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Sibling and non-sibling designs in studies investigating the risk of drug exposure during pregnancy: same results? A preliminary meta-epidemiological study.

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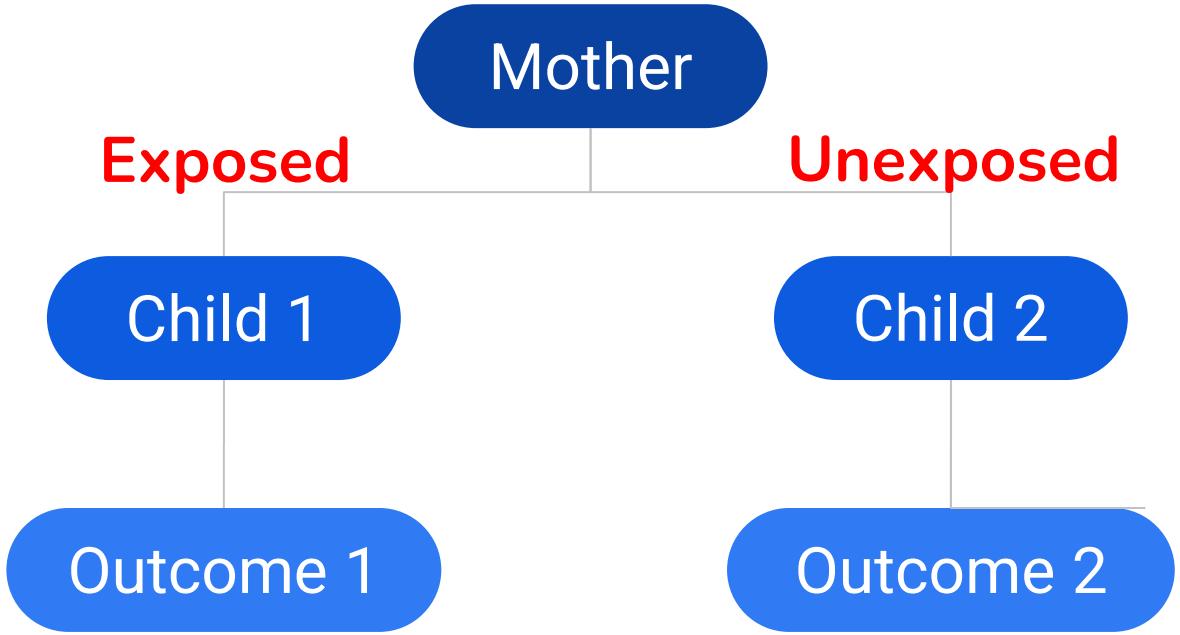
Introduction: sibling studies



- Sibling studies increasingly used, particularly for risk of drug use during pregnancy
- Better control over family-level confounding factors (e.g., genetic, environmental, or socioeconomic factors)
- But have also limitations (unshared confusion, exposure misclassification, loss of power, ...)

Sibling and non-sibling designs: same results?

Aim: Do the results of 'Sibling' studies differ from 'Non-Sibling' studies on the risks of drug exposure during pregnancy? If so, how?

Material

- **Dataset:** All available meta-analyses performed in the metaPreg project (www.metapreg.org)
- **Drugs:** All drugs with at least one study using a sibling design
- **Outcomes:** All outcomes with at least one result using a sibling design

Methods

- **Step 1:** For each outcome and drug, pooled odds ratios (OR) from sibling studies were compared to those from non-sibling studies with disease-matched control.
- **Step 2:** Ratios of Odds Ratios (RORs) computed (OR_sibling/OR_non-sibling) and pooled across drugs using a random-effects model.

→ **7 outcomes based on 17 drugs and 16 sibling studies**

Sibling and non-sibling designs: same results?

Results: strictly preliminary

Outcomes	**Pooled RORs** (ratios of ORs) (**sibling *versus* non sibling disease-matched control**)	**Interpretation**	
Attention Deficit Hyperactivity Disorder	0.79 [0.49; 1.29] (pooled ROR across 6 drugs; I2 = 47%)		Sibling results inferiors of non sibling results ; but not significantly
Autism Spectrum Disorder	0.79 [0.57; 1.11] (pooled ROR across 9 drugs; I2 = 37%)		
Severe cognitive developmental delay	1.01 [0.49; 2.09] (pooled ROR across 5 drugs; I2 = 0%)		
Major congenital malformations	1.07 [0.90; 1.27] (pooled ROR across 2 drugs; I2 = 0%)		
Congenital heart defects	0.85 [0.65; 1.11] (ROR of 1 drug; I2 = NA)		
Asthma	2.88 [0.97; 8.52] (ROR of 1 drug; I2 = NA)		Sibling results > non sibling, not significant

Sibling and non-sibling designs: same results?

Limitations

- **Overrepresentation of 5 sibling studies** that examined several drugs simultaneously, in the pooled ROR calculations.
- **Small number of studies.**

The work should continue by addressing the limitations identified here

Conclusions

- First meta-epidemiological study comparing sibling and non-sibling study results.
- **Pooled RORs** for sibling versus non-sibling **ranged from 0.7 to 2.9**, depending on the outcome.
- **Mainly inferior results for sibling design, but no significant difference between sibling and non-sibling studies.**