

Early Intervention and Newborn Screening



Advisory Committee on Heritable Disorders in
Newborns and Children

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Goals

- Provide a brief overview of Early Intervention (EI) in the United States
 - We will use “early intervention” as a generic term
 - We will use “Early Intervention” or EI when referencing the Part C Early Intervention component of the Individuals with Disabilities Education Act
- Present findings from a study to determine which current NBS conditions could be eligible for EI and in which states
- Suggest some next steps for NBS, EI and the ACHDNC

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Newborn Screening Conditions: Early Intervention and Probability of Developmental Delay

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ABSTRACT: *Objectives:* The purpose of this study is to explore which newborn screening (NBS) conditions are automatically eligible for early intervention (EI) across states and to determine the extent to which each disorder *should* automatically qualify for EI because of a high probability of developmental delay. *Methods:* We examined each state's EI eligibility policy and reviewed the literature documenting developmental outcomes for each NBS condition. Using a novel matrix, we assessed the risk of developmental delay, medical complexity, and risk of episodic decompensation, revising the matrix iteratively until reaching consensus. Three NBS conditions (biotinidase deficiency, severe combined immunodeficiency, and propionic acidemia) are presented in detail as examples. *Results:* Most states (88%) had Established Conditions lists to auto-qualify children to EI. The average number of NBS conditions listed was 7.8 (range 0–34). Each condition appeared on average in 11.7 Established Conditions lists (range 2–29). After the literature review and consensus process, 29 conditions were likely to meet national criteria for an Established Condition. *Conclusion:* Despite benefiting from NBS and timely treatment, many children diagnosed with NBS conditions are at risk for developmental delays and significant medical complexity. The results demonstrate a need for more clarity and guidance regarding which children should qualify for EI. We suggest that most NBS conditions should automatically qualify based on the probability of resulting in a developmental delay. These findings suggest a future opportunity for collaboration between NBS and EI programs to create a consistent set of Established Conditions, potentially expediate referrals of eligible children, and streamline children's access to EI services.

(*J Dev Behav Pediatr* 00:1–9, 2023) **Index terms:** newborn screening, early intervention, developmental delay.



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Net benefit figures prominently in many different arenas – medicine, economics, business, government

Therapeutic Innovation & Regulatory Science (2021) 55:129–137
<https://doi.org/10.1007/s43441-020-00197-1>

ORIGINAL RESEARCH

Predicting Regulatory Product Approvals Using a Proposed Quantitative Version of FDA's Benefit–Risk Framework to Calculate Net-Benefit Score and Benefit–Risk Ratio



Journal of Clinical Epidemiology
 Volume 137, September 2021, Pages 148–158



Original Article
The Net Benefit of a treatment should take the correlation between benefits and harms into account



Prevention and Treatment of Cardiovascular Disease - Original Research



Net benefit of statins for primary prevention of cardiovascular disease in people 75 years or older: a benefit–harm balance modeling study



FORM SSA-1099 – SOCIAL SECURITY BENEFIT STATEMENT

2020 • PART OF YOUR SOCIAL SECURITY BENEFITS SHOWN IN BOX 5 MAY BE TAXABLE INCOME.
 • SEE THE REVERSE FOR MORE INFORMATION.

Box 1. Name		Box 2. Beneficiary's Social Security Number
Box 3. Benefits Paid in 2020	Box 4. Benefits Repaid to SSA in 2020	Box 5. Net Benefits for 2020 (Box 3 minus Box 4)

What is Net Tangible Benefit And What All Are Included In It?

