HHS Public Access

Author manuscript

Am J Bioeth. Author manuscript; available in PMC 2024 July 01.

Published in final edited form as:

Am J Bioeth. 2023 July ; 23(7): 79–82. doi:10.1080/15265161.2023.2207542.

Addressing the Burdens that Newborn Screening Imposes on Underserved Communities

Meghan E. Strenk, MS,
Clinical Genetics,Children's Mercy Hospital,United States,Missouri,Kansas City

Courtney Berrios, MSc, ScM,
Genomic Medicine Center,Children's Mercy,United States,Missouri,Kansas City

Jeremy R. Garrett, PhD
Children's Mercy Bioethics Center,Children's Mercy Hospital,United States,Missouri,Kansas City

University of Missouri Kansas City,United States,Kansas City

Newborn screening (NBS) began in the 1960s by testing all newborns for a single condition —phenylketonuria, or PKU—which, when identified and treated early, significantly reduces morbidity. Over the past six decades, NBS has expanded considerably as a public health intervention for newborns born in the United States (US). Currently, the Recommended Uniform Screening Panel (RUSP), a list of conditions which the US Secretary of the Department of Health and Human Services recommends for inclusion in state NBS panels, includes 37 core conditions and 26 secondary conditions (Recommended Uniform Screening Panel). While NBS is rightly viewed as a public health success story resulting in an overall positive impact on the health and wellbeing of newborns, its impacts are not always distributed equitably among stakeholders. Realizing the true promise of NBS requires recognizing and addressing both disparities in benefits of the program and inequities in the burdens that screening can impose on patients and families.

With this in mind, we applaud Halley and colleagues for highlighting the disparate benefits of NBS across different populations. An adequate ethical evaluation of NBS must account for these salient disparities in benefits from the program. However, we cannot stop there. It is vital to attend as well to the *burdens* of NBS, which are often shouldered disproportionately by already underserved communities. In what follows, we expand on the important analysis of Halley and colleagues by (1) presenting real-world data from our NBS referral center demonstrating inequities in burdens and (2) describing how these burdens are exacerbated in rural communities that require extensive travel for care and/or in immigrant communities that may require interpreters. We conclude by (3) advocating for changes in the NBS process to reduce the inequities imposed on many underserved and marginalized populations.

In 2013, Missouri was at the forefront of expanded NBS when it became the first US state to screen newborns for four lysosomal storage disorders (LSDs): Gaucher disease,

mestrenk@cmh.edu .

Fabry disease, Pompe disease, and mucopolysaccharidosis, type 1 (MPS1). Two of these LSDs—Pompe disease and MPS1—were later added to the RUSP in 2015 and 2016, respectively (Previously Nominated Conditions). As screening for these two conditions began, several unexpected outcomes came to light. Here, we will focus on an outcome that disproportionately has affected underserved communities: namely the identification of enzyme pseudodeficiency alleles, which yield low enough enzyme levels to give positive NBS results but do not cause disease. While one MPS1 pseudodeficiency allele had been identified prior to the start of MPS1 newborn screening (Aronovich et al 1996), three additional alleles were identified during the pilot phase of Missouri's expanded NBS program (Pollard 2013). Pseudodeficiency alleles also have been identified in Pompe disease [Tajima 2007].

When screening for these conditions began, Children's Mercy Kansas City served as an NBS referral center for Missouri Region 1, which encompassed the 30 western counties of the state. In 2019, we reviewed the data from our first six years of experience doing newborn screening for these conditions (Strenk 2019). At the time, it was our practice to see all infants with an abnormal LSD newborn screen in our clinic in Kansas City for detailed physical exam and coordination of the specialty diagnostic testing necessary to either confirm a diagnosis or rule the screen a false positive. Data showed that our NBS referral pattern was inconsistent with the distribution of ethnic populations in the region we serve. In particular, compared to the Missouri Region 1 population, we received more abnormal LSD screens for babies who are Black, Asian, or Pacific Islander. For example, the Black population constituted 3.2% of Missouri Region 1 but produced 19.9% of the LSD newborn screening referrals. Similarly, Pacific Islanders made up just 0.2% of the Missouri Region 1 population but accounted for 7.4% of our referrals for LSDs.

