Medical Research Archives

European Society of Medicine

OPEN ACCESS

Published: March 31, 2024

Citation: Brunelli L, Chan K., et al., 2024. A Children's Rights Framework for Genomic Medicine: Newborn Screening as a Use Case. Medical Research Archives, [online] 12(3). https://doi.org/10.18103/mra.v12i3.5167

DOI: https://doi.org/10.18103/mra.v12i3.5167

ISSN: 2375-1924

RESEARCH ARTICLE

A Children's Rights Framework for Genomic Medicine: Newborn Screening as a Use Case

Luca Brunelli[1,*], Kee Chan[2], James Tabery[3], Warren Binford[4] and Amy Brower[2,5,6]

[1]Division of Neonatology, Department of Pediatrics, Spencer Fox Eccles School of Medicine, University of Utah
[2]American College of Medical Genetics and Genomics; kchan@acmg.net and abrower@acmg.net
[3]University of Utah, Department of Philosophy; james.tabery@utah.edu
[4]University of Colorado, School of Medicine, CU Law School; warren.binford@cuanschutz.edu
[5]Munroe-Meyer Institute, University of Nebraska Medical Center
[6]Creighton University School of Medicine; AmyBrower@creighton.edu

*luca.brunelli@hsc.utah.edu

ABSTRACT

The year 2023 marked the 60th anniversary of screening newborns in the United States for diseases that benefit from early identification and intervention. All around the world, the goal of NBS is to facilitate timely diagnosis and management to improve individual health outcomes in all newborns regardless of their place of birth, economic circumstances, ability to pay for treatment, and access to healthcare. Advances in technology to screen and treat disease have led to a rapid increase in the number of screened conditions, and innovations in genomics are expected to exponentially expand this number further. A system where all newborns are screened, coupled with rapid technological innovation, provides a unique opportunity to improve pediatric health outcomes and advance children's rights, including the unique rights of sick and disabled children. This is especially timely as we approach the 100th anniversary of the 1924 Geneva Declaration of the Rights of the Child, which includes children's right to healthcare, and the 1989 United Nations Convention on the Rights of the Child that expanded upon this aspect and affirmed each child's right to the highest attainable standard of health. In this manuscript, we provide background on the evolving recognition of the rights of children and the foundational rights to healthcare and non-discrimination, provide two examples that highlight issues to access and equity in newborn screening that may limit a child's right to healthcare and best possible outcomes, detail ways the current approach to newborn screening advances the rights of the child, and finally, propose that the incorporation of genomics into newborn screening presents a useful case study to recognize and uphold the rights of every child.

Keywords: ethics; genomic medicine; health outcomes; precision medicine; social determinants of health; children's rights, law, policy, and human rights

1. Introduction

In 1924, Eglantyne Jebb, a former British schoolteacher who founded Save the Children in the aftermath of World War I, climbed to the top of Mont Salève and outlined five principles to present to the League of Nations[1]. The Geneva Declaration[2], as it came to be known, explicitly focused on children and was the first international instrument recognizing human rights in the 20th century[1]. The Declaration stated that "mankind owes to the Child the best that it has to give," noting specifically that "the child must be given the means requisite for its normal development" and "the child that is sick must be nursed"[2]. The recognition of the inherent human rights of children was reaffirmed in 1934 by the League of Nations, expanded by the United Nations in 1959[3], and substantially expanded again in 1989 with the United Nations Convention on the Rights of the Child (CRC) – the world's first international treaty focused specifically on the rights children hold due to their unique status as children, which are in addition to the rights they also have as human beings[1,4]. Over the course of the 20th century, the rights of children to healthcare[4] (CRC, Art. 24), non-discrimination[4] (CRC, Art. 2), and the unique rights of sick and disabled children[4] (CRC, Art. 23), were recognized and documented by the international community. The international community also urged international cooperation and the development of technologies to advance children's health and well-being[4] (CRC, Art. 24). Despite the principles and goals of the CRC, the United States (U.S.) healthcare system has struggled to achieve optimal health outcomes in children.

The U.S. exhibits poor health outcomes compared to other wealthy nations. Although healthcare expenditures are more than double that of any other high-income country, clinical outcomes lag by orders of magnitude behind other industrialized nations[5–12]. The gap in health inequities has widened in the last decades while healthcare costs have continued to skyrocket[13]. Most recently, the COVID-19 pandemic further highlighted poor U.S. health outcomes and the health inequities experienced by communities of color due to the unaddressed social determinants of health (e.g., food insecurity, poverty, racism) and the structural determinants that govern the economic and social policies that affect pay, working conditions, housing, access to healthcare, and education[14]. These challenges, particularly acute in children due to their inherent vulnerability[15], have not seen any substantial improvement despite the latest technological advances and discoveries in precision and personalized medicine.

