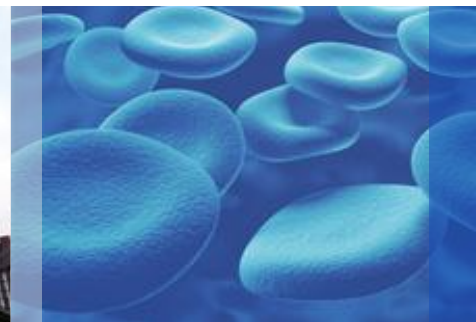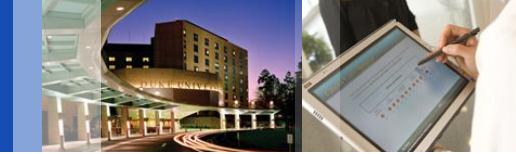# Duke Clinical Research Institute

Condition Review Process Report - Update

Alex R. Kemper, MD, MPH, MS

May 18, 2012

Meeting April 24-25, 2012

- HRSA
  - *Michael Lu*
  - *Sara Copeland*
  - *Lisa Vasquez*
  - *Debi Sarkar*
  - *Bonnie Strickland*
  - *Sarah Lunde-Feucht*
- AHRQ
  - *Denise Dougherty*
  - *Christine Chang*
- NIH
  - *Melissa Parisi*
  - *Tiina Urv*
- CDC
  - *Carla Cuthbert*
  - *Richard Olney*
- SACHDNC
  - *Joseph Bocchini*
  - *Steven McDonough*
- AMCHIP
  - *Christopher Kus*

- National Newborn Screening and Genetics Resource Center
  - *Brad Therrell*
- USPSTF
  - *Virginia Moyer*
- Community Guide
  - *Ned Caolnge*
  - *Randy Elders*
- EPC - Melissa McPheeters
- State NBS Programs
  - *Julie Luedtke*
  - *Sharmini Rogers*
  - *Anne Comeau*
- APHL
  - *Jelili Ojodu*
- Other Experts
  - *Aaron Goldenberg*
  - *Beth Tarini*
  - *Cindy Cameron*
  - *Janice Bach*
  - *Lisa Prosser*

Principles for Making Recommendations

- Recommendations are evidence based
- The outcomes that matter most are health benefits to the individual being screened
- Recommendations take into account the readiness and feasibility of screening within state public health systems
- Recommendations are not modified to accommodate concerns about insurance coverage, medico-legal liability, or legislation
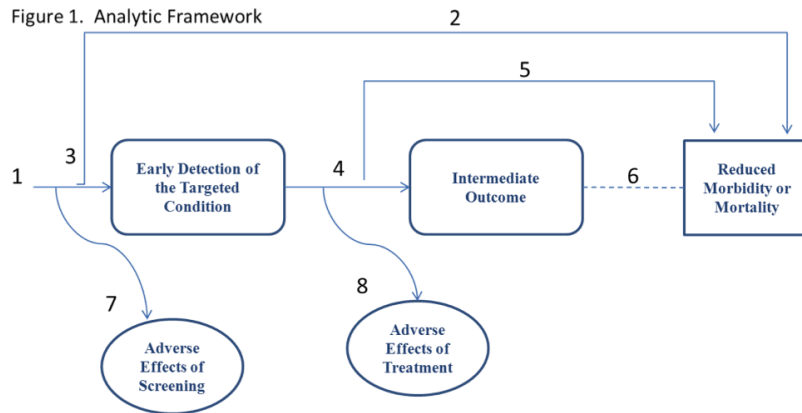
Evidence Reports

- Three components
  - *Systematic Evidence Review*
  - *Estimation of the bounds of benefit and harm*
  - *Assessment of readiness and feasibility of implementing comprehensive newborn screening from the state public health department perspective*

Analytic Framework

Figure 1. Analytic Framework

KQ1: What is the life course and spectrum of disease related to the condition?

KQ2: What is the direct evidence that screening for the condition reduces morbidity or mortality?

KQ3: What is the analytic validity and clinical validity of the screening test or algorithm?

KQ4: Are treatments available that make a difference in intermediate outcomes when the condition is caught early or detected by screening?

KQ5: Are treatments available that make a difference in health outcomes when the condition is caught early or detected by screening?

KQ6: How strong is the association between intermediate outcomes and health outcomes?
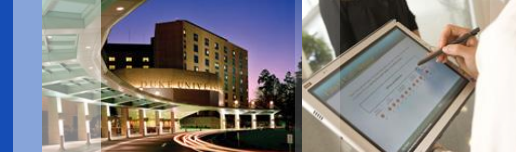
KQ7: What are the harms of the screening test?

KQ8: What are the harms of treatment?

