.00 (0.81, 1.23) and 0.70 (0.49, 1.00) respectively, per 5 μg/m3 increase in PM2.5 at the birth address.

Air Pollution Cumulative Effects on Lung Function

Ambient air pollution and children's lung function in China (Liu 2009, Environ Int)

- **11 articles** on ambient air pollution and children's lung function from 7 cities in China published from 1985 to 2006.
- Lung function significantly **lower in areas with heavy ambient air pollution** than in areas with light ambient air pollution.
- Significant negative correlation between levels of **TSP** and **SO2** and children's **FVC** and **FEV1**, as well as the levels of **NOx** and children's **MMEF**.
- Decreases of lung function for **girls** with the increasing of ambient air pollution were significantly greater for boys

Air Pollution Exposure and Lung Function in Children: The ESCAPE Project (Gehring 2013, Environ Health Perspect)

- Association between residential exposure to air pollution and lung function in **5 European birth cohorts.**
- Measured lung function at 6–8 years of age (n = 5,921)
- Estimated levels of NO2, NOx, PM2.5 absorbance, and PM2.5 at the current address were associated with **small decreases in lung function.**
- Changes in FEV1 ranged from:
  - **–0.86%** (95% CI: –1.48,–0.24%) for a 20-µg/m3 increase in **NOx** to
  - **–1.77%** (95% CI: –3.34, –0.18%) for a 5-µg/m3 increase in **PM2.5**

Air Pollution Short Term Effects on Asthma Morbidity

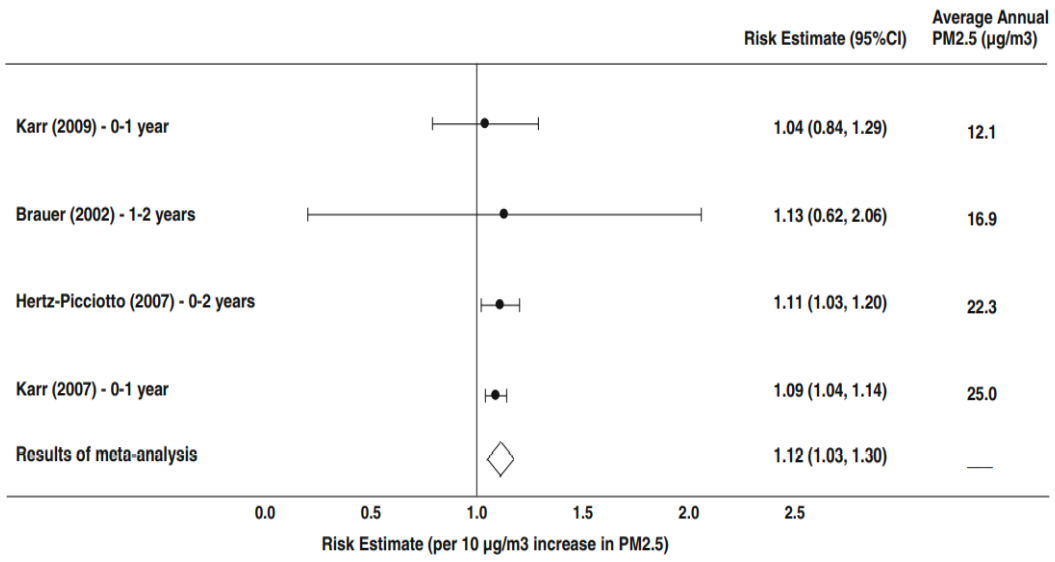
- **2 meta-analyses and 1 multicenter study**
- Daily **emergency room visits for asthma** during years 1986–92 in **Barcelona, Helsinki, Paris and London** increased significantly with **SO2** (RR **1.075**, 95% CI 1.026 to 1.126) and **NO2,** only in cold seasons (RR **1.080,** 95% CI 1.025 to 1.140). No association was observed for O3 and BC. (Sunyer 1997, Thorax)
- Meta-analysis of **87 studies** on the association of six major air pollutants with ERVs and **hospital admissions for asthma**. **Stronger associations** between ERVs/hospital admissions **in children** than in adults [**CO**: **1.018** (1.013, 1.023); **NO2**: **1.018** (1.013, 1.023); **SO2**: **1.016** (1.011, 1.022); **PM10**: **1.013** (1.008, 1.018); **PM2.5**: **1.025** (1.013, 1.037)]. (Zheng 2015, PLOS One)
- Meta-analysis of **22 studies** on **emergency departments, emergency calls, or hospitalizations** due to **asthma exacerbations** in children aged 0 to 18 years showed a significant association with **NO2** (OR: **1.040**; 95% CI: 1.001,1.081), **SO2** (OR: **1.047**; 95% CI: 1.009,1.086), and **PM2.5** (OR: **1.022**; 95% CI: 1.000,1.045). (Orellano 2017, PLOS One)

