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MCM Research and Use: Ethical Considerations

Holly Taylor, PhD, MPH
Department of Health Policy and Management
Bloomberg School of Public Health
Berman Institute of Bioethics
Johns Hopkins University

Principles and Benchmarks

- **Social value**
- **Scientific Validity**
- Fair Participant Selection
- **Favorable Risk-Benefit Ratio**
- Independent Review
- Informed Consent
- Respect for Participants

Emanuel et al 2008

Ethics of Study Design

- Social Value
  - Does the Project have social value? (Decision Point 1)
    - If no, study **cannot** go forward

Ethics of Study Design

- Social Value (con't)
  - Under what circumstances would testing a countermeasure in a pediatric setting be ethically acceptable?
    - Potential threat?
    - Reliable information regarding a potential threat?
    - Exposure in a nearby community (e.g. exposure in NYC, study to be conducted in DC)?
    - During an exposure event?
    - Post-event?

Ethics of Study Design

- Scientific Validity
  - Is the study design valid?
    - Is there uncertainty about potential benefit of the proposed intervention? (Decision Point 2)
      - If no, study **cannot** go forward as designed
      - If yes, what is the appropriate design?
        - » Phase 1 to determine safety?
        - » Equivalency trial (e.g. exposing children to two different doses of vaccine known to be effective in adults)?
        - » Randomized placebo-controlled trial?

