

Systematic Review Questions and AC Discussions

James M. Perrin, MD

Professor of Pediatrics, Harvard Medical School

Director, Center for Child and Adolescent Health Policy

MassGeneral Hospital *for Children*

Director, Evidence Review Group

Key Review Questions (2008 Discussions with AC)

- Incidence/prevalence
- Natural history
 - Timing of clinical onset
 - Severity of disease and variations
 - Genotype/phenotype
- Screening
 - Methods of screening
 - Accuracy of screening; sensitivity/specificity
 - Methods of diagnosis
 - Risks and costs

Key Review Questions II

- Treatment
 - Methods
 - Does treatment help?
 - Does early treatment help?
 - Availability
 - Risks and costs
- Critical information still needed

Possible AC Recommendations

- Recommend *adding* the condition to the core panel
- Recommend *not adding* the condition to the core panel
- Recommend not adding the condition, but instead recommend *additional studies*
- Recommend not adding the condition *now*

Category	Recommendation	Level of Certainty	Magnitude of Net Benefit
1	Recommend adding the condition to the uniform panel	Sufficient	Significant
2	Recommend not adding the condition to the uniform 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

Projects to Date

- Pompe disease
- Severe combined immunodeficiency (SCID)
- Krabbe disease
- Hemoglobin H disease (Hb H)
- Critical congenital cyanotic heart disease (CCCHD)
- (Kernicterus and bilirubin encephalopathy)

Pompe Disease

- Lack of population screening in US (or similar) population
- Case definition problems – early vs. late-onset
- General evidence re treatment for early infantile good, but complicated by CRIM – vs. CRIM +

Severe Combined Immunodeficiency

- Case definition challenging
- Lack of population screening at the time of review.
- General evidence for early identification and treatment good

Krabbe Disease

- Population screening data not conclusive
 - Challenge of early vs. late-onset
 - Especially, large number of false positives, not all followed
 - Questions re how well the test identifies children who can and will benefit from early treatment
- Diagnosis challenging
- Evidence that earlier treatment has better outcome in the short-term, but questions about long-term outcomes

Hb H

- Natural history of screen positive children unclear
- Evidence that early ID helps lacking
- Some evidence that treatment helps, but not for whom or when

Pulse Oximetry

- Case definition is challenging

Key Questions affecting AC Decisions

- Test issues
 - Test characteristics
 - Including early vs late, etc.
 - Population testing data
- Value of early identification
- Treatment helps – but not a major question in most conditions

Less Critical Data

- Incidence/prevalence
- Natural history – alone

Summary

- Certain topics more relevant to AC decision-making
- ERW focus on identifying information most helpful to the Advisory Committee

Possible Recommendations

Recommend *adding* the condition to the core panel

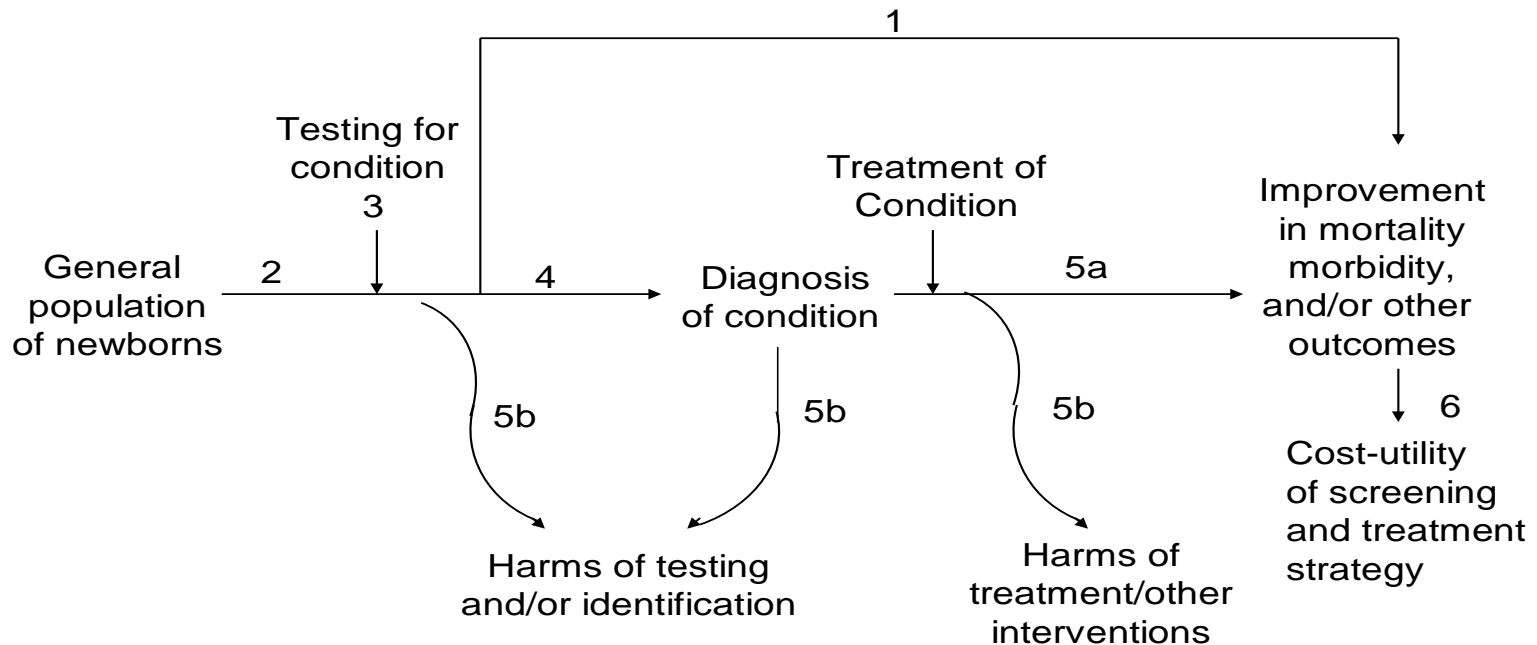
Recommend *not adding* the condition to the core panel

