Evidence Review Group: Past to Present

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Introduction

• 2007 - MCHB agreement with MassGeneral Hospital for Children and Duke Clinical Research Institute to outline and test a process for systematic evidence review development

• 2008 - MCHB expanded scope to include specific evidence reviews to help the AC inform their decision making
Guiding Principles

• Adapt established evidence review processes for screening or treatment programs

• Transparency in data abstraction and review

• Recognition of the special challenges regarding evidence about rare diseases

• Public access and input to the process
ERG Members

- **Anne Comeau, PhD**
  New England Newborn Screening Program/UMass Medical School (public health screening perspective)

- **Nancy S. Green, MD**
  Columbia University (public health/newborn screening)

- **Alex R. Kemper, MD, MPH, MS**
  Duke University (epidemiology/methods/newborn screening)

- **Lisa A. Prosser, PhD**
  University of Michigan Health System (economics/cost/benefit analyses)

- **Denise Queally**
  Consumer (PKU Family Coalition)

- **Alixandra A. Knapp, MS**
  MGH/Harvard (project coordinator)

- **Danielle R. Metterville, MS, CGC**
  MGH/Harvard (genetic counselor)

- **James M. Perrin, MD**
  MGH/Harvard (policy, chronic conditions)
Evidence Review Procedures

• Objectives of Review
  – Provide timely information to the AC in their consideration of additions to routine newborn screening

• Clear conflict of interest policy
  – Include all staff, consultants, and collaborators

• All decisions by AC
  – ERG makes no recommendations
Development of Key Questions and Case Definition

• Assemble Technical Expert Panel for each condition to refine case definition and discuss pertinent key questions

• Case definition agreed upon by the ERG and the AC Nomination and Prioritization Committee
Systematic Review Methods: Literature Review

- Study selection, data abstraction, and review
  - Medline, OVID In-Process, and Other Non-Indexed Citations for all relevant screening studies on nominated condition over 20 year period

- Inclusion/exclusion criteria
  - Peer-reviewed published literature
  - English language only
  - Human studies only
  - Review consensus statements as guides, not for abstraction
  - Pertinent material: meets case definition, answers key question

- Data abstraction and quality assessment
  - Three investigators review all abstracts and independently abstract a subset of articles (~20%)
  - Standard quality assessment methods
Systematic Review: Expert Contact

• Consultation with key investigators and advocates via systematic questionnaires and conference calls re key questions, impact and severity estimates, and identification of relevant unpublished data

• Analyses of (any) additional raw data from unpublished sources
Evidence Review
Results and Summary

• Results
  – Follow order and content of main questions
  – Decision analyses/decision model findings (outcomes tables)

• Summary
  – Key findings in summary and table form
  – Indicate where evidence is absent and what information would be most critical
    • What do we not know and level of uncertainty
    • What new information/studies would most help AC decisions

• All decisions by AC – evidence group makes no recommendations
Evidence Key Questions

Overarching question

– Is there direct evidence that screening at birth leads to improved outcomes for the infant or child screened or for the child’s family?
Evidence Key Questions

Condition

• Is there a case definition that can be uniformly and reliably applied?
• Natural history and spectrum of disease?
• Incidence and severity of condition health impact
Evidence Key Questions

Screening Test

• Analytic validity?
• Utilities: sensitivity, specificity, predictive values
• Clinical validity of screening test, in combination with the diagnostic test
• Timing of screening and follow-up
• Population-based screening evidence
Evidence Key Questions

Treatment

• Does treatment of screen-detected condition improve important health outcomes compared with waiting until clinical detection?
• Are treatments standardized, widely available, and if appropriate, FDA approved?
• Are there subsets of affected children more likely to benefit from treatment that can be identified through testing or clinical findings?
Benefits, Harms, and Costs

• What are benefits of treatment?
  – Maximum number of potential beneficiaries

• Harms or risks of
  – Screening
  – Diagnosis
  – Treatment

• What are costs
  – Screening, diagnosis, treatment, delayed treatment, failure to diagnose in newborn period
Challenges

- Lack of clear case definition (variants along a spectrum of disease severity) (Krabbe Disease)
- Rare conditions
  - High severity (often fatal outcomes)
  - Lack of randomized trials in almost all cases
- Population studies of screening for rare conditions often require several years even in large populations to document sensitivity and specificity (SCID)
- Evidence regarding these conditions typically lacks costs and benefits information across all potential outcomes
- Critical sources of information for rare conditions may be unpublished (Pompe Disease)
ERG Final Reports

• Nov 2008 – Pompe Disease
• May 2009 – Severe Combined Immunodeficiency
• Sept 2009 – Krabbe Disease
• May 2010 – Hemoglobin H Disease
• Sept 2010 – Critical Congenital Cyanotic Heart Disease
• May 2011 – Neonatal Hyperbilirubinemia (preliminary)
Other ERG Activities

- March 2010 – *Genetics in Medicine* publication on ERG Process
- May 2010 – *Pediatrics* publication on Severe Combined Immunodeficiency evidence review
- Sept 2010 – *Genetics in Medicine* publication on Krabbe disease evidence review
- May 2011 – *Journal of Pediatrics* publication on Hb H disease evidence review
Thank you