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The Ethical Hazards and Programmatic Challenges of Genomic Newborn Screening

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Advances in next generation sequencing technologies have the potential to spur better integration of genetic testing into patient care. Appropriate utilization of these technologies will require the capacity to manage, interpret, and communicate very large amounts of personal genetic information.[1] Since the clinical infrastructure necessary to support these activities is currently limited,[2] it is likely that the earliest applications of whole-genome sequencing will be restricted to settings where genetic testing is already a routine part of clinical or public health practice, such as state newborn screening (NBS) programs.

The use of next-generation sequencing holds forth the promise of enabling detection of much larger numbers of deleterious genetic variants, thereby expanding the number of pediatric disorders evaluated without significantly increasing the costs of NBS.[3] These important public-health goals may encourage early adoption of whole-exome and whole-genome sequencing by state NBS programs. However, if implemented by state programs, the use of new sequencing technologies may have a number of undesirable effects that threaten the moral foundation and core mission of one the nation's most successful public health initiatives.

For nearly half a century, state NBS programs have tested millions of children annually to identify medical conditions that, if untreated, result in severe physical, mental, or developmental harms. The child welfare considerations that support these public health initiatives are compelling, and have prompted most states to require NBS for all children, often with significant limitations on parents' ability to request an exemption. The moral justification for compulsory NBS screening derives from the state's interest in protecting its most vulnerable citizens from preventable harm. While the diseases evaluated by these programs are exceptionally rare, the opportunity to intervene and dramatically alter a child's

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life course and expectancy has been regarded as sufficient to trump any claims of parental autonomy.

As programs have evolved over the last 40 years there have been a number of challenges to the moral justification on which mandatory newborn screening was founded. With the introduction of tandem-mass spectrometry in the mid-1990s, state screening programs began evaluating greater numbers of metabolic and genetic conditions. Whereas it was typical for states to test for an average of five conditions in 1995, by 2005 states were testing for an average of 24 genetic diseases, an increase of more than 350%.[4] Some states evaluate dozens of additional conditions, including diseases that affect children at a later stage in development and others for which the benefits of early intervention are limited.

Critics have questioned whether in adding these new conditions, state NBS programs have strayed too far from their core aims as public-health programs. For these critics, NBS is justifiable as a compulsory, state-supported activity to the extent that these programs protect the welfare of newborn children by identifying diseases of early onset that require immediate medical action in order to avert a catastrophic outcome.[5] Others have voiced concerns about the lack of clinical data establishing the utility of expanded screening.[6] These objections signal a more basic worry about expanded NBS screening—that more expansive screening may fail to meet the moral requirements necessary to justify compulsory testing.

These debates may be amplified as states consider using next generation sequencing within NBS programs. Several national discussions have begun to consider use of genome sequencing technologies in NBS, including a recent meeting convened by the National Institutes of Health.[7] If these technologies are used by state NBS programs, several ethical hazards will need to be navigated. First, multiplexed forms of genetic testing have already raised questions about the ability of clinicians to interpret and effectively communicate the deluge of genetic data generated by these genotyping methods.[2] Use of genomic methods in NBS would amplify these concerns, as program directors struggle to decide what information should be disclosed to parents. Returning genetic results that do not require immediate medical action or results whose clinical implications are unclear may create unwanted psychosocial burdens on parents. These and other information-management challenges will be far more common and difficult to manage if genomic sequencing methods are adopted by state health departments, with potential to overwhelm the capacity of state NBS programs.[3] While requirements to seek parental consent for NBS may help to address some of these concerns,[8] implementation of any type of consent process would require programs to make difficult decisions about what types of information to offer to parents, including for example, whether to provide parents with results regarding late-onset conditions. Before implementing genomic screening, state health departments would also need to consider available clinical resources for assuring adequate pre- and post–test counseling about genetic test results.

