# SCID Review Discussion

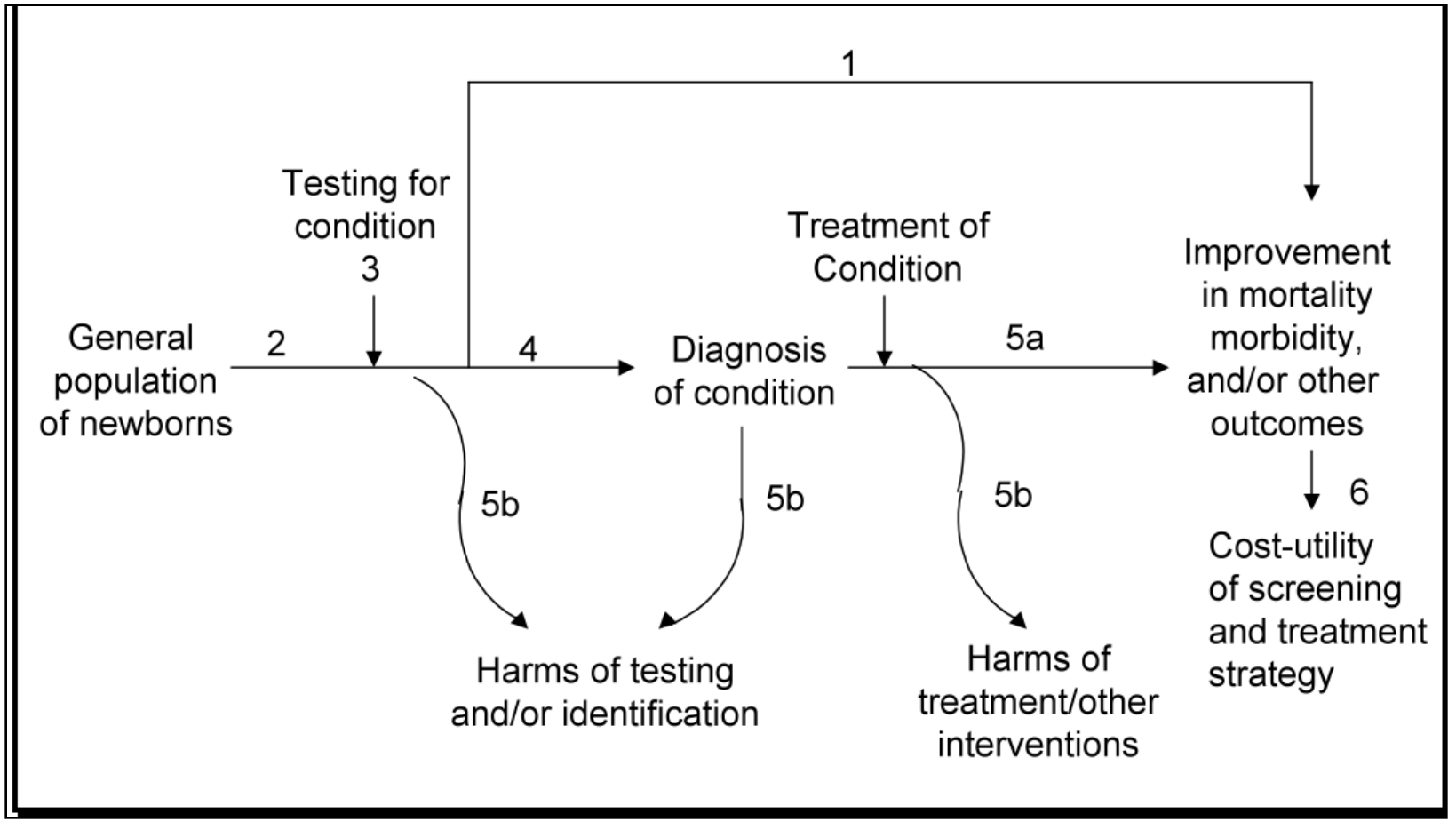
# Decision Matrix

| CATEGORY | RECOMMENDATION | LEVEL OF CERTAINTY | MAGNITUDE OF NET BENEFIT |
|---|---|---|---|
| **A.** | Recommend adding the condition to the core panel | Sufficient | Significant |
| **B.** | Recommend not adding the condition to the core panel | Sufficient | Zero or net harm |
| **C.** | Recommend not adding the condition,<br><br>Instead recommend additional studies | Insufficient, but the potential for net benefit is compelling enough to ecommend additional studies to evaluate | Potentially significant, and supported by contextual considerations |
| **D.** | Recommend not adding the condition now | Insufficient, and additional evidence is needed to make a conclusion about net benefit | Potentially significant or unknown |

# Key Questions

1. This is the overarching question for the evidence review: Is there direct evidence that screening for the condition at birth leads to improved outcomes for the infant or child to be screened, or for the child's family?
2. Is there a case definition that can be uniformly and reliably applied? What are the clinical history and spectrum of disease of the condition, including the impact of recognition and treatment?
3. Is there a screening test or screening test algorithm for the condition with sufficient analytic validity?
4. Has the clinical validity of the screening test or screening algorithm, in combination with the diagnostic test or test algorithm, been determined and is that validity adequate?
5. What is the clinical utility of the screening test or screening algorithm?
   a) What are the benefits associated with use of the screening test?
   b) What are the harms associated with screening, diagnosis and treatment?