© READ TIME: 7 MINUTES | BY AMANDA BYFORD



Advisory Committee on Heritable Disorders in Newborns and Children



NET BENEFIT/ CERTAINTY		READINESS			FEASIBILITY		
		Ready	Developmental	Unprepared			
SIGNIFICANT Benefit	Certainty	HIGH	<p>A1</p> <p>Screening for the condition has a high certainty of significant net benefits, screening has high or moderate feasibility. Most public health departments are ready to screen.</p>	<p>A2</p> <p>Screening for the condition has a high certainty of significant net benefits and screening has high or moderate feasibility. Public health departments have only developmental readiness.</p>	<p>A3</p> <p>Screening for the condition has a high certainty of significant net benefits and screening has high or moderate feasibility. Public health departments are unprepared for screening.</p>	Feasibility	HIGH or MODERATE
		MOD	<p>A4</p> <p>There is high certainty that screening would have a significant benefit; however, most health departments have low feasibility of implementing population screening.</p>				LOW
Small to ZERO Benefit	Certainty	HIGH	<p>B 1-4</p> <p>There is moderate certainty that screening would have a significant benefit.</p>				---
NEG Benefit		MOD/HIGH	<p>C 1-4</p> <p>There is high or moderate certainty that adoption of screening for the targeted condition would have a small to zero net benefit.</p>				---
---		LOW	<p>D 1-4</p> <p>There is high or moderate certainty that adoption of screening for the targeted condition would have a negative net benefit.</p>				---
---	---	---	<p>L 1-4</p> <p>There is low certainty regarding the potential net benefit from screening.</p>				---

We have been thinking about early intervention as a potential NBS benefit for a long time!

COMMENTARIES

Newborn Screening for Developmental Disabilities: Reframing Presumptive Benefit

A fundamental tenet of
newborn screening is that

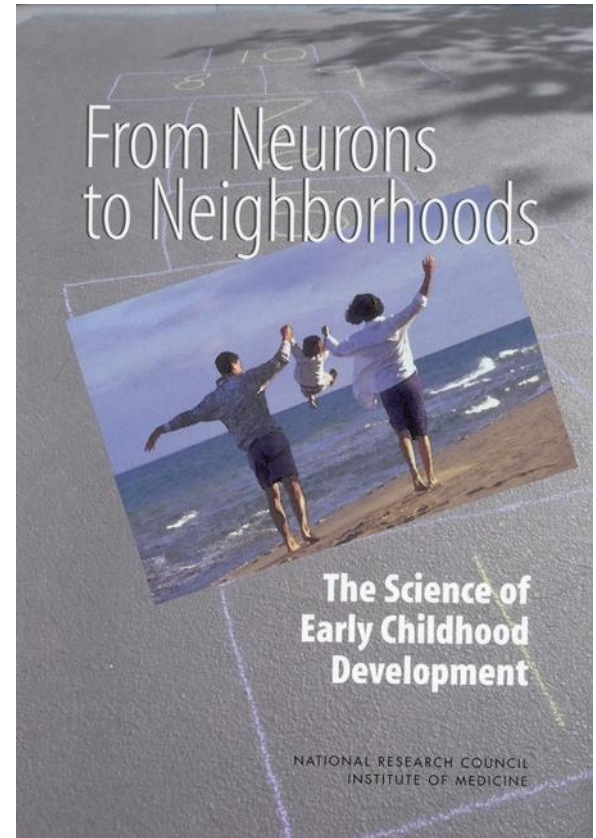
Donald B. Bailey Jr, PhD, Debra Skinner, PhD, and Steven F. Warren, PhD



(*AJPH*, 2005)

Why is early intervention important?

- The first three years of life constitute an especially formative time in human development
- Parents provide essential care, support development through everyday interactions, and advocate for their children
- Early intervention programs can support families and children by providing access to specialized interventions and therapies
- Early intervention can provide an additive benefit to medical or dietary treatments