Recommend not adding the condition, but instead recommend *additional studies*

Recommend not adding the condition *now*

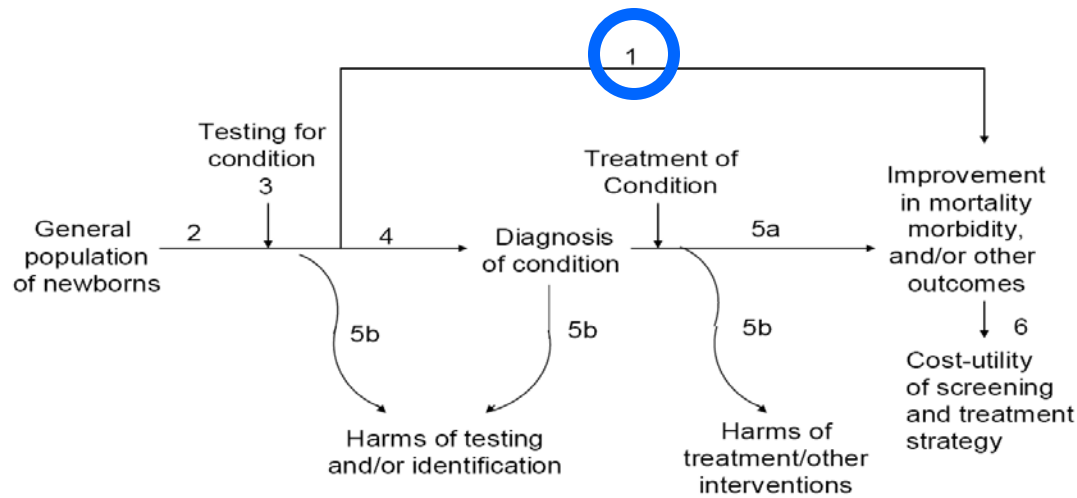
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Analytic Framework



The Decision Criteria and Process to be used in reviewing all nominations was approved and adopted by the Committee at the Feb 26-27, 2009 meeting

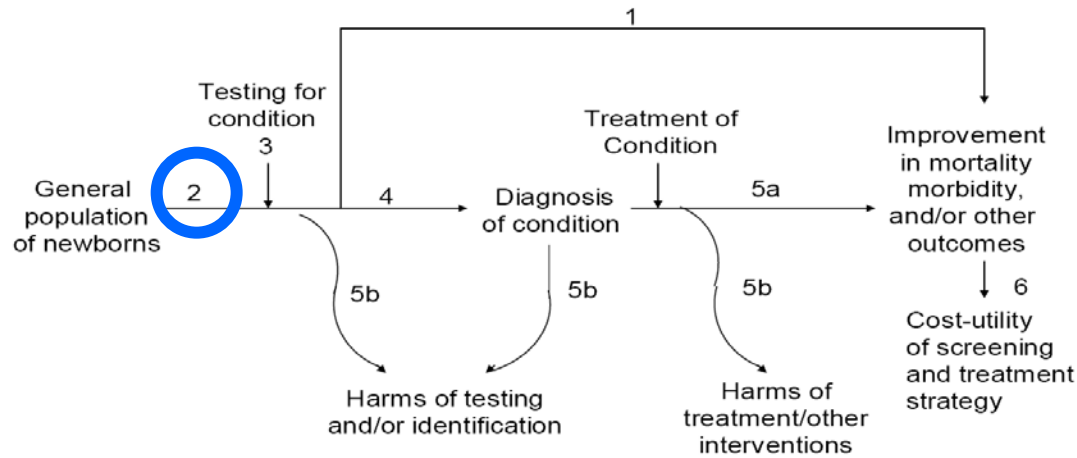
Key Question 1



Direct Evidence

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?