6. How cost effective is the screening, diagnosis and treatment for this disorder compared to usual clinical case detection and treatment?

# Analytic Framework



# Key Question 1

- This is the overarching question for the evidence review: Is there direct evidence that screening for the condition at birth leads to improved outcomes for the infant or child to be screened, or for the child's family?
- NO
- But wait for remainder of discussion!

# Key Question 2

- Is there a case definition that can be uniformly and reliably applied? What are the clinical history and spectrum of disease of the condition, including the impact of recognition and treatment?
- Yes
  - Good case definition: all serious and deadly early in life if not treated
  - Genetic heterogeneity that is not relevant to screening
  - All treated similarly and highly effective
    - Bone marrow transplant
    - Gene therapy
    - Enzyme replacement

# Key Question 3

- Is there a screening test or screening test algorithm for the condition with sufficient analytic validity?
- NO
  - Significant progress currently being made
  - Wisconsin pilot study
    - n=70,000 with no positives
    - Screening parameters within standards of other tests
  - Other pilots starting
  - No data yet on:
    - Lab variability
    - Sensitivity and Specificity
    - Quality control
    - Assay robustness
    - Ability to transfer test to other labs

# Key Question 4

- Has the clinical validity of the screening test or screening algorithm, in combination with the diagnostic test or test algorithm, been determined and is that validity adequate?
- NO
  - DNA testing (TREC) seems most robust
  - No population screening cases identified yet
  - No data on variability of clinical expression
- Diagnostic testing is highly reliable and readily available

