

Long term follow up after NBS: the Inborn Errors of Metabolism Registry

Susan A. Berry, M.D.
Nancy Vanderburg

For the
Region 4 Long Term Follow Up
and Clinical Outcomes Workgroup

Region 4 Collaborators

Metabolic Clinicians and State Health Department NBS Specialists

- ◆ Illinois
- ◆ Indiana
- ◆ Kentucky
- ◆ Michigan
- ◆ Minnesota
- ◆ Ohio
- ◆ Wisconsin

Expanded NBS: a national priority

- ◆ Justice - all should be screened equally
- ◆ NBS should improve outcomes and save lives
- ◆ NBS is only as effective as the care it prompts
- ◆ Collaboration between screening, short term, and long term team members is critical to improved outcomes
- ◆ Data sharing is essential

The potential for advancing care for babies in Region 4

- ◆ Approximately 800,000 births
- ◆ Commitment to cooperative interaction
- ◆ All states screening by MS/MS
- ◆ Selected disorders common enough to develop protocols

Treatment of Inborn Errors of Metabolism

- ◆ Reduce the offending material
- ◆ Augment activity if possible
(vitamins, cofactors, medications)
- ◆ Provide alternative fuels
- ◆ Follow up

(is this all there is? How would we know?)

How do practitioners decide how to treat inborn errors of metabolism?

- ◆ How did your mentor treat?
- ◆ What does the (text/manual/guide) say?
- ◆ What have you learned from experience?
- ◆ What does metab-I say?

We tend not to have had any uniform or organized strategy

Evidence-based medicine (EBM) in inborn errors of metabolism (IBE)

- ◆ Currency for EBM: controlled trials
- ◆ To date, very few controlled trials have been done in IBE
- ◆ Why?
 - ✎ Rare diseases
 - ✎ Primarily children

Strategies for encouraging EBM in IBE

- ◆ Collaboration between centers
- ◆ Federal and state support to encourage
- ◆ Teaching principles of EBM in clinical genetics training
- ◆ Improving precision of terminology so published reports are accessed in appropriate searches
- ◆ Publication of systematic reviews of IBE management

(adapted from Steiner: Amer J Med Genet 134A:192, 2005)

Can this even be done?

- ◆ Substantial precedent in treatment of childhood cancer
 - ✎ Also rare diseases
 - ✎ Achieved national cooperation
- ◆ Result: almost all children with cancer are treated on protocols

Challenges presented in doing trials for treatment in IBE

- ◆ Diseases are rare
- ◆ Diseases affect primarily children
- ◆ Spectrum of clinical severity
- ◆ Hard to justify testing accepted treatments that seem to work
- ◆ Who will pay?

Preliminary thought : select a condition and treat using a uniform protocol (May 2005)

- ◆ Suggested disorder: MCAD
- ◆ Incidence 1:10600 (MN) so ~ 70/yr
- ◆ Therapy critical element agreed upon (prevention of fasting)
- ◆ Other elements of treatment plan anecdotal
 - ✎ Carnitine?
 - ✎ Cornstarch?
 - ✎ Diet modification?

But: we didn't have the patients!
Where to start?

MCAD: suggested treatment and follow up protocol

- ◆ Review the suggested plans for treatment
- ◆ Identify elements that all agree are essential and that should be done uniformly
- ◆ Identify elements that are anecdotal and could be subject to randomization
- ✓ *All contributed treatment protocols so elements of difference could be characterized*

Long Term F/U Workgroup: evolution of our plan

- ◆ May 2005 - Workgroup meets and agrees to adopt the model of gathering a dataset about NBS outcomes
- ◆ We agree to focus on one disorder
- ◆ We agree to start with MCAD deficiency
- ◆ General approach is to
 - ✎ Define critical knowledge elements
 - ✎ Collect information about current treatment plans
 - ✎ Agree to work together in each state to gather data
- ◆ Apply for “mini-grant” for planning