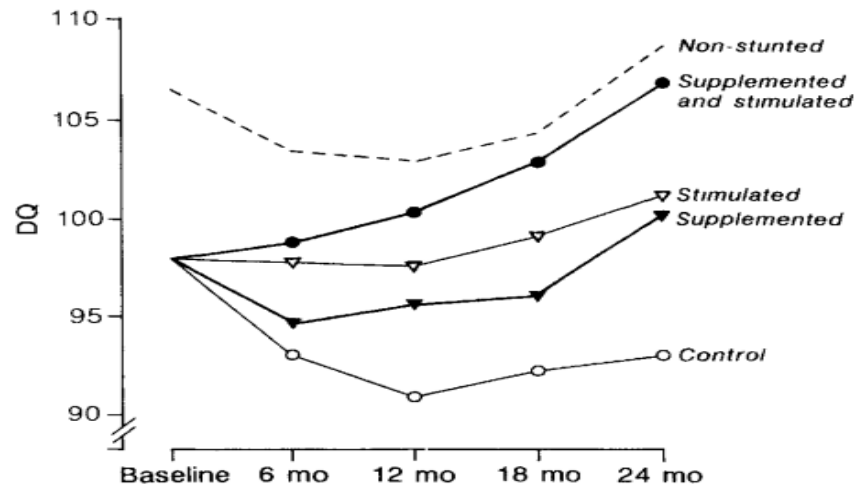
(2000)

Early stimulation has an additive effect on a nutritional supplement

Providing supplementation and early learning opportunities to malnourished Jamaican children improves development, with effects that last throughout life (Gratham-McGregor, 1991)

VOL 338: JULY 6, 1991

THE LANCET

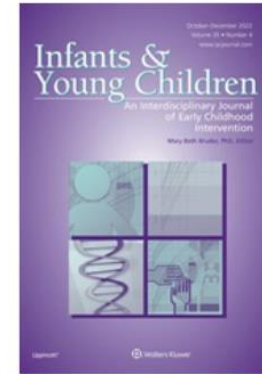


Mean DQs of stunted groups adjusted for initial age and score, compared with non-stunted group adjusted for age only.

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EI and NBS: Two programs, one goal, two paths

- EI and NBS rest on the same basic assumption:
Treatments or services for children with special health care needs or disabilities must begin as early as possible to maximize benefits
- Both are long-standing state-based programs guided by national requirements or recommendations
- Both have well-established ways to identify children and provide services
- But there are major differences in assumptions and approaches
- Unfortunately, the two programs operate in virtually independent spheres



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Early Intervention and Newborn Screening Parallel Roads or Divergent Highways?

Donald B. Bailey Jr., PhD

Early intervention in the U.S.

- Federal legislation provides guidance to states and incentives for serving infants and toddlers with disabilities
- Children must have a documented developmental delay or an “established condition” likely to lead to a delay
- Referral to EI can come from a variety of sources
- More than 420,000 babies are enrolled in 0-3 early intervention programs
- An Individualized Family Service plan forms the basis for services
- Typically provides home-based educational and therapeutic services
- Fewer than 1/3 enter before 12 months of age



Comparing Key Components of EI and NBS

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Early Intervention and Newborn
Screening

Parallel Roads or Divergent Highways?

Donald B. Bailey Jr., PhD

Component	Early Intervention	Newborn Screening
History and auspice	State-based, strong federal requirements, education auspice	State-based, minimal federal requirements, public health auspice
Entry and eligibility	Developmental delay or established condition	37 specific disorders identified by testing dried blood spots
Service models	Multidisciplinary EI or allied health services	Highly specialized medical services
Outcomes and evidence	Rate of growth in key domains, no specific evidence required	Health outcomes, screening based on rigorous evidence review
Families	Central to decision-making, family outcomes essential	No consent, family outcomes not considered in evidence reviews
Financing	Core federal funding supplemented by insurance, state funds, parent fees	Hospitals bill for screening, state fees supplement, services paid for by Medicaid or insurance

Eligibility categories for Early Intervention

Developmental Delay

- A **documented delay** in one or more domains of early development
- States must have a rigorous definition of delay but may set criteria. Common examples:
 - 2 SD below the mean in one area of development
 - 1.5 SD below the mean in 2 or more areas
 - 25% or greater delay in one or more domains

Established Condition

- A health condition that has a **“high probability” of developmental delay**
- States have discretion as to what constitutes an established condition. Common examples:
 - Chromosomal abnormalities or genetic conditions
 - Hearing or vision impairment
 - Fetal alcohol syndrome

Children who are at-risk

- Conditions that are **“at-risk” for developmental delay** in the absence of early intervention
- Most states do not serve at-risk children. Examples in the legislation include:
 - Low birthweight
 - Prenatal drug exposure
 - History of abuse or neglect

Why should we be concerned about the intersections between NBS and EI?