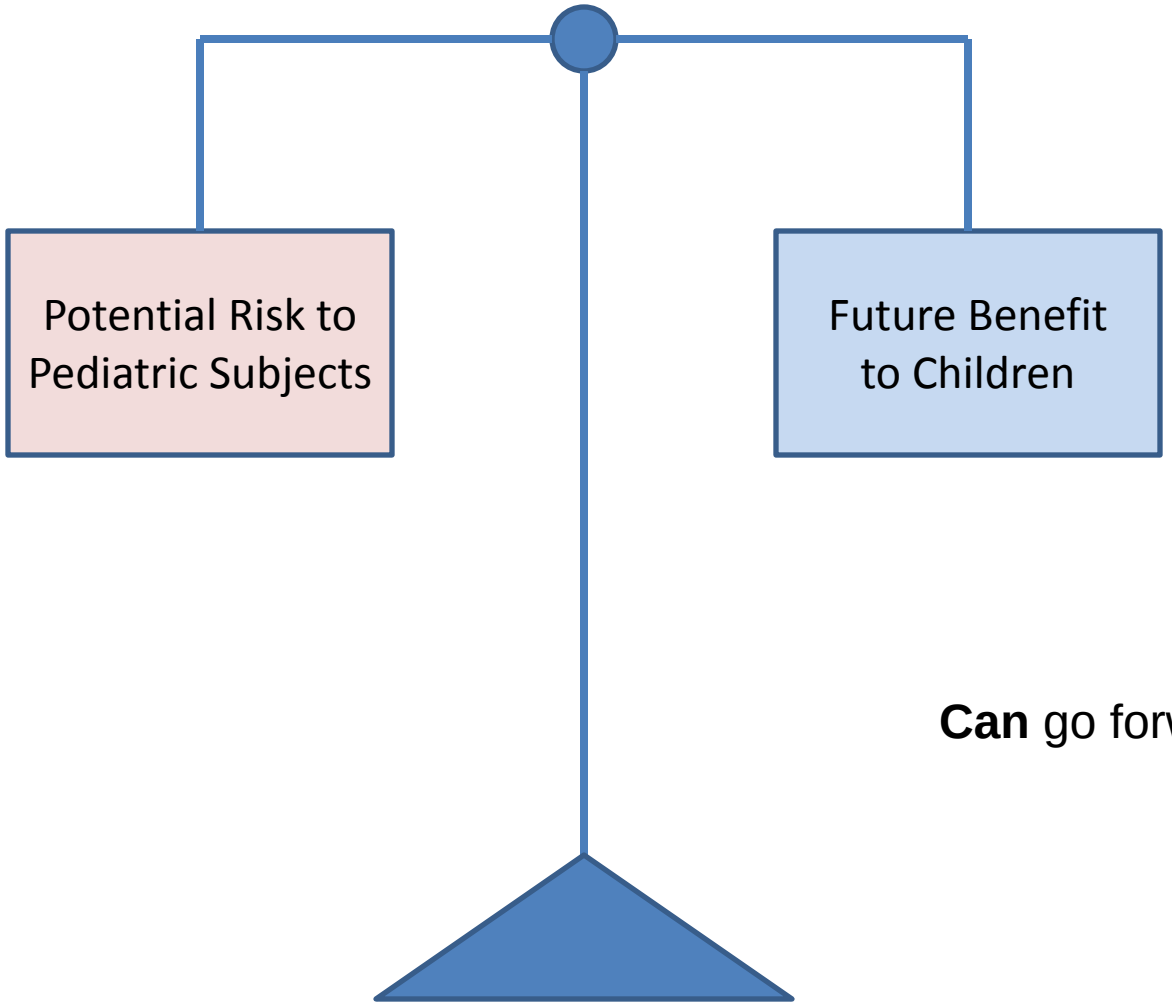
Ethics of Study Design

- Favorable Risk-Benefit Ratio
  - Do the risks to which subjects will be exposed to during the study constitute more than a minor increase over minimal? (Decision Point 3)
    - If no, study **can** go forward as designed
    - If yes, is the study too risky to conduct?
      - Physical risk of exposure to intervention
      - What is the risk of not conducting the study?

Ethics of Study Design

- Favorable Risk-Benefit Ratio
  - Are the risks and benefits to study subjects balanced? (Decision Point 4)
    - If no, study **cannot** go forward as designed
    - If yes, study **can** go forward as designed