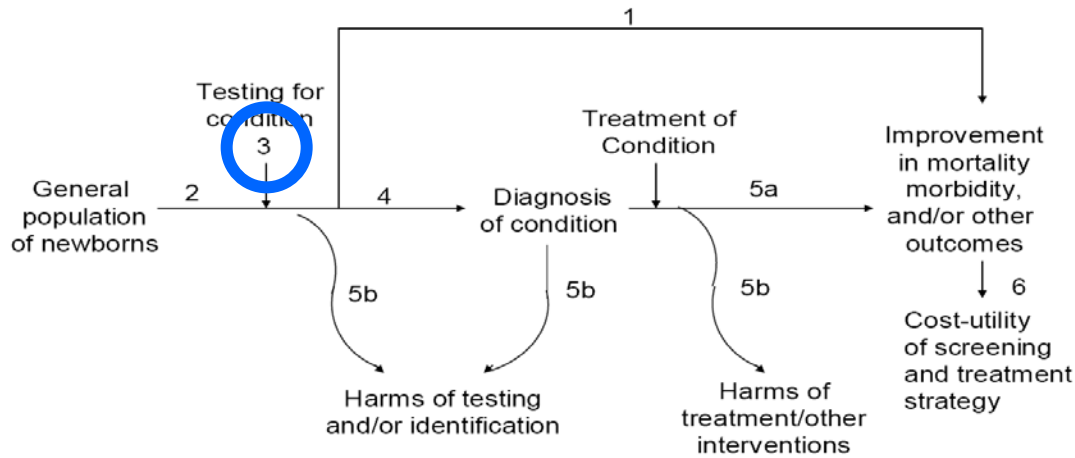
Key Question 2



Case Definition

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?