When focusing on these populations specifically, we found even more striking differences. Pseudodeficiency explained 24% of NBS referrals for Pompe disease. Of these babies with Pompe pseudodeficiency, 75% reported Pacific Islander or Asian ethnicity. Many of these families speak a rare language for which it is difficult to find an interpreter. Similarly, for MPS1, our data showed that pseudodeficiency explained 29% of positive NBS results, with 85% of those pseudodeficiencies being in Black infants.

In 2021, the NBS referral center serving the central counties in Missouri closed due to physician retirement. Those counties were re-distributed to the remaining referral centers, and our clinic now serves 55 counties including south-central Missouri. Prior to this closure, the furthest a family needed to travel to be seen in person in our clinic was 193 miles or about three hours one way. Currently, a family in the furthest county we serve would need to travel 250 miles or about four hours and 15 minutes one way to be seen in person. It's worth noting that the median household income in this county in 2021 was $36,402, and that 30% of children in the county live in poverty (Census profile: Ozark County, MO).

Our data from 2013–2019 also showed that when carrier status and pseudodeficiency are included, the NBS false positive rate was 73% for Pompe disease and 88% for MPS1. This resulted in a significant number of families who were asked to see a specialist, undergo additional testing, and wait for results. While these infants did not require long term follow

up, their families had the same stress and concern during the process of confirmatory evaluation and testing as the families whose children were ultimately diagnosed with one of these conditions. Each of these burdens is ethically significant and must be included in an adequate evaluation of the overall utility and equity of NBS programs.

Since the data above were collected, the Missouri NBS lab instituted secondary screening for both MPS1 (started 4/2020) and Pompe disease (started 7/2021) (Lacey Vermette, email message to author, March 30, 2023). Secondary screening is additional testing performed on the NBS bloodspot to separate infants who are carriers or have a pseudodeficiency from infants who truly have one of these conditions. While we have not collated or reviewed the data as we did in 2019, anecdotally, clinicians report a significant reduction in referrals of infants for additional testing for these conditions since this additional process was instituted. While this demonstrates benefit of secondary screening in terms of reducing the logistical burdens of attending appointments (travel, expense, communication, etc.), it is important to note that secondary testing does not alleviate—and may actually increase—emotional burdens for families if they are made aware of the initial screening result before an extended secondary screening process is completed, particularly in the absence of adequate and accurate counseling and education.

As we reflect on the analysis of Halley and colleagues and compare it with our own experience, several themes emerge. First, we don’t know what we don’t know until we know it. Many rare diseases are diagnosed based on clinical symptoms in a patient. NBS has allowed population screening in which all individuals with a disease can be diagnosed. This has revealed that the spectrum of disease can be broader than expected (for example, more people have LOPD than IOPD, which was unanticipated) as well as the presence of other factors that can impact the screening result (e.g., pseudodeficiencies). In addition, the distribution of disease or pseudodeficiencies may be different than anticipated (e.g., pseudodeficiencies in minority ethnicities). Secondly, more information from NBS labs (secondary screening) can promote greater equity in the process by preventing disproportionate numbers of referrals of already underserved populations, though it is important to recognize that this may reduce logistical burdens without alleviating the emotional burdens of additional testing for families.

The burdens of NBS also can affect patients and families on a more granular level. When pseudodeficiencies are more common in minoritized ethnicities, immigrant communities may be more likely to be referred for an abnormal LSD screen. Some of these communities are underserved and/or speak rare languages for which available interpretation services are inadequate or lacking entirely. Additionally, underserved families from poorer areas often have further to travel for specialty care. This is becoming more pronounced as specialty care is consolidated and current providers age and retire without sufficiently trained replacements. Finally, it is vital to appreciate that families with false positives undergo the same process as families who end up with a diagnosis but lack the same resources for support. There is no “false positive NBS” support group.

Our experience suggests several actions labs and referral centers can—and should—undertake to identify and ease the burdens of NBS, particularly for underserved populations.

1. Tracking and analyzing NBS referrals, including patient demographics and clinical follow up data, is essential for identifying screening inequities. Data should be tracked routinely, especially as new conditions are added to NBS panels or changes are made in testing processes, to identify emerging concerns and suggest potential ways to address them.

