Integrating Evidence

Richard Scheines

Carnegie Mellon University

The IRIS Process

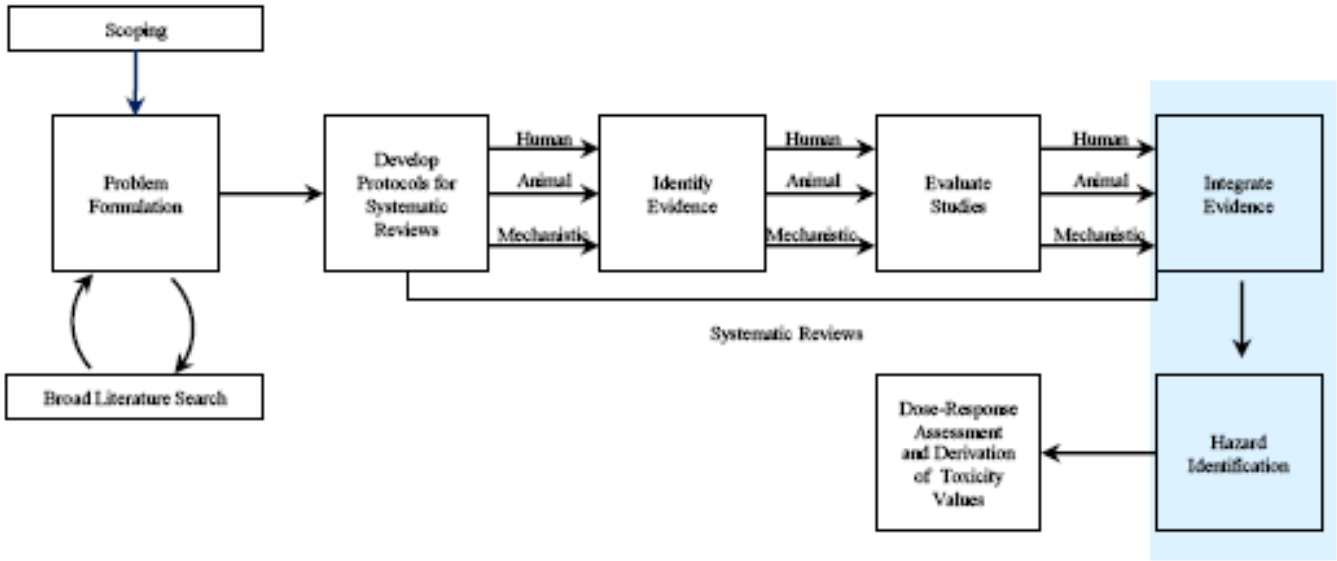
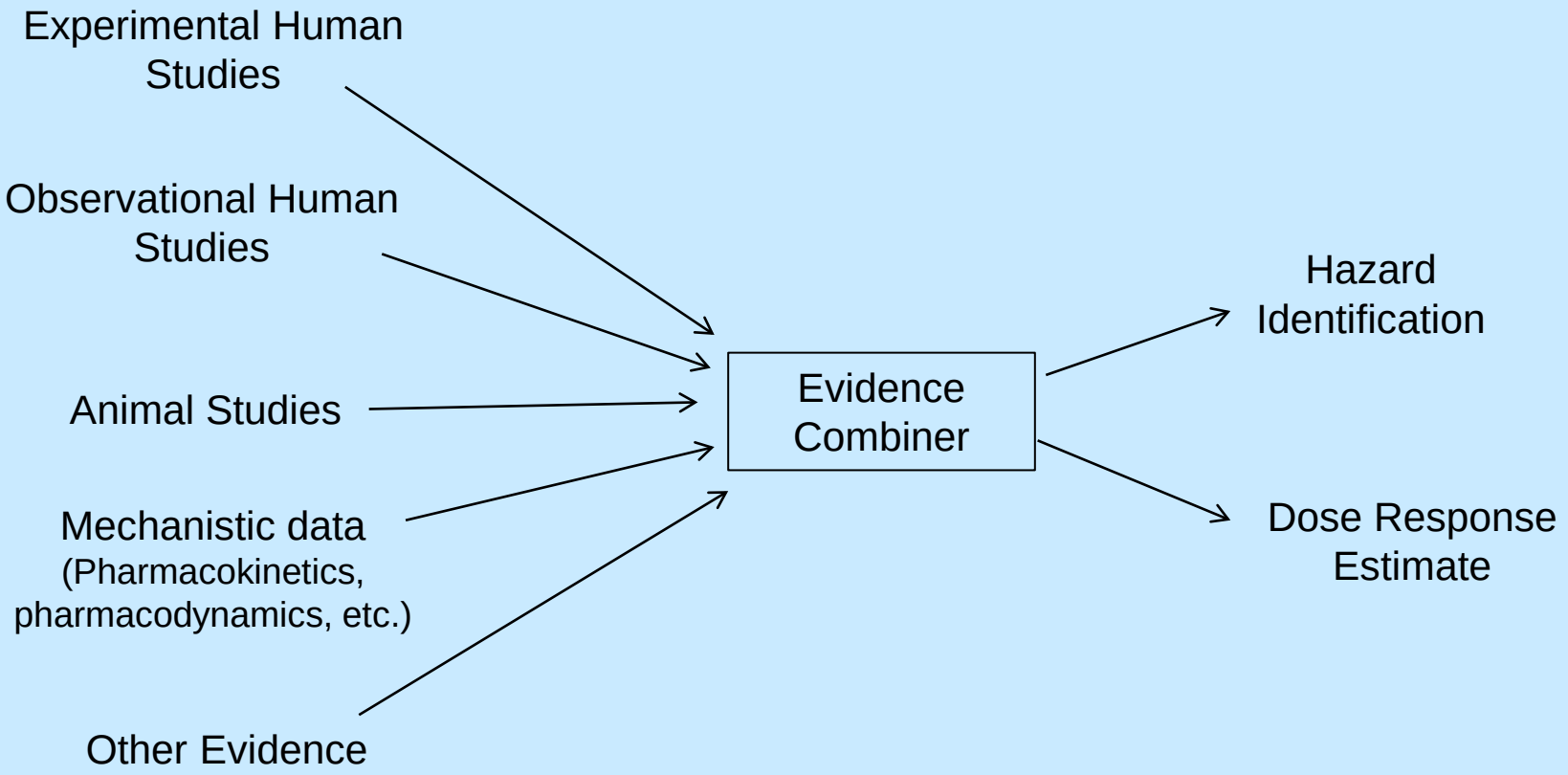