Balance Assessment



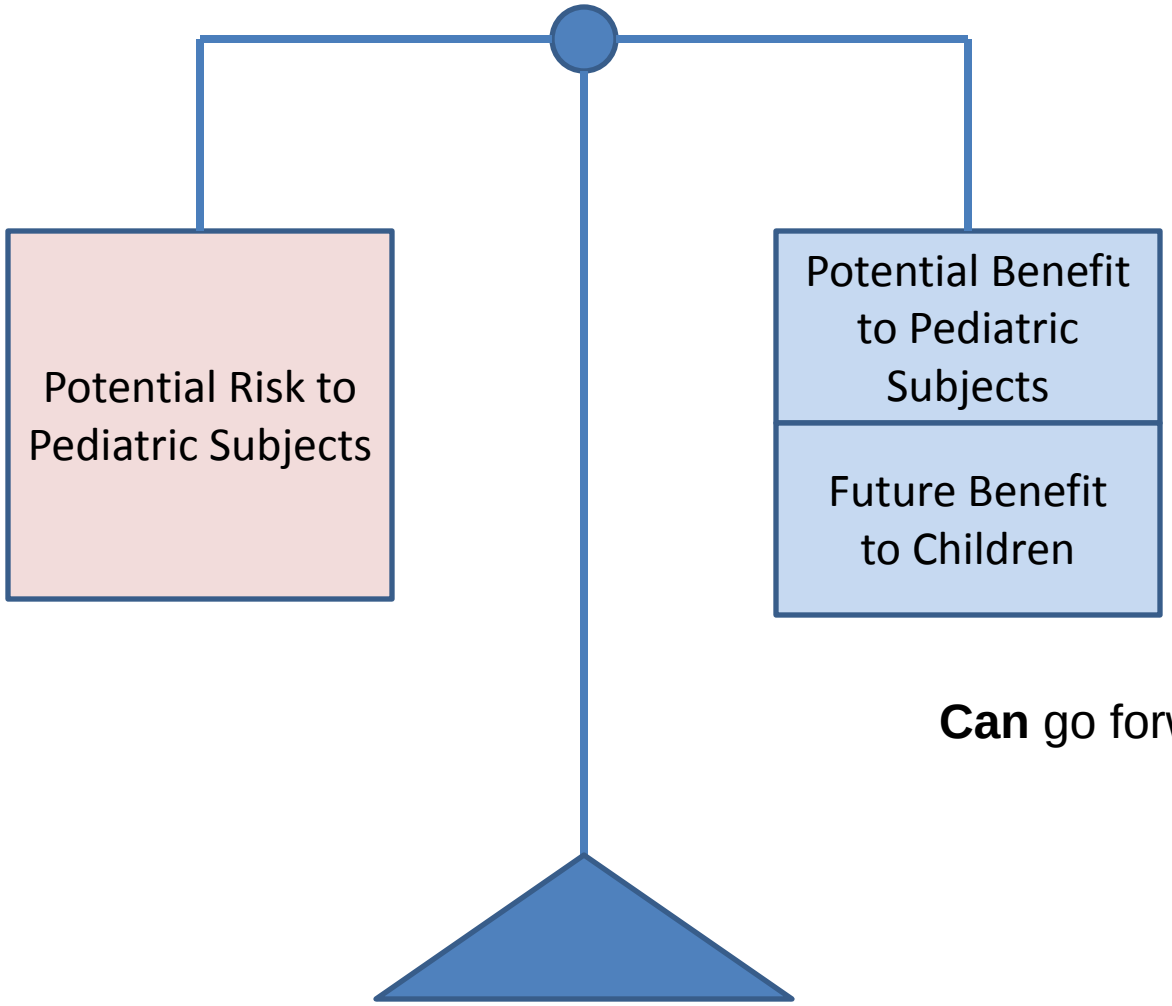
Identifiable

Not Identifiable

Can go forward as designed

Present – Before Trial

Balance Assessment



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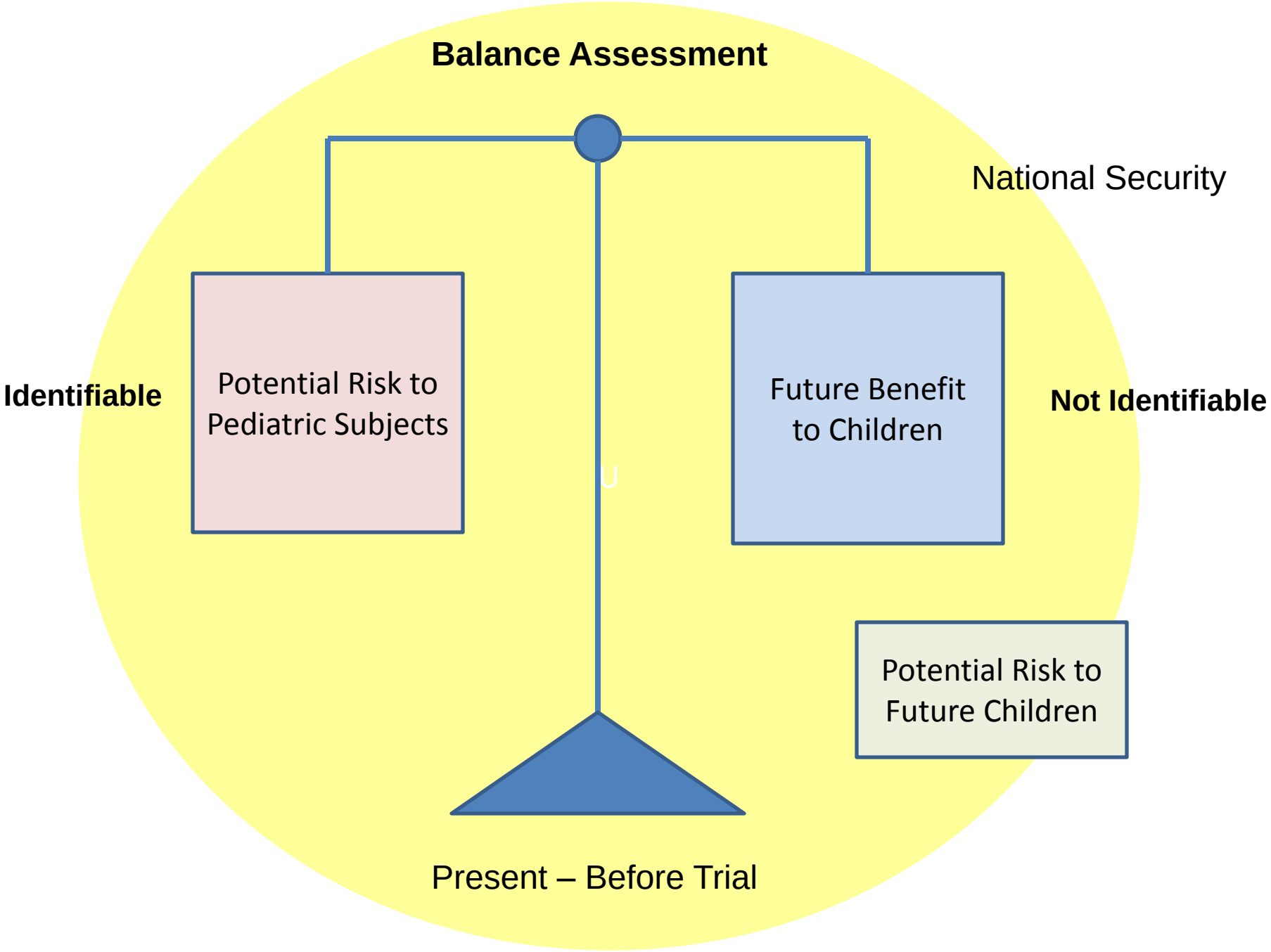