Assessing Evidence at the Key Question Level

- Consider the entire body of evidence for each key question and the coherence of the evidence
  - *Convincing*
  - *Adequate*
  - *Inadequate*

Assessing the Magnitude of Net Benefit

- After evaluating each key question, consider the magnitude of net benefit across the entire population to be screened
  - *Negative: Harms outweigh the benefits*
  - *Zero to Small: Close balance of harms and benefits*
  - *Significant: Benefits outweigh harms*
- Costs are considered as a component of feasibility, separately evaluated
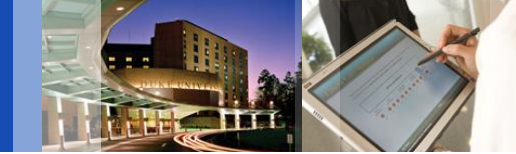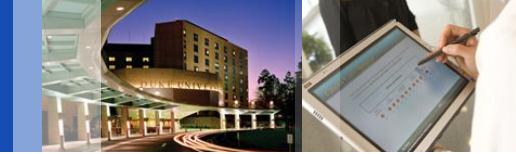
Assessing Certainty of the Evidence

- Judgment based on the following questions:
  - *Are there critical evidence gaps in any of the key questions?*
  - *To what extent are the results of the studies generalizable to newborns in the United States?*
  - *Do the studies have the appropriate research design to answer the key questions?*
  - *To what extent are the studies of adequate quality for each of the key questions?*
  - *What is the precision of the evidence for each key question?*
  - *How coherent are the studies for each key question?*

Assessing Certainty of the Evidence

- Certainty is classified into one of three categories:
  - *Low: Insufficient to have confidence in the assignment of net benefit*
  - *Moderate: Further research could change the magnitude or direction of findings within any of the key questions such that the assessment of net benefit would change*
  - *High: Assignment of net benefit is unlikely to be strongly affected by the results of future studies*

Estimation of the Bounds of Benefit and Harms

- Decision-analytic modeling
- Similar to what was done for the hyperbili report
- Key inputs
  - *Prevalence*
  - *Test accuracy*
  - *Treatment Effectiveness*
  - *Estimation of harm*
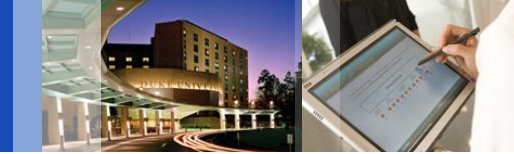
Matrix One: Net Benefit Assessment

CERTAINTY OF NET BENEFIT	MAGNITUDE OF NET BENEFIT		
	Significant	Small to zero	Negative
High	A	C	D
Moderate	B	C	D
Low	L		

A: There is high certainty that adoption of screening for the targeted condition would lead to a significant net benefit. The Advisory Committee will next evaluate readiness and feasibility of screening to develop a recommendation regarding inclusion of the condition in the RUSP.

B. There is moderate certainty that adoption of screening for the targeted condition would lead to a significant net benefit. The Advisory Committee will not further evaluate readiness or feasibility in order to develop a recommendation regarding inclusion of the condition in the RUSP.

C. There is high or moderate certainty that adoption of screening for the targeted condition would lead to a small to zero net benefit. The Advisory Committee will not further evaluate readiness or feasibility in order to develop a recommendation regarding inclusion of the condition in the RUSP.

D. There is high or moderate certainty that adoption of screening for the targeted condition would lead to small to a negative net benefit. The Advisory Committee will not further evaluate readiness or feasibility in order to develop a recommendation regarding inclusion of the condition in the RUSP.

L. There is low certainty regarding any potential net benefit from screening. The Advisory Committee will not further evaluate readiness or feasibility in order to develop a recommendation regarding inclusion of the condition in the RUSP.

Assessing Readiness

- Only for conditions with an "A" code
- Readiness depends on the current availability of
  - *Validated high-throughput approach to screening*
  - *Systems for training and education*
  - *Processes for quality assurance*
  - *Information systems*
  - *Diagnostic Services*
  - *Treatment and systems for follow-up*
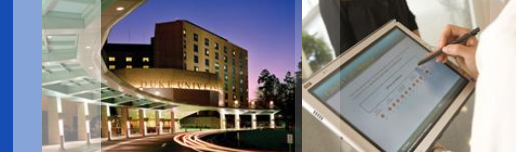
Assessing Readiness

- Readiness is classified into one of three categories:
  - *Ready*
  - *Developmental: Further work is needed*
  - *Unprepared: Significant challenges in immediately adopting comprehensive screening*
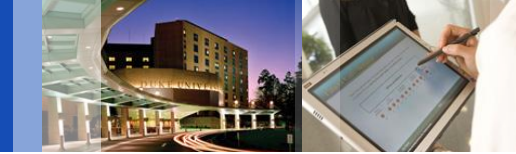
Assessing Feasibility