- Many children identified through NBS could benefit from EI
- But the path from NBS to EI is not clear:
 - State NBS programs refer children to medical services
 - Usually the medical provider (often the primary care pediatrician) must make the referral to EI
 - States vary widely in their definition of “established conditions”
 - If a NBS condition is not on the “established conditions” list, EI providers may need to wait until a delay is evident before services can be provided
- Parents may be caught in the middle
- Integration and coordination of services could enable earlier EI services and assure parents of systems-level support

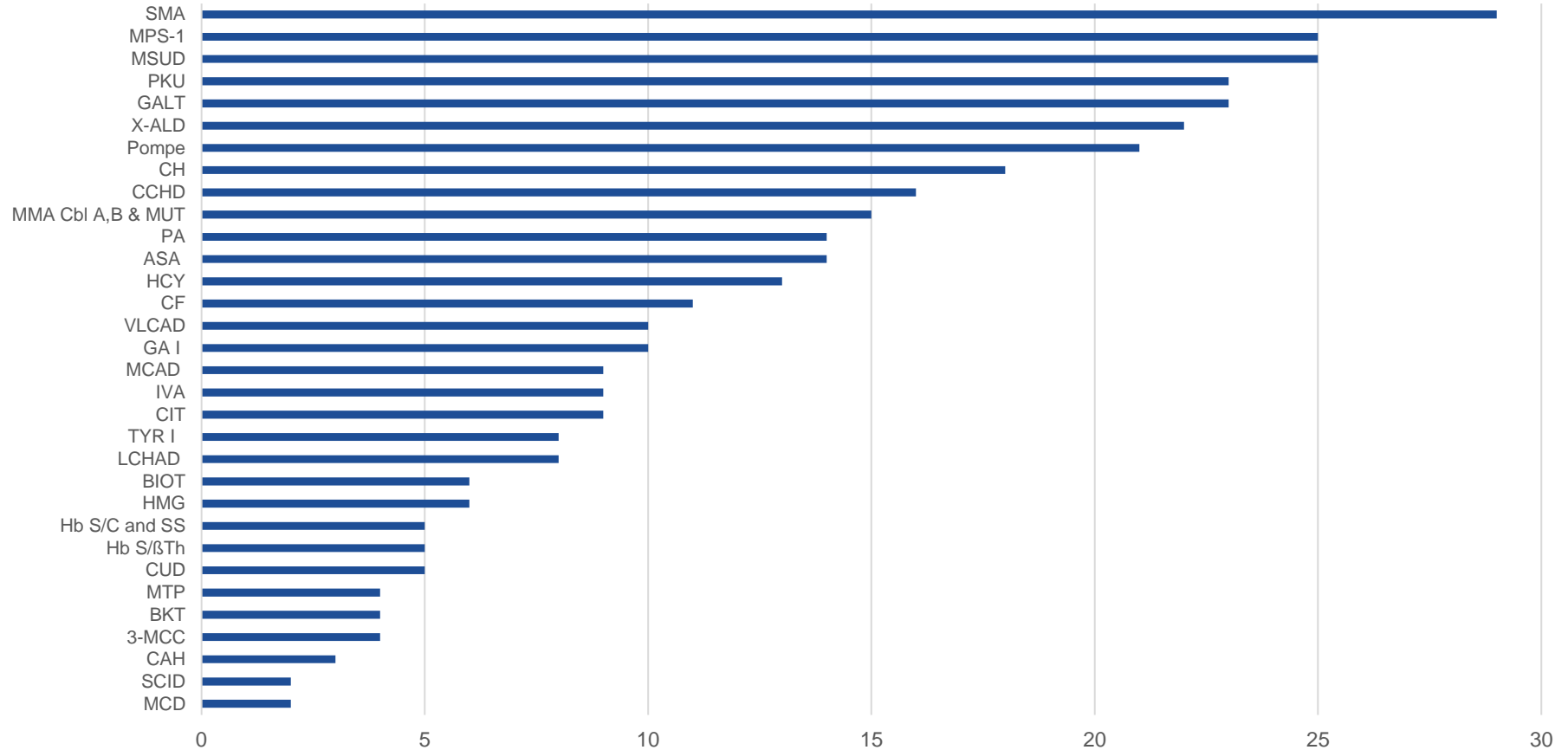
Our team has been studying links between EI and NBS