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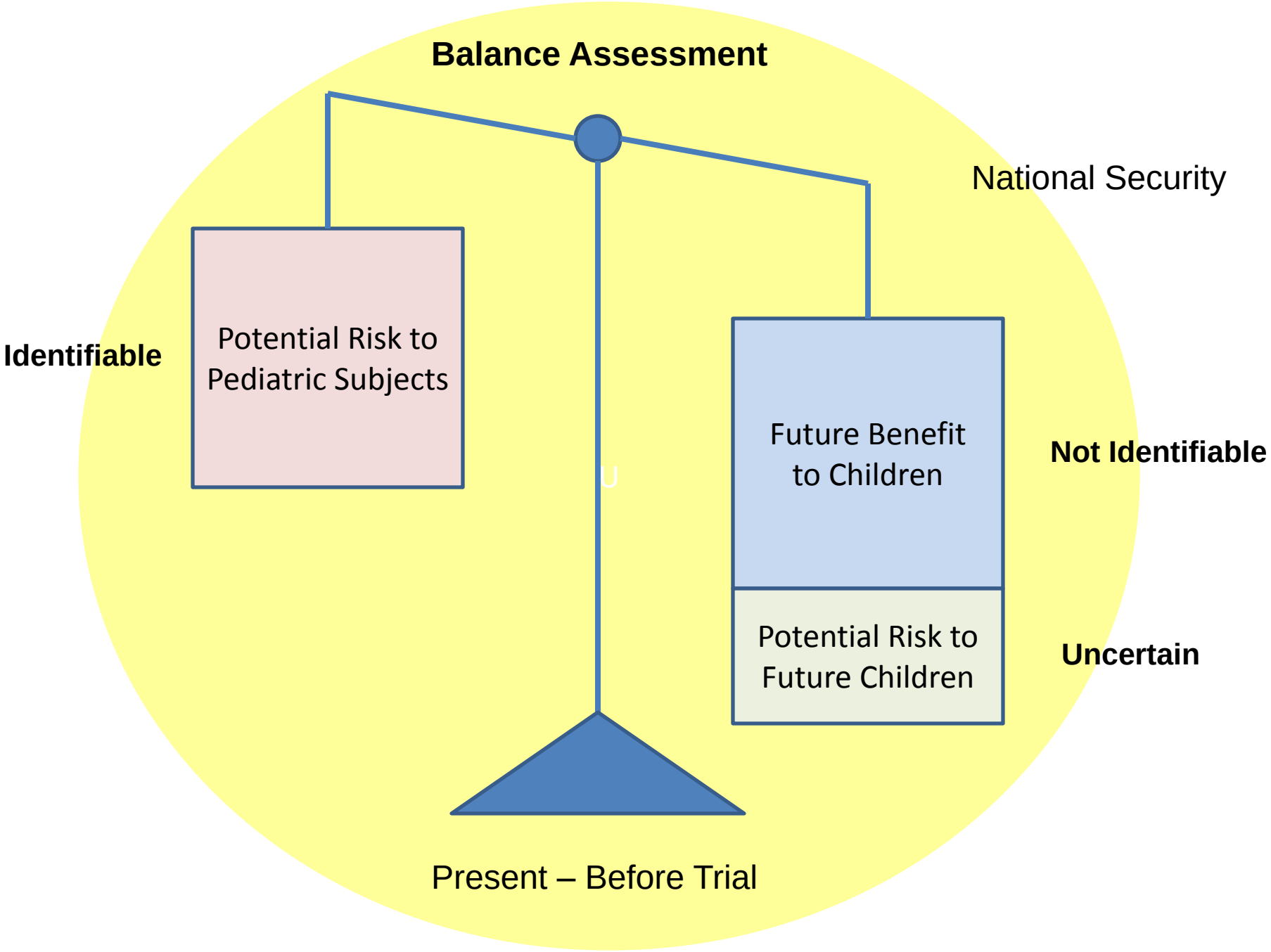
Potential Risk to Pediatric Subjects
Future Benefit to Children
Not Identifiable
Potential Risk to Future Children
Present – Before Trial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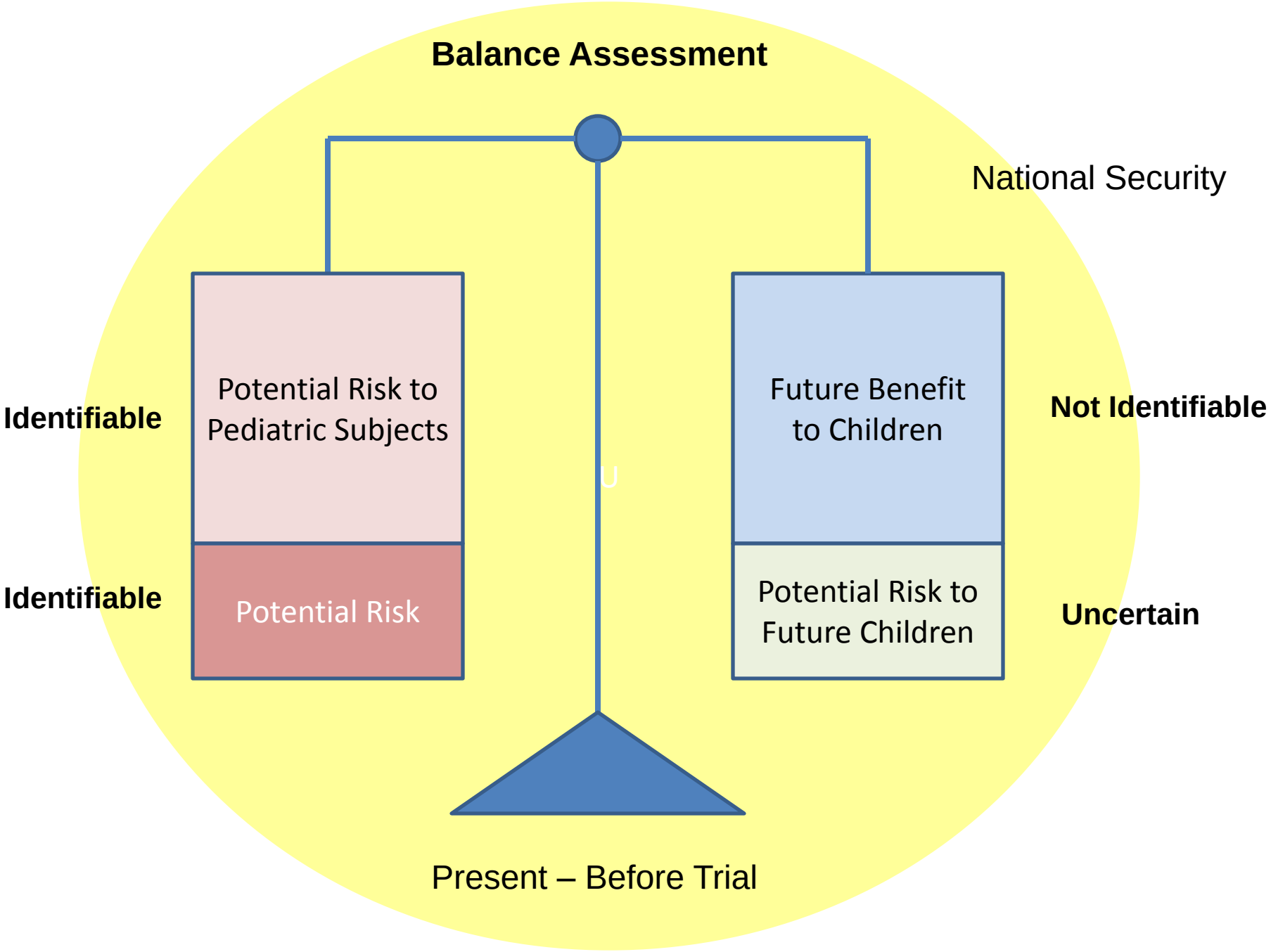
