Evidence-based environmental decisions: Bridging the gap between epidemiology and risk assessment

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FRAMING THE CONVERSATION

Judy: I’m an exposure scientist/risk assessor. I have certain data needs.

Carol: I’m an epidemiologist. What do you need?
Outline

• Background

• Epidemiology-risk assessment gap

• Risk assessment “asks”
Background

Fate and transport

Exposure measurements

Epidemiology studies

Exposure models

Toxicology data: in vitro, in vivo

Risk Assessment

Public Health Decision-Making
Epidemiology-risk assessment gap

1. Increased reliance on epi for human health risk assessment

• Target species is directly relevant - no inter-species extrapolations needed

• Reduces need for high-to-low dose extrapolations

• No/poor laboratory animal models for some health endpoints

• Minimize the use of animals in chemical testing
2. Epi ≠ Tox; should there be a GLP-equivalent?
Epidemiology-risk assessment gap

3. Large number of epi studies but often can’t be used for decision-making
Epidemiology-risk assessment gap

Over 20 years of calls for improving suitability of epidemiology studies for risk assessment:

“For epidemiologists, the lessons to be learned from this brief review should include recognition that risk assessment is now established as a policy-making tool and that epidemiologic research may have a central role to play in setting policies with substantial societal implications” Samet 1998

“recommendations emerged to help improve the utility of epidemiologic data in risk assessment” Burns et al. 2014

“...calls for establishing consensus standards for the conduct, analysis, and reporting of epidemiologic studies have been voiced in a variety of areas of research.” Goodman et al. 2010

“Despite the considerable amount of epidemiological information available, the quality of much of this evidence was rather low and many limitations likely affect the results so firm conclusions cannot be drawn... Studies that do not meet the ‘recognised standards’... are thus not suited for risk assessment.” EFSA 2017
What is needed

Guidance documents? Frameworks?

These abound, but:

- not designed to enhance collaboration and dialogue between the epidemiology and risk assessment disciplines
- developed for systematic review
- not all designed for environmental research
- met with resistance (e.g., dampening of creativity, eventual obsolescence of guidelines)
- too detailed; too specific for general use.
If you always do what you’ve always done, you’ll always get what you’ve always got.
Risk Assessment Asks

Risk Assessment

- Hazard Identification
- Dose-Response Assessment
- Exposure Assessment
- Risk Characterization


Burns/LaKind
Goals of Asks

Bridging the gap by focusing on important concepts

Improved dialogue, communication

A nudge, not a shove
Asks: Hazard Identification

- confirm health outcome
- confirm specific exposure
- report study methods fully and transparently
## Confirm health outcome

BEES-C, EPA OPP, etc.

<table>
<thead>
<tr>
<th>TIER</th>
<th>OUTCOME</th>
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</thead>
<tbody>
<tr>
<td>TIER 1</td>
<td>Measurement from a medical provider or a confirmed diagnosis</td>
</tr>
<tr>
<td>TIER 2</td>
<td>Self-reported diseases, symptoms, test scores</td>
</tr>
<tr>
<td>TIER 3</td>
<td>Single sample of a short-lived chemical or hormone</td>
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</tbody>
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Example: pyrethroid epidemiology studies and outcome

Highest confidence in birth weight and cancer

Sperm quality: 10 of 13 studies relied upon a single semen sample
Infant Health: All quality studies of infant health (birth weight, birth length, head circumference, gestational age)
Development: 1 of 8 studies relied upon medical confirmation of developmental delay and autism spectrum disorder
Respiratory outcome: 12 of 13 studies relied upon self report
All cancer studies based upon medical confirmation

Burns and Pastoor, 2018
Option: test reliability of a sample
High agreement increases confidence in the self reported outcome

- Agricultural Health Study
- Enrollment of prospective cohort (~80,000 participants)
- Serendipitous repeated interviews with ~4,000 subjects

<table>
<thead>
<tr>
<th>Symptom Reported*</th>
<th>% Exact Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessive tiredness</td>
<td>82</td>
</tr>
<tr>
<td>Headaches/dizziness</td>
<td>76</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>92</td>
</tr>
<tr>
<td>Skin irritation</td>
<td>79</td>
</tr>
</tbody>
</table>

*Response categories for symptoms from pesticide use were: never or rarely, sometimes, and frequently/almost always

Blair et al., 2002
Asks: Exposure Assessment

- Describe source-to-intake pathway (conceptual model)
- Provide complete exposure data
- Describe direction and magnitude of error
• Describe source-to-intake pathway (conceptual model)
• Describe complete exposure data, including data quality

Completeness

Quality

Exposure and biological relevance
Specificity
Method sensitivity
Contamination
Stability
Adjust for matrix dilution
Ability to use data to estimate exposure over window of interest
Ability to establish that exposure precedes effect

LaKind et al. Environ Int 73C:195-207.
• Describe direction and magnitude of error
ICC = intraclass correlation coefficient = proportion of variability explained by between subject variation

ICC < 0.40 – poor reproducibility
ICC > 0.40 - fair to good reproducibility
ICC ≥ 0.75 excellent reproducibility
For an ICC of .75, ~40% of people may be incorrectly classified regarding their exposure.
Asks: Dose-Response

- Describe shape of curve
- Describe and evaluated concordance with previous results
- Describe direction and magnitude of error
Describe shape of curve
Describe shape of the curve

Quartiles show more information than beta coefficients

Linear regression results:
• A = -2.6 (95% CI: -4.6 to -0.6)*
• B = -0.7 (95% CI: -2.2 to 0.8)
• C = -2.0 (95% CI: -3.8 to -0.1)*

*Statistically significant

Adapted Fig 1 from Factor-Litvak et al. PLoS ONE 9(12): 2014
Describe and evaluate concordance with other studies

- Example: 4 case control studies of non-Hodgkin lymphoma (NHL)

  Similar question: How many days did you use pesticide “x”?
Exposure categories vary widely

At > 15 days per year, different study populations are labeled as medium, high and highest.

Reporting similar cut-points would foster direct comparison.
Summary

• From the risk assessor:
  • want to use epidemiology data
  • don’t have much flexibility in their needs

• From the epidemiologist:
  • want my data to have impact in public health
  • don’t have much flexibility to control dose and data collection
  • funding issues and participant burden issues
Summary

Let’s keep talking

• From the risk assessor – This is what I need
  • Hazard Identification: confirm outcome, confirm exposure, describe methods
  • Dose-response: describe curve, concordance, define error
  • Exposure-assessment: give source, describe data, define error

• From the epidemiologist – I see what you need
  • Study design
  • Analysis
  • Reporting
Thank you. Questions?