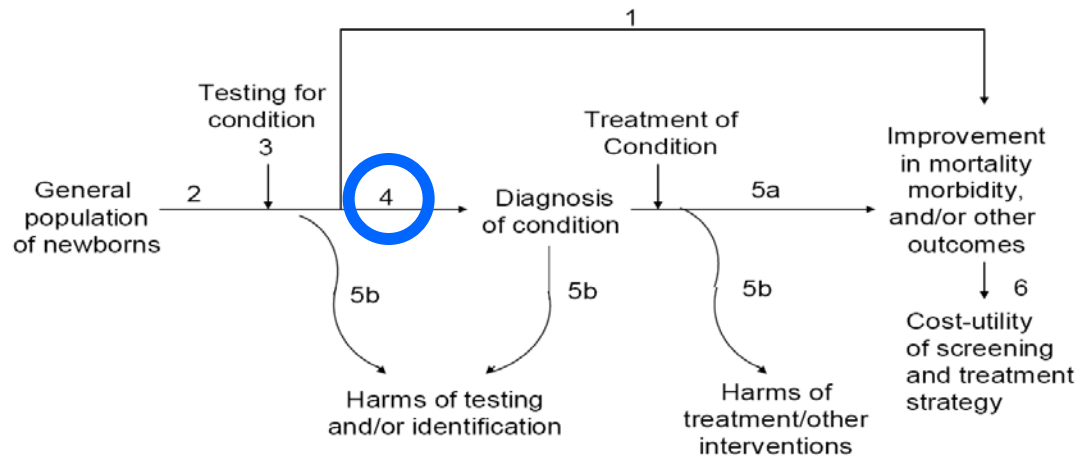
Key Question 3



Screening Test

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

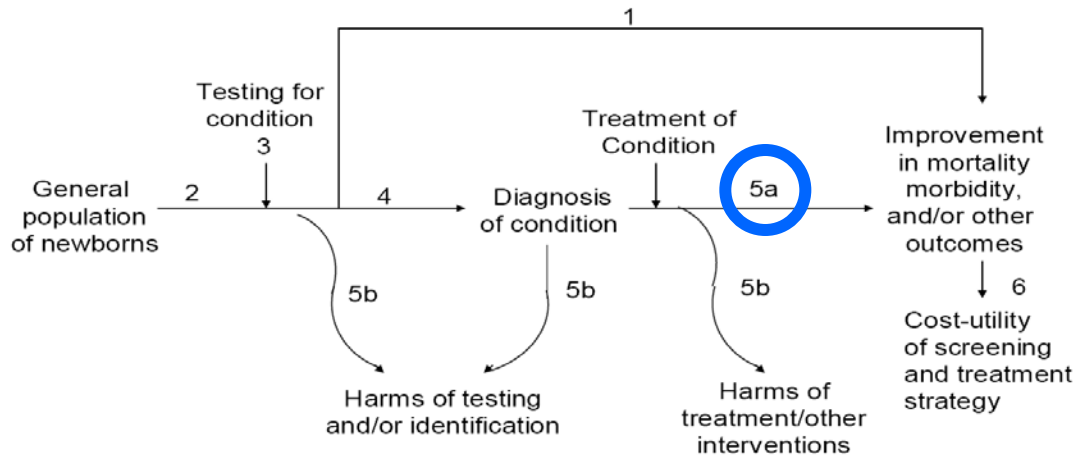
Key Question 4



Clinical Validity

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?

Key Question 5a

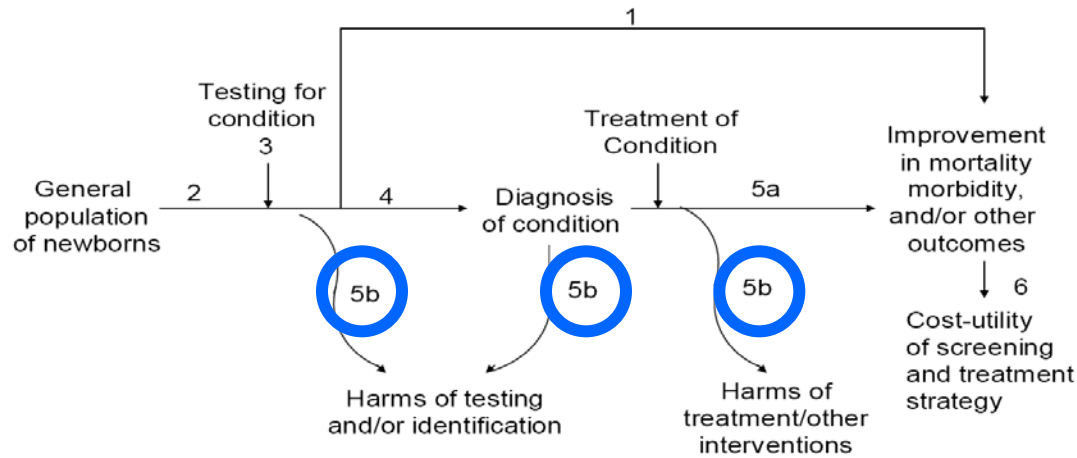


Benefits

What is the clinical utility of the screening test or screening algorithm?

- **5a**: What are the benefits associated with use of the screening test?

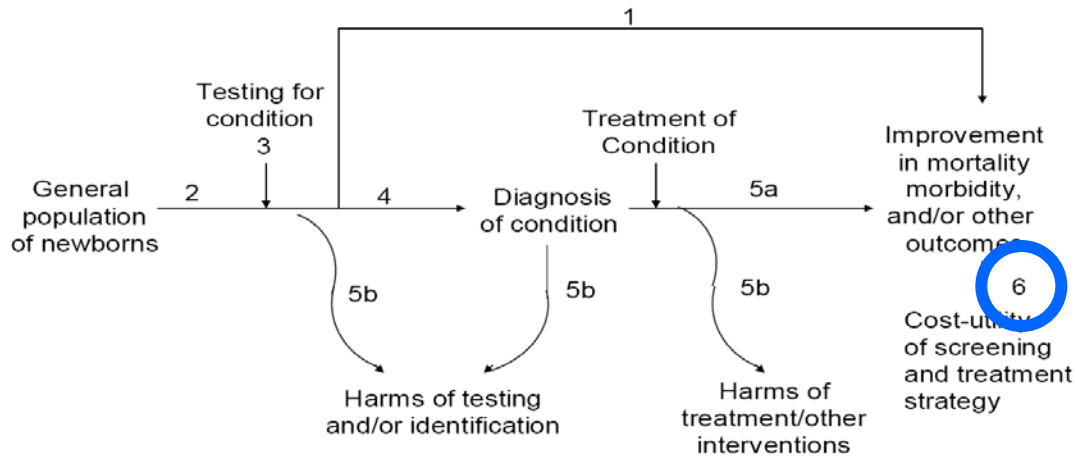
Key Question 5b



Harms

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

Key Question 6



Cost Effectiveness

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

Translating Evidence into Recommendations

- Judgment regarding the **magnitude of net benefit** (benefits minus harms)
- Judgment of the **adequacy of evidence** in answering the key questions
- Judgment of the **certainty of net benefit**