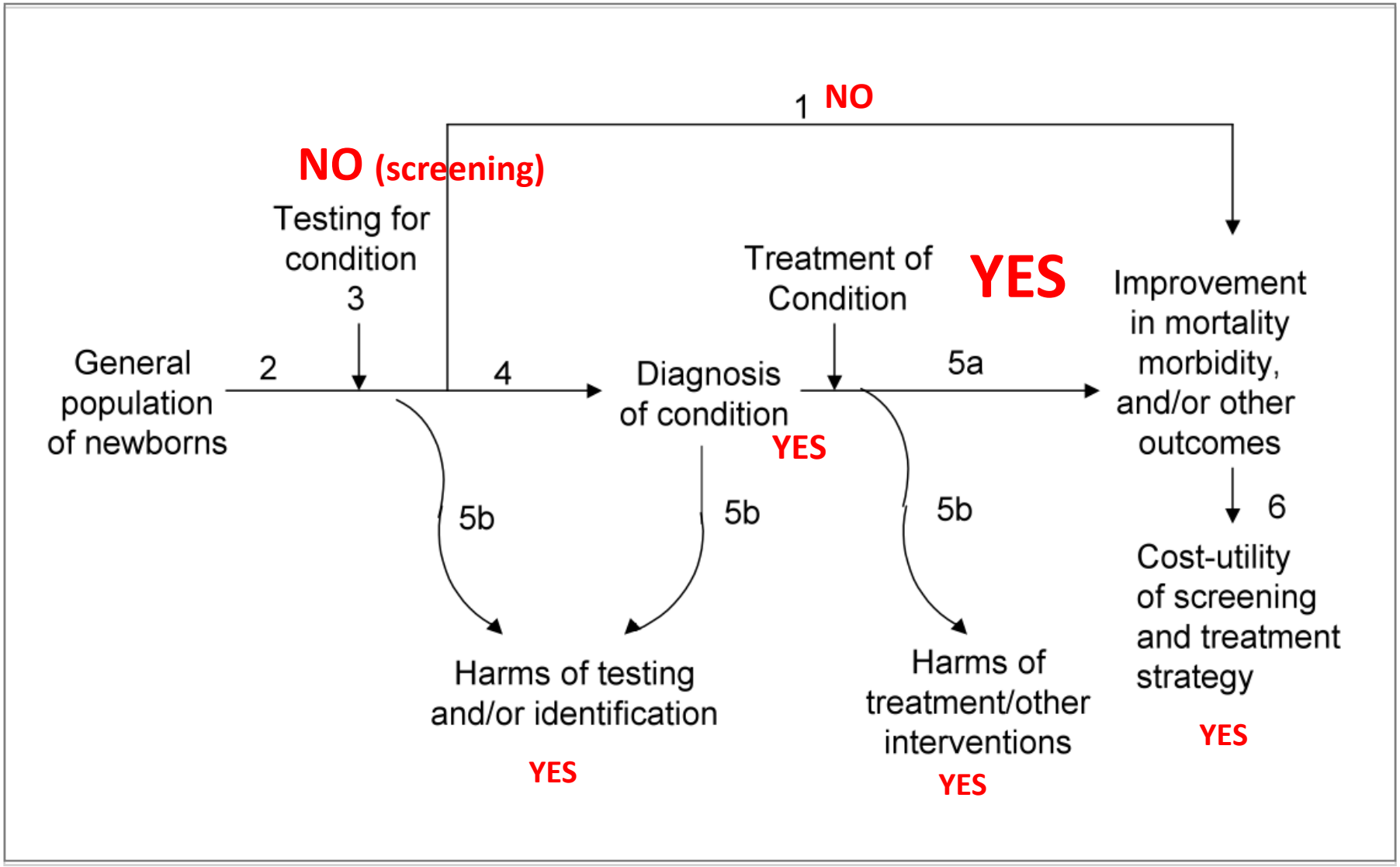
# Key Question 5

- What is the clinical utility of the screening test or screening algorithm?
- What are the benefits associated with use of the screening test?
  - Compelling benefit if diagnosis and treatment prior to 3.5 months or symptoms
  - Reduction of morbidity and mortality of identified cases
  - Additional cases missed without screening
- What are the harms associated with screening, diagnosis and treatment?
  - None identified or anticipated

# Key Question 6

- How cost effective is the screening, diagnosis and treatment for this disorder compared to usual clinical case detection and treatment?
- Yes
  - Minimal formal analysis
  - Probably beneficial based on cost of transplant *versus* treatment of disease diagnosed late

# Do We Have Enough Information?



# Summary

- Strong reasons for screening
- Gold standard diagnostic test
- Compelling treatment data drives the issue
- Inadequate evidence for analytic validity of screening test
- Recommend
  - Additional screening studies
  - Demonstration of technology transfer to broader base of labs

# Recommendation

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