Air Pollution Short Term Effects on ALRI

- 1 meta-analysis and 1 multicenter study

- A systematic review and meta-analysis of ambient particulate air pollution and **hospitalizations** for acute lower respiratory infections (ALRI) in young children. From **4 eligible studies** the relative risk of **ALRI** per 10 µg/m3 of **PM2.5** was estimated to be **1.12** (1.03, 1.30). (Mehta 2013, Air Qual Atmos Health)

- Overall association of **ozone** and **emergency department (ED) visits** among 5–18 year olds in **Atlanta** (OR = **1.08**, 95% PI: 1.06, 1.11), **Dallas** (OR = **1.04**, 95% PI: 1.01, 1.07) and **St. Louis** (OR = 1.03, 95% PI: 0.99, 1.07). The stronger ORs were observed in **low SES areas**. (Lenick 2017, Environ Health)



Mehta 2013, Air Qual Atmos Health

Air Pollution Short Term Effects on Pneumonia and Otitis Media

- 2 meta-analyses and 2 studies on multi-cohort combined data

- Meta-analysis of **17 studies** on short-term association between ambient air pollution and **hospitalization** of children due to **pneumonia**. The ER% per **10 unit increase** of pollutants was **1.5%** (95% CI: 0.6%-2.4%) for **PM10**, **1.8%** (95% CI: 0.5%-3.1%) for **PM2.5**, **2.9%** (95% CI: 0.4% -5.3%) for **SO2**, **1.7%** (95% CI: 0.5%-2.8%) for **O3**, and **1.4%** (95% CI: 0.4%-2.4%) for **NO2**. (Nhung 2017, Environ Pollut)
- Association between air pollution and **parent report of physician-diagnosed pneumonia** in **10 European birth cohorts**. Adjusted odds ratios (ORs) were elevated and statistically significant for all pollutants except PM2.5 (e.g., OR = **1.30**; 95% CI: 1.02, 1.65 per 10-μg/m3 increase in **NO2** and OR = **1.76**; 95% CI: 1.00, 3.09 per 10-μg/m3 **PM10**). (MacIntyre 2014, Environ Health Perspect)
- Associations between **8 particulate matter elements** and **parental reports of physician-diagnosed pneumonia** between 0-2 years in **7 European birth cohort** studies (n= 15,980). Pneumonia was weakly associated with **zinc derived from PM10** (OR: **1.47** (95% CI: 0.99, 2.18) per 20 ng/m3 increase). No other associations with the other elements were observed. (Fuertes 2014, Int. J. Hyg. Environ. Health)
- Meta-Analysis of **12 studies** of PM concentration and the development of **otitis media** (OM). Pooled odds ratios for each 10 μg/m3 increase in **PM2.5** and **PM10** concentration were **1.032** (95% confidence interval (CI), 1.005–1.060) and **1.010** (95% CI, 1.008–1.012), respectively. (Lee 2020, Int. J. Environ. Res. Public Health)

Air Pollution Short Term Effects on Respiratory Mortality

- **Effects of air pollution on infant and children respiratory mortality in four large Latin-American cities (Gouveia 2017, Environ Pollution)**
  - Evaluated the effect of air pollution on children respiratory mortality in four large urban centers: **Mexico City, Santiago in Chile**, **Sao Paulo** and **Rio de Janeiro in Brazil.**
  - Daily **time-series** of mortality due to respiratory diseases in infants and children, and levels of PM10 and O3
  - For **PM10 10 unit increase** the percentage increase in risk of death due to respiratory diseases in infants in a fixed effect model was **0.47%** (0.09-0.85).
    - For respiratory deaths in children **1-5 years old**, the increase in risk was **0.58%** (0.08-1.08)
    - A **higher effect** was observed for **lower respiratory infections (LRI)** in children 1-14 years old [1.38% (0.91-1.85)].