- Feasibility considers the
  - *Availability of screening technology, diagnostic testing, treatment, follow-up*
  - *Direct costs to the public health system*
  - *Other indirect or induced costs*
- Classified into one of three categories:
  - *High: Resources for screening are available and cost of screening is balanced against other public health obligations*
  - *Moderate: Resources not readily available but implementation is possible within the financial constraints of public health programs*
  - *Low: Resources for screening are not available or the cost of screening is prohibitive*

Assessment of Readiness and Feasibility

- Key informant interviews from representative states
- Guided interview – questions specific to the condition
- Costs likely difficult to assess, but ranges will be informative

Matrix Two: Readiness and Feasibility

FEASIBILITY	READINESS		
	Ready	Developmental	Unprepared
High	1	3	5
Moderate	2	4	6
Low	7		

1. Screening for the targeted condition is highly feasible and most state public health programs are ready to begin comprehensive newborn screening.
2. Screening for the targeted condition is moderately feasible and most state public health programs are ready for comprehensive newborn screening.
3. Screening for the targeted condition is highly feasible and most state public health programs have developmental readiness for comprehensive newborn screening.
4. Screening for the targeted condition is moderately feasible and most state public health programs have developmental readiness for comprehensive newborn screening.
5. Screening for the targeted condition is highly feasible and most state public health programs are unprepared to implement comprehensive newborn screening.
6. Screening for the targeted condition is moderately feasible and most state public health programs are unprepared to implement comprehensive newborn screening.
7. Implementation of screening for the targeted condition has low feasibility.

Combining both matrices….

NET BENEFIT		READINESS			FEASIBILITY
		Ready	**Developmental**	**Unprepared**	
Significant Benefit	**High Certainty**	**A1** Screening for the condition is BENEFICIAL, and is Feasible for most PH systems to obtain needed resources. Most PH programs are Ready to implement. **The condition is recommended to be added to the RUSP.**	**A3** Screening for the condition is BENEFICIAL, and is Feasible for most PH systems to obtain needed resources. Most PH programs have Developmental Readiness to implement. SOME WORK is required for PH systems to Become Ready	**A5** Screening for the condition is BENEFICIAL, and is Feasible for most PH systems to obtain needed resources. However, most PH programs are Unprepared and Not Ready to implement. SIGNIFICANT WORK is required to Prepare and Ready PH systems.	**High Feasibility**
		A2 Screening for the condition is BENEFICIAL. It is Moderately Feasible for most PH programs to obtain needed resources. Most PH programs are Ready to implement screening. SOME RESOURCES are needed by most PH systems.	**A4** Screening for the condition is BENEFICIAL. It is Moderately Feasible for most PH programs to obtain needed resources. Most PH programs have Developmental Readiness to implement. SOME RESOURCES are needed by most PH systems and SOME WORK is required for PH systems to Become Ready.	**A6** Screening for the condition is BENEFICIAL. It is Moderately Feasible for most PH programs to obtain necessary resources. Most PH programs are Unprepared and Not Ready to implement. SOME RESOURCES are needed by most PH systems and SIGNIFICANT WORK is required for PH systems to Become Prepared and Ready .	**Moderate Feasibility**
		A7 Screening for the condition is BENEFICIAL. However, there is Low Feasibility that most PH systems can obtain needed resources. Most PH programs are Unprepared and Not Ready to implement. SIGNIFICANT RESOURCES are needed by most PH systems and SIGNIFICANT WORK is required for PH systems to Become Prepared and Ready			**Low Feasibility**
	Moderate Certainty	**B** Specific research is required to address uncertainty regarding the net benefit of screening for the condition.			----
Small Benefit	**High or Moderate Certainty**	**C** There is high or moderate certainty that adoption of screening for the targeted condition would lead to a small to zero net benefit. The Advisory Committee will not further evaluate readiness or feasibility in order to develop a recommendation regarding inclusion of the condition in the RUSP.			----
Neg Benefit		**D** There is high or moderate certainty that adoption of screening for the targeted condition would lead to small to a negative net benefit. The Advisory Committee will not further evaluate readiness or feasibility in order to develop a recommendation regarding inclusion of the condition in the RUSP.			----
Low Certainty of Net Benefit		**L** There is low certainty regarding any potential net benefit from screening. The Advisory Committee will not further evaluate readiness or feasibility in order to develop a recommendation regarding inclusion of the condition in the RUSP.			----

Next Steps

- Advisory Committee will need to approve decision-making process
  - *Document in final revision with meeting attendees*
  - *Plan: Vote at the next Advisory Committee meeting*
- Methods for evidence review similar to what has been done in the past – does not require a vote and we can move forward on new topics

Questions?