Project	Research questions	Project status
1. NBS condition review	<ul style="list-style-type: none">• What NBS conditions are on state's EI established conditions lists (e.g., auto-qualify children for EI)?• What NBS conditions put children at risk for "high probability of developmental delay"?	<i>Publication in Journal of Developmental and Behavioral Pediatrics</i>
2. EI and NBS coordinator survey	<ul style="list-style-type: none">• Are EI and NBS programs coordinating to serve children?• Are the program leaders familiar with the other program?	<i>Analysis complete; paper under review</i>
3. Caregiver survey	<ul style="list-style-type: none">• To what extent are children being identified, referred, and enrolled into EI after a NBS diagnosis?	<i>On-going recruitment of caregiver participants</i>
4. Develop template of benefit	<ul style="list-style-type: none">• Could Early Intervention services be considered as part of the "net benefit" equation as new conditions are added to NBS panels?	<i>Ongoing</i>

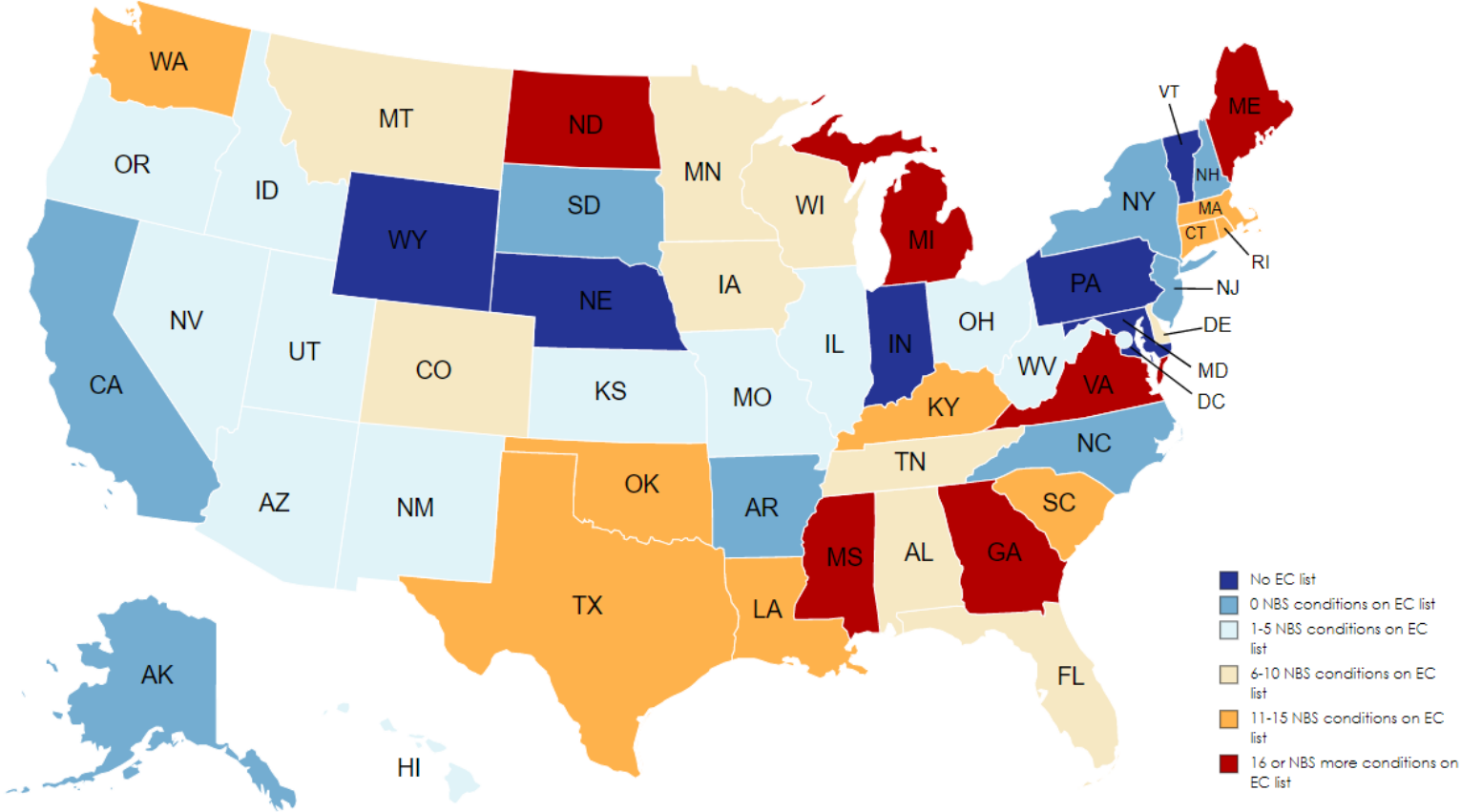
Question 1: Which NBS conditions are considered “established conditions,” by state?