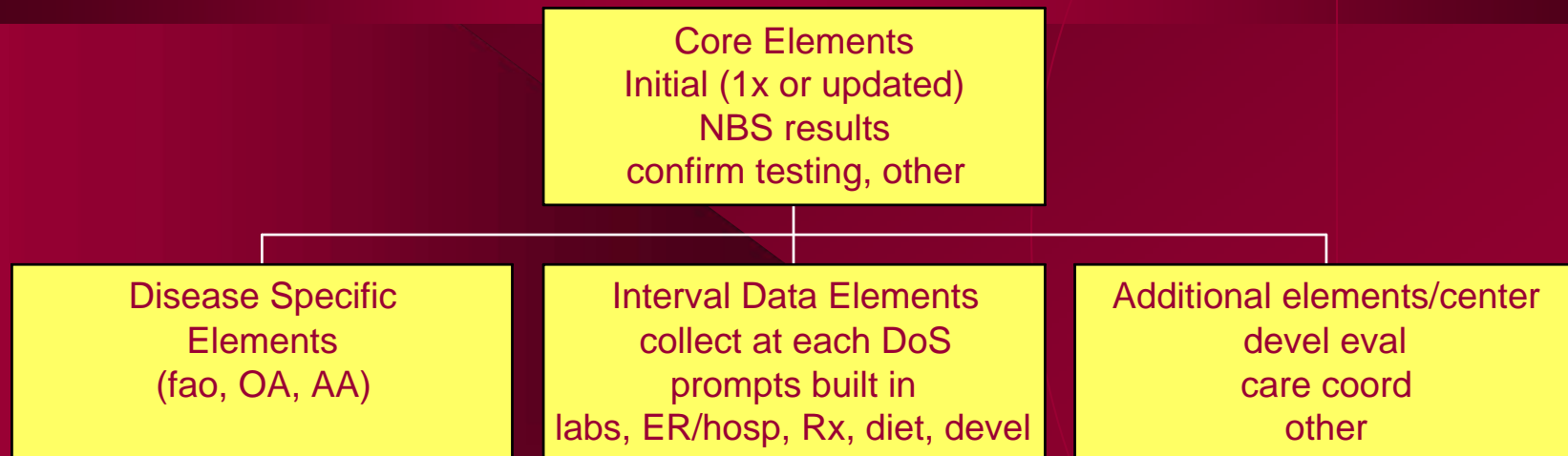
Step 2: Minigrant proposal

- ◆ Each state has a metabolic clinician lead identified
- ◆ Metabolic leads not in workgroup are added to group
- ◆ All states share their treatment protocols for conditions
- ◆ Draft elements for registry are assembled
- ◆ Funding is requested / awarded for a planning meeting for deriving consensus on data elements
- ◆ All metabolic clinician leads attend a one day gathering
- ✓ *All agree to the elements for inclusion*

Critical planning agreements

- ◆ Data: ease of entry
- ◆ Web based with option of paper checklist for use during visits
- ◆ Local control of PHI
- ◆ All participants have access, but at varying levels
 - ✎ Local enrolling centers
 - ✎ Departments of Health
- ◆ All agree to shared participation in studies and in subsequent publication
- ◆ All agree to serve as advisory group to plan for access to database for projects
- ◆ Initial projects to define natural history, outcomes
- ◆ *Ultimate plan is to request that enrolled subjects become potential participants in trials*

Plan: a relational database



Goal: add other disorders, keeping core and interval elements, adding disease-specific elements, center-specific elements

Where are we now?

- ◆ Achieved agreement on registry elements
- ◆ Selected a probable “host” using Web-based EMR technology
- ◆ Engaged the majority of treating centers in Region 4
 - ✎ Added additional metabolic leads in larger states
- ◆ Have sought IRB approval for the registry at UMN
 - ✎ Pilot in MN
- ◆ Will share IRB protocol for others
- ◆ Anticipating needs for funding ongoing
- ◆ Plan for integration of registry into other efforts

What next?

- ◆ We really have to enter subjects
- ◆ Initiating projects (Shawn McCandless, for example)
- ◆ Can we pick a strategy?
 - ✎ Generally uniform f/u and reporting
 - ✎ consensus questions to ask
- ◆ If successful, add additional conditions
 - ✎ OA - 3MCC deficiency?
 - ✎ AA - (decide??)

Acknowledgements

- ◆ Nancy Vanderburg - Co-Leader
- ◆ Kristi Bentler
- ◆ Carolyn Anderson
- ◆ All Committee Members
- ◆ All State Metabolic Leads

Dedicated to the memory of Becky Wappner