Air Pollution Cumulative Effects and Autism

- **2 meta-analyses and 1 study on multi-cohort combined data**

- Meta-Analysis of **23 studies** of multiple airborne pollutants **prenatal exposure** and **autism spectrum disorder (ASD)**. Significant summary ORs of **1.07** (95% CI: 1.06, 1.08) per 10-μg/m3 increase in **PM10** exposure (n = 6 studies) and **2.32** (95% CI: 2.15, 2.51) per 10-μg/m3 increase in **PM2.5** exposure (n = 3 studies). **Unexplained statistical heterogeneity** across the individual study estimates meaning that the effect could be larger or smaller. (Lam 2016, PLOS One)

- Meta-analysis of **25 studies** on **maternal exposure** to outdoor air pollution by trimester of pregnancy and risk of **ASD in children**. **Frequentist meta-analysis** yielded significant pooled ORs, **1.06** (1.01,1.11) for **PM2.5** and **1.02** (1.01,1.04) for **NO2**. **Bayesian meta-analysis** showed similar ORs, **1.06** (1.00,1.13) for **PM2.5** and **1.02** (1.00,1.05) for **NO2**. **Third trimester** appeared to have higher pooled ORs for PM2.5, PM10, and ozone. (Chun 2020, Environ Pollut)

- Air pollution exposure during **pregnancy** and **childhood autistic traits** assessed between 4 and 10 years of age in **4 European cohort studies** (n= 8,079 children). Prenatal air pollution exposure was **not associated** with autistic traits within the borderline/clinical range. (Guxens 2016, Environ Health Perspect)

Air Pollution Cumulative Effects and Psychomotor Outcomes

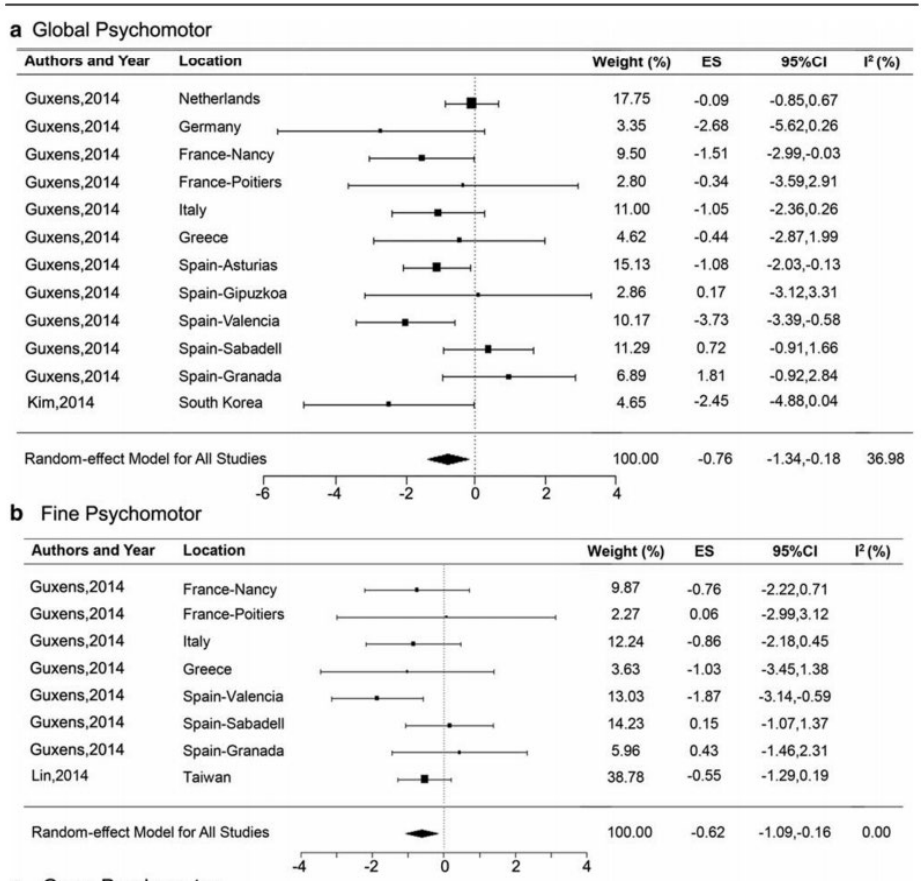
1 meta-analysis and 2 studies on multi-cohort combined data

- **4 multi-cohort** data studies found evidence of **association** of air pollution, especially motorized traffic pollutants, **with delayed psychomotor development** during childhood. (Sentis 2017, Environ Int; Lubczyńska 2017, Environ Int; Guxens 2014, Epidemiol; Fuertes 2016, Environ Int)

- **Synthesis of 8 European-cohorts data** found **no air pollution association** with **depressive and anxiety symptoms** or **aggressive** symptoms in children. (Jorcano 2019, Environ Int)

