Methods Development for Assessment of Environmental Exposures for Pregnancy Outcomes

WORKSHOP ON ADVANCING SYSTEMATIC REVIEW FOR CHEMICAL RISK ASSESSMENT

ANNA Z. POLLACK, PHD
ASSISTANT PROFESSOR
GEORGE MASON UNIVERSITY
APOLLAC2@GMU.EDU
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

Selevan et al. 1987; Weinberg et al. 1992; Schisterman et al. 2013
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
Acknowledgements – Pregnancy Working Group

Emily Harville, Tulane University
Glinda Cooper, EPA
Audrey Galizia, EPA
Amanda Persad, EPA
Michelle Cawley, ICF