Methods Development for Bias Assessment of Environmental Exposures for Male Reproductive Outcomes

Workshop on Advancing Systematic Review for Chemical Risk Assessment

Jane S. Burns, ScD
Research Scientist
Harvard T.H. Chan SPH

Courtney Lynch, PhD
Assistant Professor
Ohio State University

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Male Reproductive Outcomes

- Puberty Development
- Reproductive Hormones
  - Puberty
  - Adult
- Semen parameters
- Time to pregnancy/Fecundity

Epidemiologic Methods for Evaluation of Bias

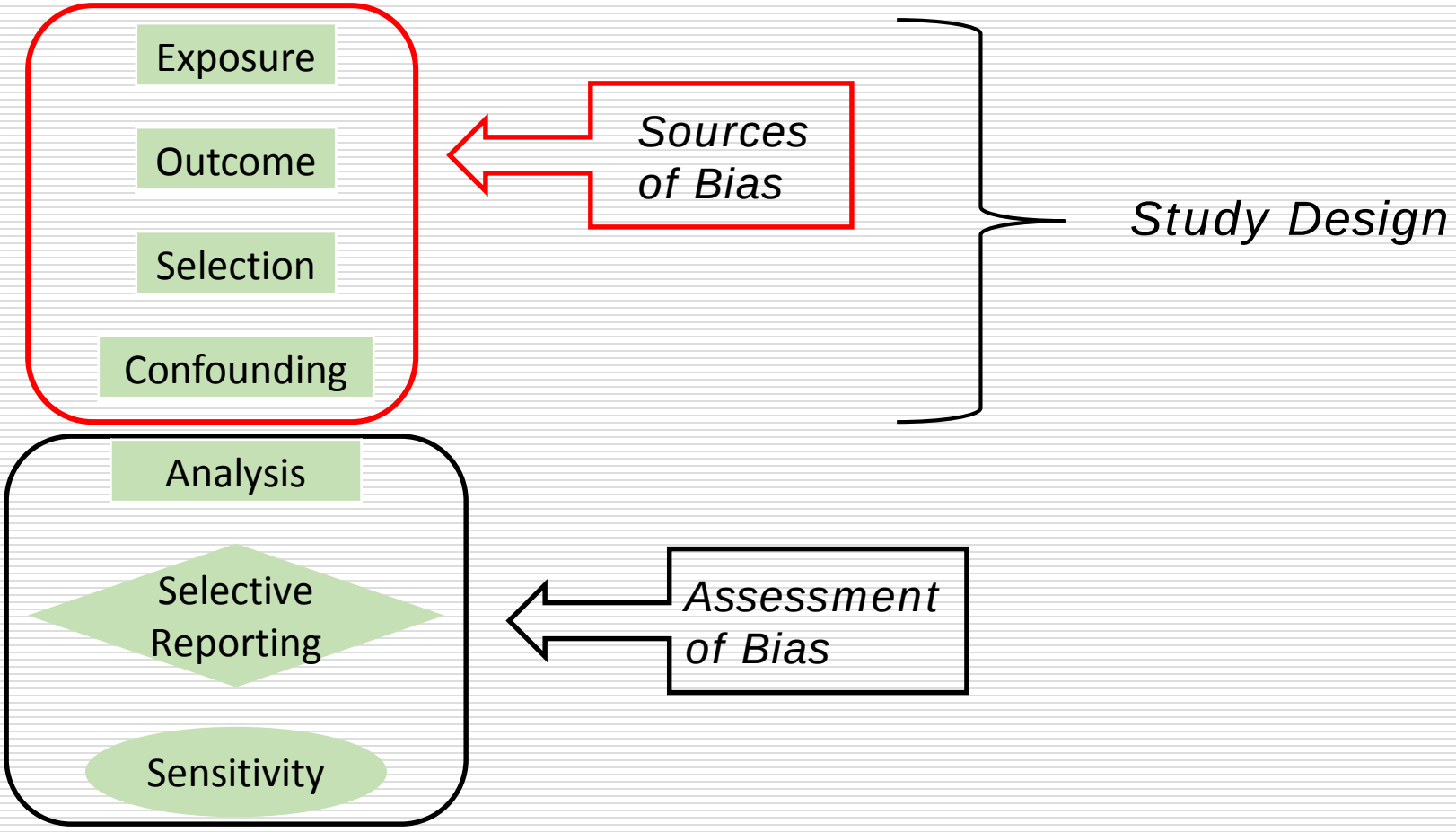
Sources of Bias:

