

# Virtual Mentor

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## POLICY FORUM

### Emerging Dilemmas in Newborn Screening

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Newborn screening is an initiative designed to identify infants with serious health conditions who could benefit from early detection and treatment. Begun in the 1970s and governed at the state level, newborn screening expanded gradually as cost-effective tests developed or new treatments were discovered, and has recently undergone an unprecedented phase of growth and change. While many embrace and encourage these changes, they create a number of dilemmas that must be addressed to ensure that the practice grows in a rational and ethical fashion.

A report issued by the American College of Medical Genetics (ACMG) in 2006 established a template for grading the suitability of screening for newly proposed conditions [1]. Based on expert ratings of 87 conditions, the report recommended that all states screen for 29 core conditions and disclose the results of an additional 25 secondary conditions that are obligatorily detected by tandem mass spectrometry when screening for the core conditions. The report, together with advocacy initiatives, prompted broad changes in state screening programs. In 2005, most states screened for fewer than 10 conditions; currently, most screen for at least 25 conditions, a total that continues to increase. To address cross-state discrepancies and provide states with ongoing guidance, a Secretary's Advisory Committee on Newborn Screening for Heritable Disorders was established by the U.S. Department of Health and Human Services. Recognizing the need for a coherent national program of coordinated research, the National Institute of Child Health and Human Development issued a contract to build the infrastructure for a National Newborn Screening Translational Research Network. This network will link state programs and clinical centers, develop a national research informatics system, establish a research repository of residual dried blood spots, and facilitate research on conditions proposed for testing or laboratory tests.

For the most part, newborn screening enjoys wide public support and strong endorsement by the public health community. But developments in screening technology have made it possible to identify conditions for which there is no immediate treatment—a long-standing criterion for selecting which conditions to screen. A number of bioethicists have questioned whether disclosing results for untreatable conditions is desirable.

In December of 2008, the President's Council on Bioethics issued a report that examined many issues associated with expanded screening [2]. A major theme

reflected in the report and expressed by some bioethicists was that mandatory screening was expanding too rapidly nationwide without adequate consideration of the potential harms that could occur when disclosing information about conditions for which: (1) the natural history has not been described, (2) the potential range of impact of the genetic change is unknown (including the possibility that some identified children will be unaffected), and (3) treatments are not available. Disclosure under these circumstances could cause parental anxiety, disrupt parent-child bonding, contribute to hypervigilant parenting, lead some parents to try unproven treatments in anticipation of possible symptoms, result in stigmatization or discrimination, or cause the child to worry.

Our own work with fragile X syndrome (FXS) exemplifies these issues [3]. FXS, a trinucleotide repeat expansion disorder, is the most common inherited form of intellectual disability. Located on the X chromosome, the *FMR1* gene affects the production of a protein (FMRP) known to be essential for normal brain development. Males with FXS have moderate to severe intellectual impairment and can have co-occurring conditions such as anxiety, hyperactivity, or autism. Females are typically more mildly affected. There is considerable variability in the effects of the gene mutation on both males and females. Diagnosis of FXS typically does not occur until around 3 years of age, which limits timely access to early intervention programs and can result in the birth of a second child with FXS prior to the diagnosis of the first [4, 5]. Newborn screening would identify children much earlier, but this action has several implications for which concerns have been raised [6]. For example:

- There is currently no effective medical treatment that would prevent or reduce the consequences of FXS.
- Screening will identify some children who are phenotypically normal.
- Screening will identify children who are carriers and are at increased risk for adult-onset conditions such as premature ovarian insufficiency or neurological symptoms that include tremor and ataxia.

How should we make decisions about screening for a heterogeneous group of conditions such as those caused by changes in the *FMR1* gene? State-mandated genetic testing of children rises to a level of scrutiny that should invoke a moral and ethical analysis. We suggest that traditional criteria for decision making (being able to treat the condition, doing no harm) should be revised to a more nuanced goal in which benefits are maximized while harms are minimized. Using this definition, we offer several factors to consider when making decisions about newborn-screening policy:

- For the most part, the potential harms of expanded screening are speculative. Although it is possible that each harm could occur in isolated situations, there is no empirical evidence that any would occur at such a frequency or be so long-lasting that it would warrant withholding information from parents and children. Screening decisions should not be made on the mere assumption of harm but, rather, should recognize that harm also occurs if information gained from screening is not shared with families.

- Most research shows that parents want information relating to their child’s health and their family, even when biomedical treatments are not available. Information itself should be considered as a potential benefit from screening, even when no treatment is available.
- Benefit has historically been narrowly defined and limited to improved health. Policy decisions should weigh other potential benefits for the child (e.g., preventing secondary conditions, enhancing development, maximizing quality of life), family (e.g., avoiding financial and emotional costs of the “diagnostic odyssey,” enabling advocacy, knowing reproductive risk), or society (e.g., assuring equitable access to timely information, accelerating understanding of genetic variations and consequences, enabling treatment discovery, maximizing efficient public health services).
- Relying on benefit as the primary guiding moral principle devalues other equally salient moral frameworks, rights, and duties (e.g., distributive justice, social justice, fairness, equity, duty to inform, right to know).
- We should consider the possibility that it would be morally untenable *not* to report potentially useful health-related information and examine social and legal ramifications of the failure to disclose such results.

Inevitable advances in technology will identify hundreds of genetic variants at relatively low cost, radically changing both the possibilities and the realities of newborn screening. What would we do if whole-genome sequencing suddenly became cheap enough to use for newborn screening? How would we decide whether and how to disclose genetic information such as an increased susceptibility to Alzheimer’s disease or cardiovascular disease? What is the appropriate demarcation between private-market screening and public health screening? Would limiting public health screening to a few treatable conditions lead to a burgeoning private market for expanded screening that exacerbates discrepancies in equitable access to health-related information?

Ultimately, the line separating disclosed results from those not reported (i.e., deciding whether a result is clinically relevant) will become increasingly difficult to draw. Technological advances, gene discovery, genotype-phenotype association studies, and treatment research will make the customary state-by-state, condition-by-condition approach to research outdated, and it will be nearly impossible for health policy to keep up with this rapidly shifting landscape.

Research is needed on issues, using a few prototype conditions that exemplify the concerns that bioethicists consider problematic. This research should examine broad questions of family adaptation to complicated, nuanced, presymptomatic information and identify the supports families need to assure that the disclosure of such information results in benefit rather than harm. Assessing medical and genetic literacy, developing novel methods of obtaining consent, and promoting and evaluating informed decision making will necessarily be part of next-generation newborn screening. Research must also examine methods by which families can become knowledgeable about the benefits and limitations of screening to enable

them to make knowledgeable decisions about what information they want. Only a systematic and integrated research agenda such as this can provide the data needed to adequately inform newborn-screening policy decisions.

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