

Methods Development for Assessment of Environmental Exposures for Pregnancy Outcomes

WORKSHOP ON ADVANCING SYSTEMATIC REVIEW FOR CHEMICAL RISK ASSESSMENT

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Pregnancy Outcomes

- Spontaneous abortion
 - Early loss <12 weeks
 - Clinical loss 12-20 weeks

- Preterm birth
 - <37 weeks gestation

Evaluation Categories

- Outcome ascertainment
- Study population selection
- Confounders
- Analysis strategy

Population Selection – Preterm Birth

- **Ideal**

- Study entry protocol described and occurred by the first trimester or early in the second trimester of pregnancy

- **Good**

- Entry into study occurred later in pregnancy (second trimester, after 20 – 22 weeks), with potential of missing some preterm births
- Retrospective cohort created from well-defined population

- **Adequate/Limited**

- Entry late in pregnancy (3rd trimester) with potential of missing early preterm births
- Little information on selection strategy, sampling framework, respondents vs. non-respondents

- **Critically deficient**

- Population selected in such a way that an association is created due to study design, e.g., if cases taken from clinic where exposed workers are treated, or from a high-exposure geographic area, while controls taken from a clinic where exposure would be lower

Challenges – Spontaneous Abortion

- Lack of consensus on ideal study design/ selection approach
 - Pre-pregnancy cohort gets all spontaneous abortions but recruits pregnancy planners
 - Planners differ from non-planners
 - Population-based sampling methods miss early spontaneous abortions but include non-planners

Challenges – Pregnancy Outcome

Selection

- Truncation: missing person time that can result in selection bias
- Left truncation (or staggered entry) can induce bias that could be opposite of what would be expected and loss of precision
- Higher dose of chemical early in pregnancy could cause spontaneous abortion but early losses not detected

Challenges - Overall

- Not quite knowing where there was
- Tendency to focus on known aspects of bias
 - Confounding
 - Bias toward the null
- Need for additional practical methodological work on implications for selection bias and information bias – or accessible methods pieces in the subject areas
 - Absent a known direction of effect, difficult to draw inference on a particular study
- Older studies more limited on analysis approach

Looking Ahead

- Potential benefit to have groups come together for a call – relevant cross cutting issues
- Evaluate select aspects without specific endpoint in mind
 - Analysis approach, confounding
- Limited by type of studies we reviewed
 - There may be other relevant issues that were not covered
- Optimistic that protocol will result in a fairly well conducted evaluation of a set of studies

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