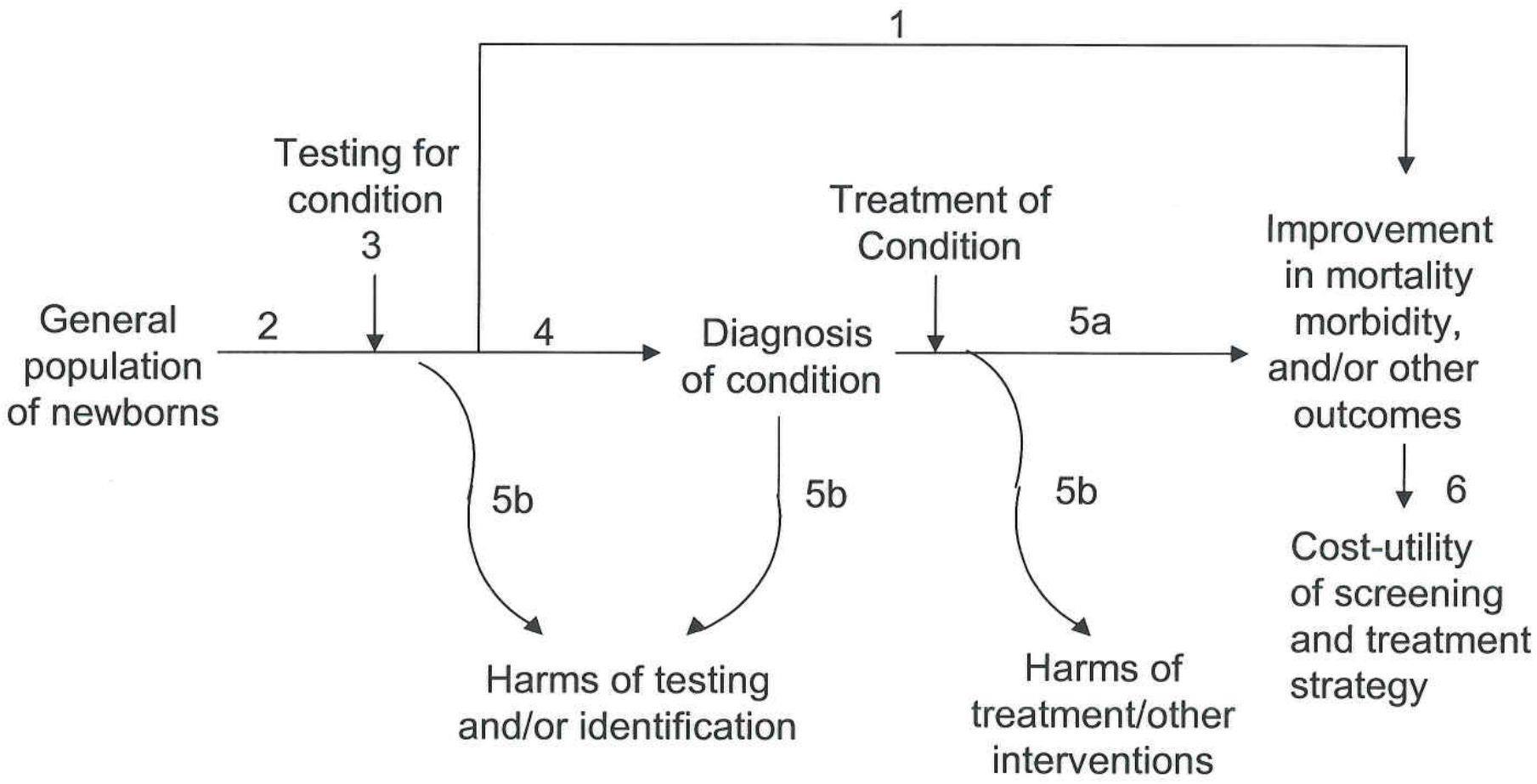
Decision Criteria and Process

Advisory Committee on Heritable Disorders in Newborns and Children February 26-27, 2009

Workgroup work status

- Analytic framework and key questions are set
- Minor editing of introductory sections still needed
- Need to decide how much discussion of how the decision of certainty of net benefit needs to be in the body vs. appendix
- Decision matrix needs some fine tuning
- Study design/quality appendices need additional work

Figure 1—Analytic Framework



Key question 1

- (Overarching question): 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?

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?

Key question 3

- Is there a screening test or screening test algorithm for the condition with sufficient analytic validity?

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?
  - » Is the evidence sufficient to conclude that we know what the clinical validity is?
  - » Is this level of clinical validity sufficient to justify testing?

Key question 5

- What is the clinical utility of the screening test or screening algorithm?
- **5a:** What are the benefits associated with use of the screening test?
- **5b:** What are the harms associated with screening, diagnosis and treatment?

Key question 6

- How cost effective is the screening, diagnosis and treatment for this disorder compared to usual clinical case detection and treatment?

Weighing the evidence

- Evaluate study quality
- Determine adequacy of evidence for each key question
- Determine adequacy of evidence across the key questions

Evaluate study quality

- Study design
- Threats to internal validity
- Threats to external validity/generalizability

Determine adequacy of evidence

- *Adequate evidence:* the observed estimate or effect is likely to be real, rather than explained by flawed study methodology, and the Advisory Committee concludes the results are unlikely to be strongly affected by the results of future studies
- *Inadequate evidence:* the observed results are more likely to be the result of limitations and/or flaws in study methodology rather than an accurate assessment, and subsequent information is more likely to change the estimate or effect enough to change the conclusion

Critical appraisal questions for determining adequacy

1. Do the studies have the appropriate research design to answer the key question?
2. To what extent are the studies of high quality (internal validity)?
3. To what extent are the studies generalizable to the US population (external validity)?
4. How many studies and how large have been done to answer the key question (precision of the evidence)?
5. How consistent are the studies?
6. Are there additional factors supporting conclusions

Translation into recommendations

- What is the magnitude of net benefit (are the benefits of screening, diagnosis and treatment minus the harms significant?)
- What is the overall adequacy of evidence (does the evidence overall meet the standards for having adequate quality?)
- What is the certainty of net benefit/harm (is the Committee sufficiently certain that the research supports a conclusion that benefits exceed harms or not?)

Decision Matrix

CATEGORY	RECOMMENDATION	LEVEL OF CERTAINTY	MAGNITUDE OF NET BENEFIT
1.	Recommend adding the condition to the core panel	Sufficient	Significant
2.	Recommend not adding the condition to the core panel	Sufficient	Zero or net harm
3.	Recommend not adding the condition, but instead recommend additional studies	Insufficient, but the potential for net benefit is compelling enough to recommend additional studies to evaluate	Potentially significant, and supported by contextual considerations
4.	Recommend not adding the condition now	Insufficient, and additional evidence is needed to make a conclusion about net benefit	Potentially significant or unknown

Category 1

- The Committee has sufficient certainty of significant net benefit to recommend adding the condition to the core panel

Category 2

- The Committee has sufficient certainty of no net benefit, or of net harm, to recommend not adding the condition to the core panel
- NOTE: this is “evidence of no benefit”, not “no evidence of benefit”

Category 3

- The evidence in insufficient to make a recommendation, however, there is compelling potential for net benefit and the Committee wants to make a strong recommendation for additional studies, such as pilot studies, to fill in the evidence gaps

Category 4

- The evidence is insufficient to make a recommendation
- There is insufficient evidence of potential net benefit to lead the Committee to want to make a strong recommendation regarding pilot studies
- An example might be a condition for which there is currently no treatment, and no evidence of other benefits that might be realized through early detection

Discussion