Evidence Review Group: Past to Present

James M. Perrin, MD
Professor of Pediatrics, Harvard Medical School
MGH Center for Child and Adolescent Health Policy
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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
- March 2011 – Established Evidence Evaluation Methods (EEM) Workgroup
- May 2011 – *Journal of Pediatrics* publication on Hb H disease evidence review

Thank you