VIEWPOINT

Newborn Screening
Evolving Challenges in an Era of Rapid Discovery

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Newborn screening is designed for presymptomatic identification of serious conditions for which there are effective treatments. Because newborn screening programs in the United States are operated by states, there has historically been considerable cross-state variability in screened conditions and thus a need for a mechanism to guide states.

The Discretionary Advisory Committee on Heritable Disorders in Newborns and Children, which was appointed by the Secretary of the US Department of Health and Human Services (DHHS), conducts a rigorous evidence-based review of nominated conditions with 4 primary considerations: (1) the condition represents a significant public health problem, (2) there is an accurate and low-cost screening test, (3) treatments exist with proven efficacy, and (4) states are capable of screening and follow-up.

After considering the magnitude and the certainty of the net benefit and feasibility of implementation, the committee makes a recommendation to the DHHS Secretary, who determines whether the condition should be added to the Recommended Uniform Screening Panel (RUSP).[1]

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Emerging Disrupters

The committee's work has been highly successful, reducing cross-state variability and providing a scientific basis for policy decisions. But the landscape of newborn screening is rapidly evolving, and 4 disruptive trends now require consideration of new alternatives.

A Slow, Condition-by-Condition Review in an Era of Rapid Discovery

The very nature of a thoughtful and rigorous evidence review and the inevitable political sensitivities inherent in providing national guidance to states have meant that the pace of decision making is slow. In 2010, the Secretary approved the initial RUSP, which had 29 conditions recommended by the American College of Medical Genetics[2] and was endorsed by the committee in 2005. Since then, the committee has recommended only 4 additional conditions for the RUSP, 3 of which have been accepted by the Secretary (severe combined immunodeficiency, critical congenital cyanotic heart disease, and Pompe disease) and 1 (mucopolysaccharidosis I) is still under consideration.

Eight conditions have been reviewed but not recommended (spinal muscular atrophy, Niemann-Pick disease, neonatal hyperbilirubinemia, Krabbe disease, hemoglobin H disease, Fabry disease, adrenoleukodystrophy, and 22q11.2 deletion syndrome). Even though a careful and deliberative process can be justified, a central question is whether this condition-by-condition approach is sustainable in an era of rapid advances in gene discovery, disease mechanisms, and targeted therapeutics.

Frustration by Patient Advocates

Many families of children with conditions not included on the RUSP are frustrated by what they perceive as an unduly burdensome and restrictive process, arguing that early identification can result in substantive benefits for both children and families—reducing the diagnostic odyssey, providing access to supportive services, informing families of reproductive risk, and providing the opportunity to enroll in experimental treatment studies. Patient advocates are increasingly requesting states to screen for additional conditions.

For example, despite the committee's conclusion that Krabbe disease was not ready for newborn screening, advocates in several states secured legislation mandating the addition of Krabbe disease and other conditions to their state's panel.[3] Frustration with the slow pace of decision making is understandable, but when states add conditions that the committee has not reviewed or does not recommend, it will reintroduce the cross-state variability that the committee has worked to reduce and evokes the possibility of adding conditions for which there is insufficient science, that are difficult for states to screen or provide services for, or that have the potential for unintended harmful consequences.

Commercial Options

Recognizing consumer demand for information about any condition that could affect their child's health, commercial companies have entered the genetic testing market, offering expanded screening for a fee. In one regard, this option is reasonable because if people want information beyond that provided by the public health system, they should pay for it.

A primary concern evoked by commercial options is that they are expensive, increasing disparities in access to important health information. Often the commercial panels provide results but offer little or no follow-up. Because the tests typically are not ordered

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by the child's physician, it becomes the family's responsibility to seek appropriate care.

Changes in Screening Technology

A fourth disrupter is the inevitability of new, more accurate, and cost-effective ways of screening. Genetic testing in newborn screening could identify hundreds of significant genetic variants, only a few of which meet criteria for the RUSP.[4] This would force a complete reconceptualization of screening because decisions will be required about the types of information that should be disclosed and whether parent choice for return of results should become part of newborn screening.

A Potential Solution

There is now a critical need to determine the feasibility of a voluntary expansion of screening offered shortly after birth, providing a choice for those families who want to know about other conditions. An expanded panel should be offered under a research protocol with opt-in informed consent, providing opportunities to determine prevalence, detect patterns of early symptom onset, examine genotype-phenotype relationships, and test presymptomatic treatments. The data obtained through such an enterprise could more rapidly advance understanding of diseases and treatments and reduce the length of time for appropriate conditions to be added to the RUSP.

The notion of an expanded panel system is not new,[5-7] but no serious effort has been launched to test feasibility, costs, and benefits because of the obvious challenges and enormity of such an undertaking. How might such a system work? What would the criteria be for selecting conditions and who would make those decisions? How and when should information be presented to ensure a voluntary and informed decision? How much would it cost to screen and provide counseling, follow-up support, and services? What uptake rate would be needed to justify expanded screening as a public health service? What data are needed to determine whether the net benefits of such a program are worth the effort and expenditure?

Because of the emergence of new challenges to newborn screening, these questions are no longer sufficient limitations to reject the possibility of a voluntary expansion, and planning efforts have been initiated to establish and test a model for how this might work. Activities include partnering with key states and patient advocacy groups, determining criteria for conditions that would fit in an expanded panel, developing and testing models for public awareness and informed consent, and establishing protocols for activities ranging from screening to follow-up. These efforts are needed to understand the necessary data and infrastructure required to launch a functional program.

These emerging disrupters are real. They challenge the current state of newborn screening, and advocates are shifting the question from why screen to why not screen. A voluntary alternative has the possibility of balancing competing interests and could ensure a rational process for newborn screening policy.

ARTICLE INFORMATION

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