- We used an existing data base and contacted state EI coordinators to get the exact wording of each state’s “established conditions” definition
- We then identified the specific established conditions (if any) listed by state
- We determined whether and which RUSP conditions were on each state’s established conditions list

Frequency each NBS condition is included on states EC list



NBS condition review: How many NBS conditions are included on states' Early Intervention Established Condition list?



Question 2: Which conditions on the RUSP have a high probability of needing EI services even after treatment?

- We developed a matrix to characterize risk of delay in treatment-altered natural history, extent of medical complexity, and likelihood of episodic decompensation
- We conducted a literature review to identify neurodevelopmental outcomes and medical risks associated with each RUSP condition
- Two authors who are medical experts independently classified each condition in terms of risk of delay in treatment-altered natural history, extent of medical complexity, and likelihood of episodic decompensation
- The first author met with the two experts to reach a consensus rating for each condition

NBS condition review: Matrix to assess “high probability of developmental delay”

	Low Risk of DD in Treatment-Altered Natural History	Moderate Risk of DD in Treatment-Altered Natural History	High Risk of DD in Treatment-Altered Natural History
Low medical complexity	Yellow	Red	Red
Moderate medical complexity	Yellow	Red	Red
High medical complexity	Red	Red	Red

Children with conditions in the red cells should automatically qualify for EI

Children with conditions in the yellow cells should be monitored and evaluated as needed for EI

Which NBS conditions put children at risk for “high probability of DD”?

	Low Risk of DD in Treatment- Altered Natural History	Moderate Risk of DD in Treatment- Altered Natural History	High Risk of DD in Treatment- Altered Natural History
Low medical complexity	3-MCC BIOT CUD MCAD*	CH	GALT
Moderate medical complexity	CAH* MCD* PKU TYR I	BKT* HMG* IVA* VLCAD*	ASA* HCY*
High medical complexity	CF SCID Hb S/ β Th Hb SC Hb SS	CCHD GAI* LCHAD* MTP* X-ALD	CIT* MMA Cbl A,B* MMA MUT MPS-1 MSUD* PA* Pompe SMA

Children with conditions in the **red cells** should automatically qualify for EI (26 of 34 NBS conditions).