A second area of concern centers on how states would utilize the vast amounts of information generated by uses of genomic technologies in NBS. State storage of this data may lead some parents to view genomic evaluation of newborns as a form of research. As a result, if NBS continues to be a mandatory test—required of all children with limited options available to parents who wish to avoid participation—members of the public who feel their privacy is being violated may mobilize politically in opposition to mandatory NBS programs. These concerns are already evident in current debates about the storage and use of residual NBS bloodspots for research, which has resulted in fears of higher numbers of parents opting out of testing and lawsuits by parents in Texas and Minnesota.[9]

Lastly, genomic screening would represent an even greater departure from the core public health aims served by NBS than other recent extensions of these programs. Since its inception, NBS has saved thousands of children from the effects of devastating genetic diseases. While program improvement should always be a goal, the use of genomic sequencing methods has a significant potential to erode the moral foundation of NBS further, resulting in greater numbers of children with genetic disease going undetected. Many parents will voice significant objections to the government sequencing their child's genome, especially if this is done in the context of a compulsory public health program, undermining public confidence in state NBS programs and potentially threatening their political tenability. Some have suggested that a tiered consent process in which some tests are mandatory and others are elective may help to address these concerns.[10] Implementing this approach in state NBS programs would represent a dramatic shift away from the core public health principles that have anchored public support for these programs, potentially resulting in larger numbers of parents choosing to forego screening altogether.

This collection of moral and practical concerns highlights how the use of genomic technologies poses a significant threat to state NBS programs, as these programs move ever further from their core protectionist mission. In this regard, the use of genome sequencing methods in state NBS programs may undermine the child welfare goals upon which mandatory NBS programs are founded. As our ability to interpret data generated by next generation sequencing increases, ongoing dialogue between screening programs, genome scientists, primary care providers and parents will be essential for assessing where, and how, these technologies should be used. While the implementation of genomic technology may improve the quality of newborn screening, premature adoption of these tools could ultimately put newborns at risk.

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References

1. Ormond KE, Wheeler MT, Hudgins L, et al. Challenges in the clinical application of whole-genome sequencing. Lancet. 2010; 375:1749–1751. [PubMed: 20434765]
2. Sharp RR. Downsizing genomic medicine: approaching the ethical complexity of whole-genome sequencing by starting small. Genet Med. 2011; 13:191–194. [PubMed: 21311340]
3. Clayton EW. Currents in Contemporary Ethics. J Law med Ethics. 2010; 38:697–700. [PubMed: 20880251]
4. Tarini BA, Christakis DA, Welch HG. State newborn screening in the tandem mass spectrometry era: more tests, more false-positive results. Pediatrics. 2006; 118(2):448–456. [PubMed: 16882794]
5. Grosse SD, Boyle CA, Kenneson A, Khoury MJ, Wilfond BS. From public health emergency to public health service: the implications of evolving criteria fore newborn screening panels. Pediatrics. 2006; 117(3):923–929. [PubMed: 16510675]
6. Botkin JR, Clayton EW, Fost N, et al. Newborn screening technology: proceed with caution. Pediatrics. 2006; 117:1793–1799. [PubMed: 16651338]
7. National Institute of Child Health and Human Development, National Institutes of Health; Newborn Screening in the Genomic Era: Setting a Research Agenda. Website. http://www.nichd.nih.gov/about/meetings/2010/121410.cfm. [Accessed October 25, 2011]
8. Ross LF. Mandatory versus voluntary consent for newborn screening? Kennedy Inst Ethics J. 2010; 20(4):299–328. [PubMed: 21338027]

9. Lewis MH, Goldenberg A, Anderson R, Rothwell E, Botkin J. State laws regarding the retention and use of residual newborn screening blood samples. Pediatrics. 2011; 127(4):703–712. [PubMed: 21444595]

10. President's Council on Bioethics. Washington, D.C.: 2008 Dec. The changing moral focus of newborn screening: an ethical analysis by the President's Council on Bioethics. Available at http://www.bioethics.gov/reports/newborn_screening/index.html [Accessed December 20, 2011]