Selection – who is in the study

Information – dependence between exposure and outcome measurements, e.g. recall bias

Confounding

Evaluation Categories



Method Evaluations Between Working Groups

Consistency:

- Confounding
- Analysis

Specific adaptations for:

- Selection
- Outcomes

Generalization of Exposure Evaluation

- *Evaluation framework for other environmental exposures for future applications*

Assessment Outcomes Example 1

Pubertal Development

- Tanner stage for genitalia and pubic hair
  - Visual inspection
  - Established criteria
- Testicular volume (TV)
  - Testes measurement
  - Prader orchidometer

Pubertal Development

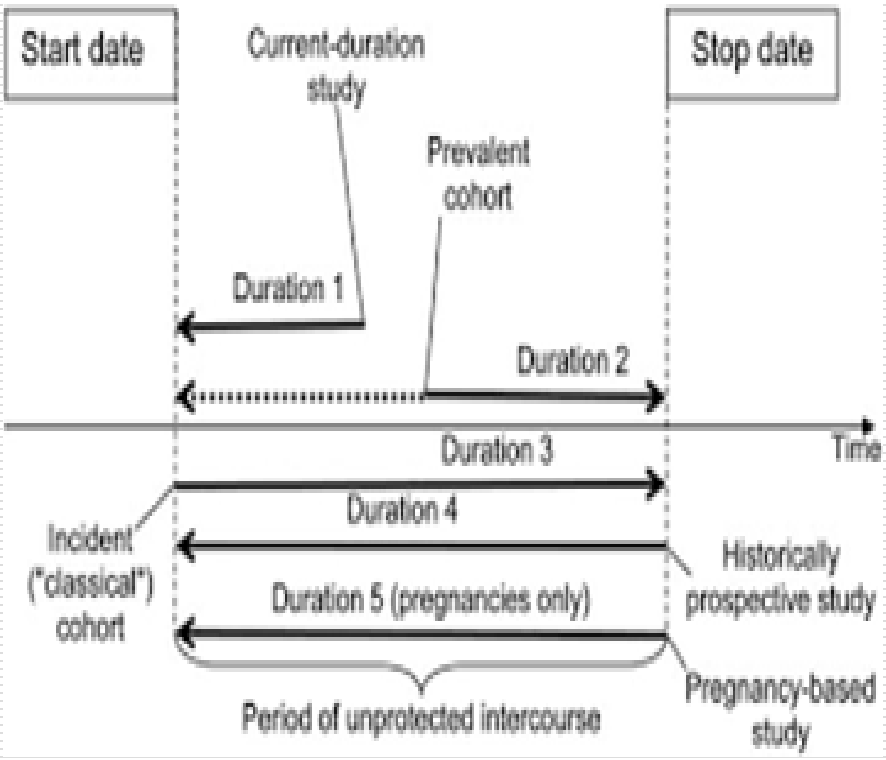
- Comparison of stages
  - Cross-sectional
  - Longitudinal
- Pubertal milestones
  - Onset of puberty
    - Tanner stage 2
  - Sexual maturity
    - Tanner stage 5

Assessment Outcomes Example 2

Time to pregnancy – a measure of fecundability

- Pregnancy
  - Self-report
  - Pregnancy test

1) Current duration approach
2) Prevalent cohort
3) Prospective enrollment
4) Retrospective recall (tried)
5) Retrospective recall (pregnant)



Slama et al., 2013

Assessment of Epidemiologic Methods in Studies

- Analysis
  - Exposure/Outcome measurements
  - Confounding adjustment
  - Effect modification and mediation
- Reporting
  - Description of data
    - Study population
    - Exposure levels
    - Outcomes
    - Potential confounders
  - Results
    - Crude
    - Adjusted
  - Sensitivity results

Applying Protocol to Evaluating Studies – Biomarkers!

- Was appropriate matrix selected?
- Was sample collection and storage appropriate?
- Were appropriate laboratory methods used?
- Did the laboratory meet recognized clinical/research standards?
- Were LODs and CVs reasonable?
  - low values may be difficult to detect
  - some biomarkers are more difficult to measure

Biomarker assessment is specific and requires expertise

Logistics of Developing Protocol – "Living virtual lives"

Teleconferences and email

- Small group helped
- Split outcomes amongst external consultants
  - allowed for individual's expertise in development
  - reviewed protocols together
- EPA/IRIS personnel shared experiences of other groups and evolving protocols
- Applying protocols during development process to actual epidemiology studies helpful

Optimistic that these protocols will be useful tools for future evaluation and transparency.