Children with conditions in the **yellow cells** who are at risk for episodic decompensation (asterisked) should automatically qualify for EI (3 of 34 NBS conditions).

Children with all other conditions in the **yellow cells** should be monitored and evaluated as needed for EI (5 of 34 NBS conditions).

NBS condition review: Three exemplar conditions

Condition	Medical complexity	Risk of DD in Treatment-Altered Natural History	Recommendation
Biotinidase deficiency (BIOT)	Low	Low	Affected children should be monitored and evaluated as needed for EI
Severe Combined Immunodeficiencies (SCID)	High	Low	Affected children should be auto-eligible for EI
Propionic Acidemia	High	High	Affected children should be auto-eligible for EI

Could EI be considered as part of the “net benefit” equation as new conditions are added to NBS panels?

- Potentially, but a mechanism to assess whether the condition would be eligible for EI would be helpful for the ACHDNC

	2	1	0
Developmental delay with treatment	High probability	Moderate probability	Low probability
Medical complexity after treatment	High medical complexity	Moderate medical complexity	Low medical complexity
Number of states condition is automatically eligible	16 states or more	7-15 states	6 states or fewer
Recommendations for EI, EI-related services, and/or developmental monitoring	Clinical care recommendations	Patient advocacy group recommendations	None

0 = Lowest possible score, children unlikely to be automatically eligible for EI

9 = Highest possible score, children with that condition are very likely to be eligible for EI

Biotinidase Deficiency

Score = 2

	2	1	0
Developmental delay with treatment	High probability	Moderate probability	Low probability
Medical complexity after treatment	High medical complexity	Moderate medical complexity	Low medical complexity
Number of states condition is automatically eligible	16 states or more	7-15 states	6 states or fewer
Recommendations for EI, EI-related services, and/or developmental monitoring	Clinical care recommendations	Patient advocacy group recommendations	None

Severe Combined Immunodeficiency

Score = 5

	2	1	0
Developmental delay with treatment	High probability	Moderate probability	Low probability
Medical complexity after treatment	High medical complexity	Moderate medical complexity	Low medical complexity
Number of states condition is automatically eligible	16 states or more	7-15 states	6 states or fewer
Recommendations for EI, EI-related services, and/or developmental monitoring	Clinical care recommendations	Patient advocacy group recommendations	None

Propionic Acidemia

Score = 8

	2	1	0
Developmental delay with treatment	High probability	Moderate probability	Low probability
Medical complexity after treatment	High medical complexity	Moderate medical complexity	Low medical complexity
Number of states condition is automatically eligible	16 states or more	7-15 states	6 states or fewer
Recommendations for EI, EI-related services, and/or developmental monitoring	Clinical care recommendations	Patient advocacy group recommendations	None

Conclusions and recommendations

○ **Conclusions**

- Considerable variability exists across states in definition and inclusion of Established Conditions
- Of 34 NBS conditions examined, we suggest that 29 (85%) should be considered Established Conditions, compared with the current average we found of 7.8

○ **Recommendations**

- NBS and EI programs could build or expand 2-way communication channels
- NBS could be a designated Child Find source for EI
- EI programs could adopt definitions and standards so that all appropriate NBS conditions are consider Established Conditions
- EI and NBS could coordinate efforts to collect and track data
- ACHDNC could consider likely eligibility for EI when weighing net benefit

Caveats

- At the present time, EI is unlikely to be the primary benefit that the ACHDNC should consider
- But EI would likely be an **additive** benefit to almost any medical or dietary treatment
- It will be almost impossible to conduct an evidence review of the benefits of EI for a particular nominated condition
- We recognize that EI is not as comprehensive or intensive as we would hope
- Nonetheless, it enjoys wide support and almost every survey done of families reports high satisfaction with services and outcomes

Current funding

- The John Merck Fund
- Helmsley Charitable Trust
- Juvenile Diabetes Research Foundation
- Traverre Therapeutics



Thank you

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