- Meta-analysis of **10 studies** estimated that per 10 µg/m3 increase of **NO2** during pregnancy was associated with a – **0.76 point decrease in global psychomotor** (95% CI, – 1.34, – 0.18) and a **– 0.62 point decrease in fine psychomotor** for children (95% CI, – 1.09, – 0.16). Further studies are needed for determining the effects of prenatal air pollution exposure on attention, IQ, and behavior. (Shang 2020, Environ Sci Pollut Res)

Shang 2020, Environ Sci Pollut Res



Air Pollution Cumulative Effects and Leukemia

4 meta-analyses

- Childhood leukemia was positively associated (OR=**1.53**, 95% CI=1.12, 2.10) with **residential traffic** exposure among **7 studies** using a **postnata**l exposure window. There was no association (OR=0.92, 95% CI=0.78, 1.09) among **4 studies** using a **prenatal exposure window** (e.g. pregnancy period or birth address). (Boothe 2014, Am J Prev Med)

- Meta-analysis of **26 (6 ecologic and 20 case-control) studies** showed for **NO2** exposure an OR of **1.21** (95% CI 1.04 – 1.41) for **ALL** and 1.06 (95% CI 0.51 – 2.21) for AML; For **benzene** exposure OR were 1.09 (95% CI 0.67 – 1.77) for ALL and **2.28** (95% CI 1.09 – 4.75) for **AML**.

Estimates were generally **higher for exposures in the postnatal period** compared to the prenatal period. (Filippini 2016, J Environ Sci Health C Environ Carcinog Ecotoxicol Rev)

- Meta-analysis of **15 studies** of exposure to **traffic density or traffic-related air pollution** published from 1999 to 2014, the summary relative risk was **1.48** (95% CI: 1.10, 1.99; n = 12); it was **higher for AML** (sRR = **2.07**; 95% CI: 1.34, 3.20) than for **ALL** (sRR = **1.49**; 95% CI: 1.07, 2.08). (Carlos-Wallace 2015, Am J Epidemiol)

- Meta-analysis of **29 case–control and cohort studies** found **little association** between disease risk and **traffic indicators** near the child's residence for most of the exposure range.
- In contrast, **benzene** exposure was **positively** and approximately **linearly** associated with risk of childhood **leukemia**, particularly for **AML**, among children **under 6 yrs** of age.
- Exposure to NO2 showed **little association** with leukemia risk except at the highest levels. (Filippini 2019, Environ Health Perspect)

Air Pollution Cumulative Effects and Congenital Heart Defects

2 meta-analyses

- Meta-analysis of **5 studies** (3 cohort and 2 case-control) evaluated **maternal exposure** to **PM2.5** during the **first trimester** (weeks 1–12) of fetal development and found **no association** with congenital heart defects
- atrial septal defect, OR = 0.65 (95% CI, 0.37 to 1.15);
- ventricular septal defect, OR 1.02 (95% CI, 075 to 1.37); and
- tetralogy of fallot, OR = 1.16 (95% CI, 0.78 to 1.73. (Hall 2019, JBI Database System Rev Implement Rep)

- Meta-analysis of **26 studies** on the relationship between **maternal air pollution exposure** and CHDs risk in the offspring showed that
- High versus low **CO exposure** was associated with an increased risk of **tetralogy of Fallot** OR =**1.21**, 95% CI: 1.04-1.41,
- Increased risk of atrial septal defects (**ASDs**) was found for each **10 unit increment in PM10** and **Ozone** (OR = **1.04**, 95% CI: 1.00-1.09; OR = **1.09**, 95% CI: 1.02=1.17).
- Categorical **NO2 exposure** was associated with an increased risk of **coarctation of the aorta** (OR for high versus low = **1.14**, 95% CI: 1.02-1.26).
- Analyses for other combinations yielded none statistically significant associations. (Hu 2020, Chemosphere)

Conclusion and Perspectives

- Extensive body of knowledge has accumulated on associations between air pollution and children's health, both from an epidemiological and mechanistic standpoint.
- Overall, primarily positive and few null associations have been reported for cumulative and short term effects on pediatric respiratory morbidity in terms of hospitalizations and ED visits for overall respiratory, asthma and ALRI-pneumonia.
- Positive relationships were more frequently reported between TRAP related pollutants NO2, $PM_{10,}$ and $PM_{2.5}$
- More attention should be paid to the association between air pollution and other pediatric diseases, such as those affecting the nervous system and hematological malignancies.
- Future studies should focus on the mechanisms implicating air pollution in causing harmful effects in children, especially in respiratory, CNS and hematological diseases.
- More intervention studies are needed to reduce children's exposure to air pollution and linking of the findings with possible policy decisions and prevention measures

Thank You!