2. Telehealth is a valuable tool for reducing burdens for families who are geographically distant from referral centers. Telehealth access became easier and more available due to the COVID19 pandemic, but its extension to underserved communities who live far from the specialty care required for the workup of an abnormal newborn screen is ongoing. Healthcare providers and organizations should advocate for expanding and accelerating ongoing access to and reimbursement for telehealth services.

3. Changes to NBS analytics and follow-up processes should regularly be considered and evaluated to eliminate or mitigate burdens imposed on underserved communities. The addition of second tier screening or adjustments in cutoffs can reduce notifications and referrals that turn out to be false positives. However, the implementation of these practices must be evaluated to ensure that they have the intended impact.

4. It is incumbent upon healthcare providers and bioethicists who are aware of inequitable benefits and burdens of NBS to advocate for changes to the system. Halley and colleagues highlight the pressures upon patients and families with rare diseases to advocate for themselves and emphasize how this advocacy often is essential to adding new conditions to NBS panels. This has genuinely benefited many children who thereby receive earlier interventions for rare conditions. Yet for underserved communities disproportionately burdened by NBS false positives, there is no advocacy group. Most parents do not know others who have required follow-up for a newborn screen, especially not for the same condition, and parents experiencing a false positive may wish to move on from their experience. These parents therefore are less likely to advocate for change without the motivation, knowledge, and advocacy skills built out of necessity by those impacted by rare disease. This puts the onus on our healthcare and ethics communities to advocate on their behalf.

In conclusion, it is unarguable that when considering the benefits versus burdens of NBS, the balance certainly falls toward overall benefit to the health and well-being of newborns and children. However, these benefits are not always distributed equitably, and they also are accompanied by significant—and similarly disparate—burdens. Recognizing only the aggregate successes of NBS prevents us from seeing its inequities, and it is only in addressing these that we can fully realize the full potential of NBS for improving public health.

Authorship Acknowledgment

Courtney Berrios and Jeremy Garrett contributed equally as senior authors on the manuscript, and we wish to acknowledge them as co-senior authors.

Funding Acknowledgement

Courtney Berrios' work on this commentary was supported by a CTSA grant from NCATS awarded to the Frontiers Clinical and Translational Science Institute at the University of Kansas (# UL1TR002366). The contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH or NCATS.

Sources:

Aronovich Elena L., Pan Dao, and Whitley Chester B.. "Molecular genetic defect underlying alpha-L-iduronidase pseudodeficiency." American journal of human genetics 58, no. 1 (1996): 75. [PubMed: 8554071]

Tajima Youichi, Matsuzawa Fumiko, Aikawa Sei-ichi, Okumiya Toshika, Yoshimizu Michiru, Tsukimura Takahiro, Ikekita Masahiko et al. "Structural and biochemical studies on Pompe disease and a "pseudodeficiency of acid α-glucosidase"." Journal of human genetics 52 (2007): 898–906. [PubMed: 17805474]

Pollard L, Braddock SR, Christensen KM, Boylan DJ, Smith LD, A Heese B, M Atherton A, Lawson CE, Strenk ME, Willing M, Manwaring L, Wood TC. "Inborn errors of metabolism: from identification to treatment." (Abstract 82, presentation at the American Society of Human Genetics 63rd Annual Meeting, Boston, MA: October 23, 2013.

Strenk M, N Gadea R, Heese BA, Gannon JL. "Newborn screening for four Lysosomal Storage Disorders: One center's experience over six years." (Poster, presented at the National Society of Genetic Counselors 38th Annual Education Conference, Salt Lake City, UT, November 5–8, 2019

"Recommended Uniform Screening Panel." HRSA. Health Resources and Services Administration, March 30, 2023. https://www.hrsa.gov/advisory-committees/heritable-disorders/rusp.

"Previously Nominated Conditions". HRSA. Health Resources and Services Administration, April 3, 2023. https://www.hrsa.gov/advisory-committees/heritable-disorders/rusp/previous-nominations

"Census profile: Ozark County, MO". Census Reporter. March 29, 2023. http://censusreporter.org/profiles/05000US29153-ozark-county-mo/>