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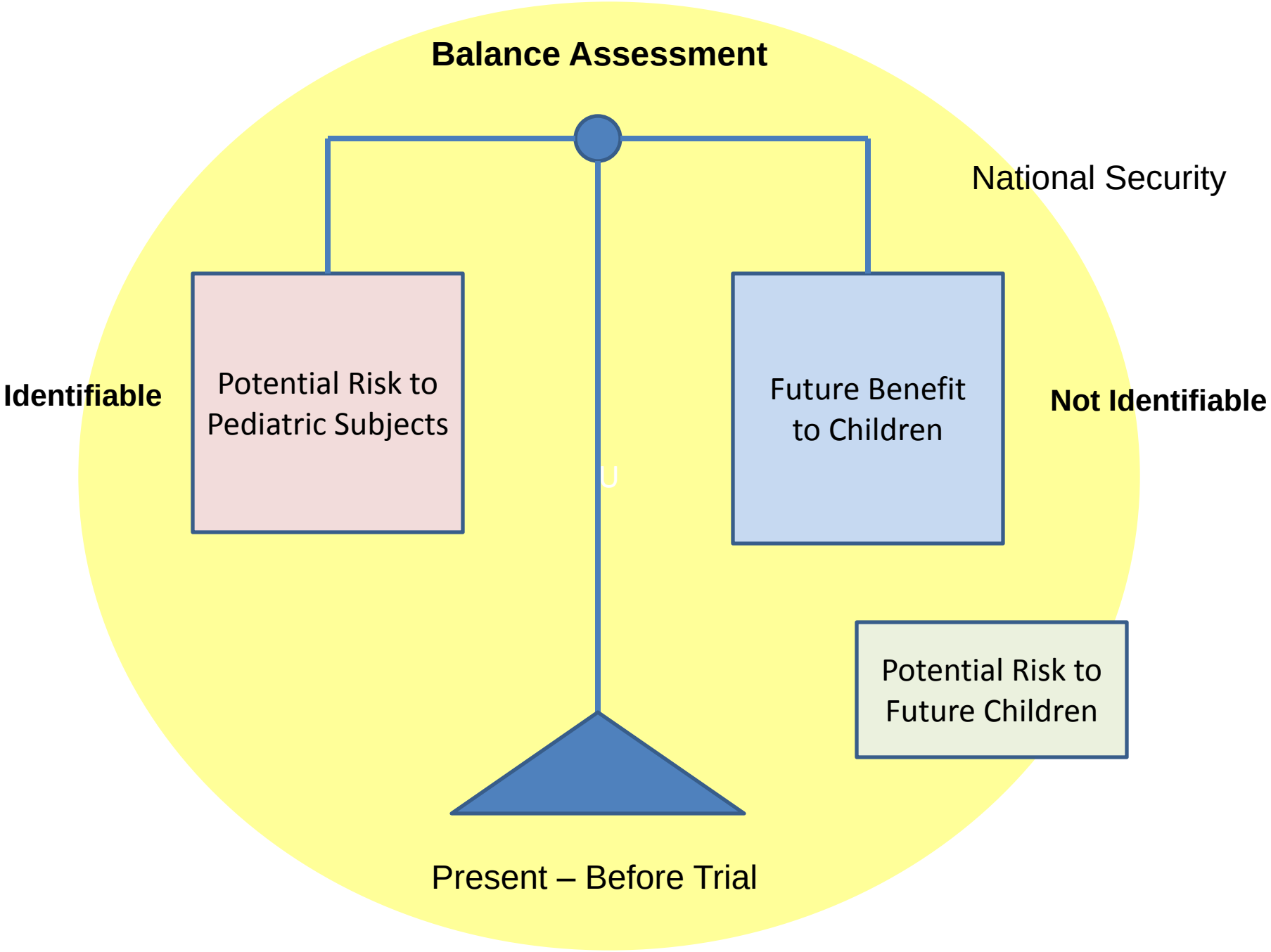
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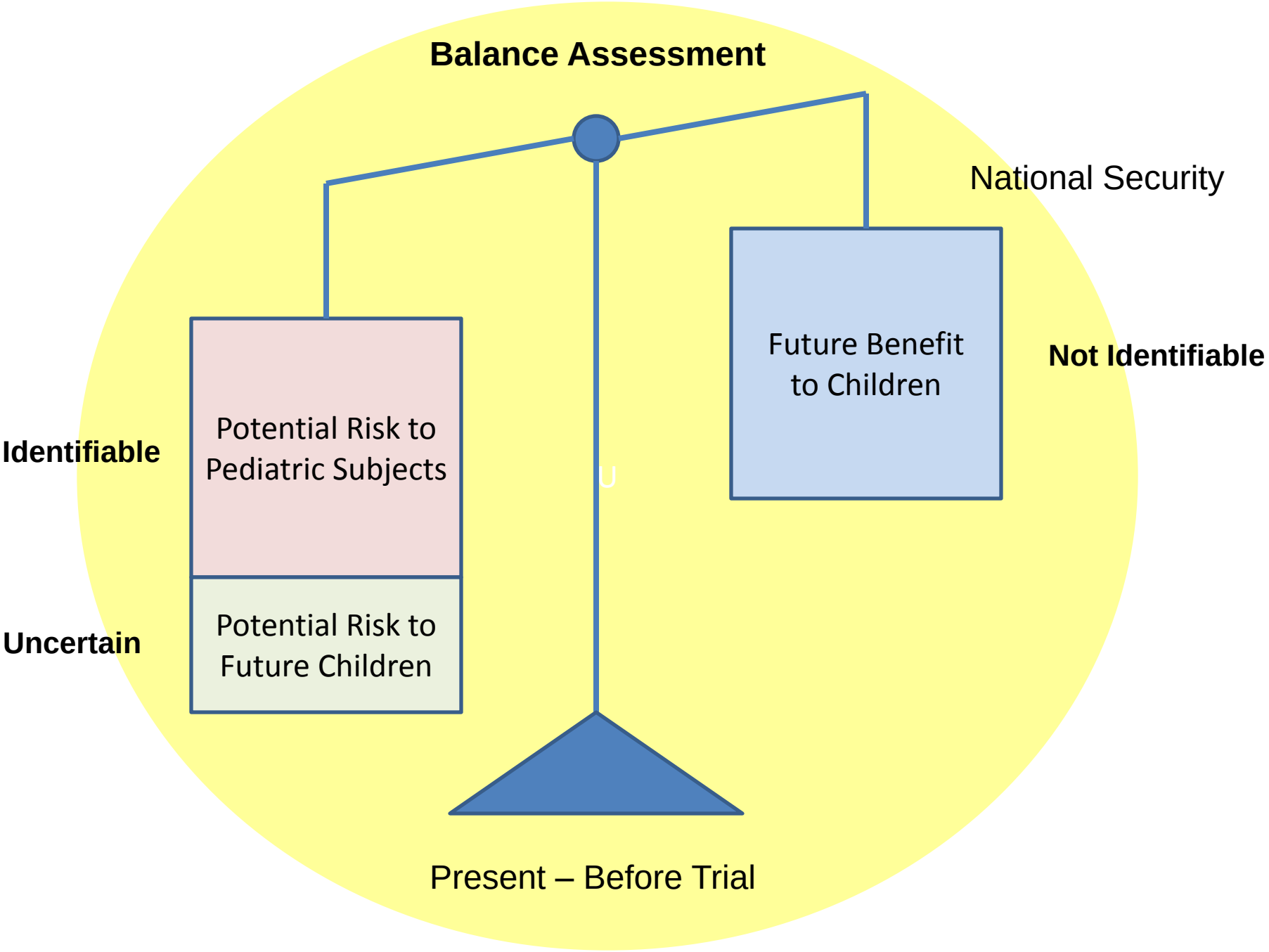
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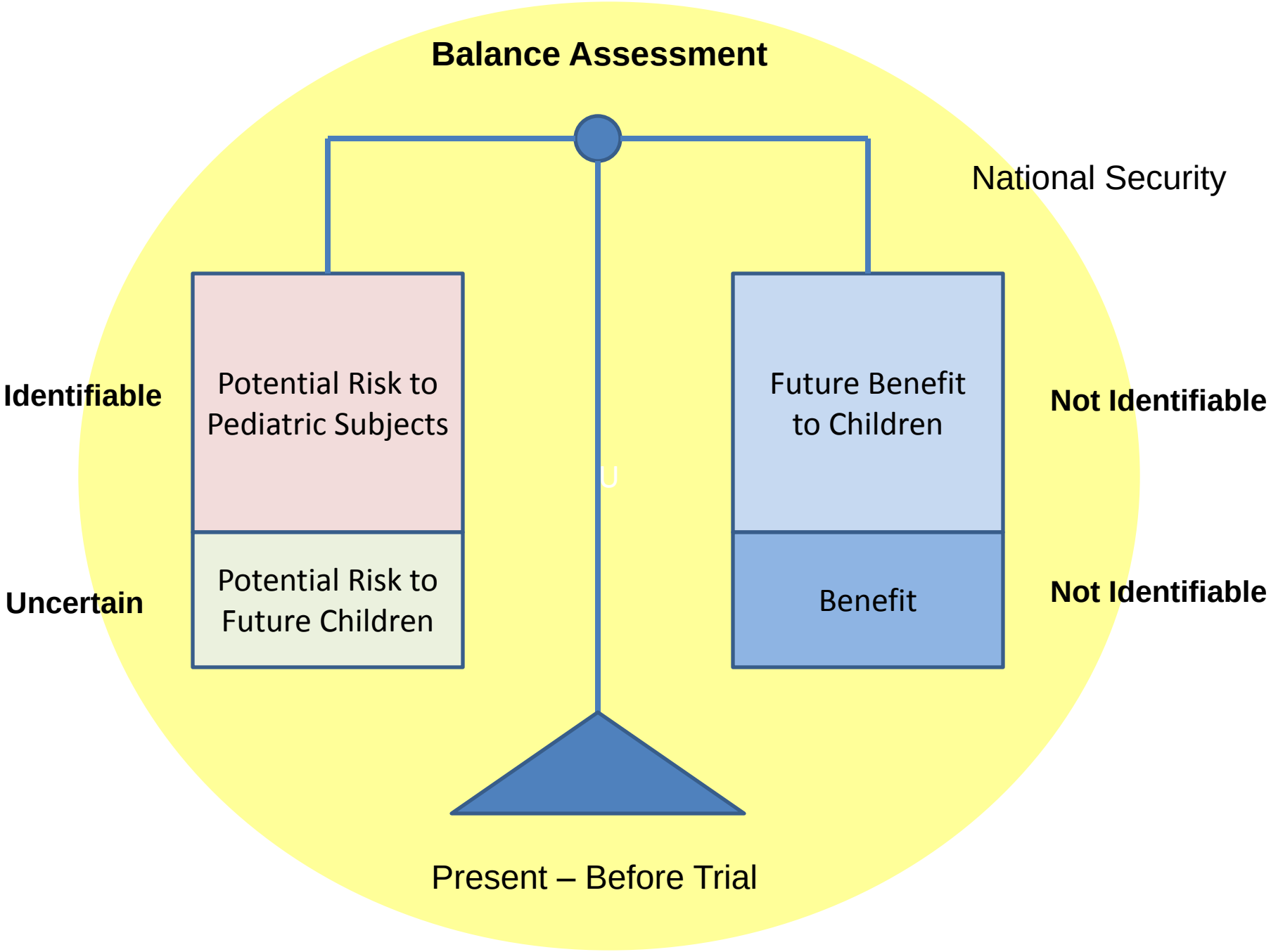
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Benefit
Not Identifiable
Present – Before Trial

Consequences of Non-Action

- Intentional release
  - Post-exposure prophylaxis
    - Known risk
  - Post-exposure vaccination under IND
    - Unknown risk

Adult ⇨ Child Vaccination

- Lack of safety
  - Vaccinia for Smallpox
    - Infants with eczema are more likely to develop disseminated vaccinia
- Lack of efficacy
  - Plain Polysaccharide Vaccine for Pneumococcal Pneumonia
    - Under 2 years (use Pneumococcal Conjugated Vaccine)
  - Influenza
    - Under 6 months, rely on mother's antibodies

Source: Peter Patriarca, MD Biologics Consulting Group, Inc.

Consequences of Action

- Approvable for use?
  - Need for additional trials?
- Added to stockpile for future use?
- Intentional release
  - Post-exposure prophylaxis
    - Known risk
  - Post-exposure vaccination
    - More known risk?