FIGURE 6-1 The IRIS process; the hazard-identification process is highlighted. The committee views public input and peer review as integral parts of the IRIS process, although they are not specifically noted in the figure.

Combining Evidence



Problems

1. Wide variation in evidence base
   - E.g., arsenic: lots of evidence of all types
   - Many chemicals: little or no human evidence,
     small number of animal studies.
   - Most chemicals: no human or animal evidence,
     only mechanistic models

Problems

2. How to combine different types of evidence depends on the goal

- Output: Hazard Identification
  - Categorical/Qualitative judgment
    - (Yes, No)
    - (Sufficient, Probable, Suggestive, Inadequate, etc.)
  - Quantitative judgment of hazard
    - Pr(Hazardous) = .3, Pr(Not Hazardous) = .7

- Output: Dose - Response
  - Parameterized Dose-response function
  - Best estimate *with* uncertainty (confidence intervals?)

Hazard Identification: Strategies

Organizing Principles

- Mechanism
  - Pro: models should improve over time, and are often all we have
  - Cons: most epidemiological or experimental evidence is mechanism agnostic, and often compelling

- Evidence type (human, animal, mechanistic)
  - Pros: methodological pros and cons of each kind somewhat understood
  - Cons: does not help us understand how evidence types cross relate

- Alternative interpretations
  - Pros: holistic view of evidence, fits scientific practice
  - Cons: hard to systematize

Current Options

Guided Expert Judgment

- E.g. IARC, IRIS
- Evidence & loose guidelines → Experts → Judgment (e.g., Suggestive of causation)
  - Pros: experts are often very good at complicated scientific judgment
  - Cons: hard to make transparent or explicit and thus replicable

Structured Processes

- Recipe like, algorithmic, e.g. GRADE, NTP-Grade
  - Pros: transparent and replicable
  - Cons:
    - still requires large amounts of expert judgment
    - algorithms come with no epistemic guarantees

Alternative: Bayesian Approach

Pros:

- Theoretically defensible as a method for combining evidence
- Explicitly embraces alternative interpretations (exclusive hypotheses)
- Models evidential inter-relationships (e.g., mechanistic knowledge that bears on the relevance of the animal model)
- Explicitly incorporates all types of uncertainty
  - E.g. uncertainty in the measurement of exposure in human epi studies
  - Uncertainty in the relevance of the animal model
- Explicitly characterizes posterior uncertainty
- Hazard-ID and Dose-Response in a single framework
- Allows for smooth and principled updating as new evidence comes in
- Computation no longer an obstacle
- Becoming mainstream

Bayesian Approach

Cons:

- Not easy to implement in many situations
- Still requires expert judgment to construct and “seed” the model

NRC Recommendations

Near Term Future:

- Guided Expert Judgment → but make it more transparent

  or

- Structured Process → customized to the needs of IRIS (e.g., NTP – Grade)

Medium Term (1-3 years) – develop *in parallel*:

- Bayesian Approach