As the 21st century dawned, findings from the Human Genome Project promised precision and personalized medicine for children and adults[16]. The hope has been that deciphering the information encoded in the human genome would lead to better prediction, diagnosis, treatment, and management of human disease, improving human health on a population scale. The promise has been to eliminate the traditional, one-size-fits-all approach to healthcare and focus on providing the proper treatment to the right patient at the right time, thereby cutting the costs of healthcare in the U.S., decreasing health disparities[17] while fulfilling the right of every individual member of the next generation to the "highest attainable standard of health"[4] (CRC, Art. 6.2). Although molecularly designed therapies are revolutionizing treatment and improving

health outcomes in select conditions like cystic fibrosis (CF)[18] and spinal muscular atrophy (SMA)[19], overall pediatric health outcomes in the U.S. remain poor[13–20].

Among several initiatives launched in the U.S. to help fulfill children's rights and improve pediatric outcomes, newborn screening (NBS) represents a uniquely innovative program that incorporates several of the core principles of the CRC. NBS is well positioned to help advance health equity for children because, since its initiation in the 1960s, all newborns are offered a screen, and parents, families, and advocacy groups have played pivotal roles in advancing policies and practices that consider the benefits and harms of neonatal screening that occurs on a population basis. Over the last 60 years, NBS has served as a model that recognizes and upholds the fundamental human rights of every child because most newborns, regardless of birth location, family income, or education, receive screening. Physiological screening of hearing and critical congenital heart disease takes place in birthing hospitals, while state-based public health laboratories perform blood-based screening for sixty-three conditions. The involvement of and public investment in state-based public health programs and the use of the public health mandate to screen all newborns are key components that enable the delivery of screening to all newborns in the U.S.

Over the last decade, significant attention in the NBS community has shifted towards the research and public health implementation of genomic-NBS (g-NBS)[20,21], an expansion of NBS technologies incorporating genomic sequencing into routine screening. This has led to several research and public health initiatives[22–24]. The new g-NBS is emerging as a potential mechanism to screen, diagnose, and possibly treat hundreds if not thousands of genetic conditions, thus showing the potential of bringing the promises of personalized medicine to every newborn while recognizing the rights of children to healthcare and the best possible outcome. This expansion of NBS to include genomics presents challenges and obstacles that need to be overcome, but these efforts can provide a useful framework for children's rights and genomics medicine.

The purpose of this manuscript is to outline the evolving recognition of the rights of children and the foundational rights to healthcare and non-discrimination, provide two examples that highlight issues to access and equity in newborn screening that may limit a child's right to healthcare and best possible outcomes, detail ways the current approach to newborn screening advances the rights of the child, and finally, propose that the incorporation of genomics into newborn screening presents a useful case study to recognize and uphold the rights of every child. This is a model of genomic medicine that is personalized and precise, acknowledges the rights of the child, and catalyzes change to advance the health and well-being of all children.

2. Relevance of the Convention on the Rights of the Child for the United States

While the 100th anniversary of the birth of international children's rights provides an auspicious occasion to reflect on global progress in the recognition and fulfillment of children's rights, including their healthcare rights, some

might mistakenly believe that it is an irrelevant measure to use in the U.S. since it remains the only recognized country in the world that has not yet ratified the CRC. As with many aspects of U.S. identity and legacy, its relationship to children and their rights is no exception.

The U.S. was not a member of the League of Nations and never had the opportunity to either recognize or later reaffirm the 1924 Declaration on the Rights of the Child. However, when the League of Nations was dissolved following World War II, the U.S. played a significant role in the formation of the United Nations (U.N.) and the prioritization of its work. Indeed, former First Lady Eleanor Roosevelt was well known for her human rights advocacy, including for children, and the U.S. voted in favor of the 1959 U.N. Declaration of the Rights of the Child.

Twenty years later, the U.S. dominated the 10-year drafting process of the CRC, submitting more content during the drafting process and making more changes to other countries' content than any other drafting party[25]. The CRC broke records for the number of signatories submitted on the first day and quickly became the most widely ratified human rights treaty in the history of the world. Today, every recognized country is a party except the U.S., which signed but has not yet ratified the CRC[1]. The U.S. went on to ratify both the first and second optional protocols to the CRC on children in armed conflict and child trafficking, respectively. Furthermore, the U.S. Supreme Court cited the near-universal ratification of the Convention as evidence of international customary law in *Roper v. Simmons* (which held that it was unconstitutional to impose the death penalty for crimes committed when the offender was a child).

Despite the U.S.'s failure to ratify the CRC, the otherwise universal ratification of the treaty, the U.S.'s status as a signatory of the treaty, the U.S.'s extensive participation in the drafting of the CRC, and the recognition of the treaty as evidence of customary law—at least with regard to some children's rights—collectively compel its applicability to the U.S., at least in aspirational principles. Indeed, the American Academy of Pediatrics (AAP) endorsed the CRC and supports its ratification[26]. A 2010 AAP policy statement further lauded the CRC as a foundational document for future policy implementation, noting that "the promotion and protection of children's rights can be used to guide the work of pediatricians as clinicians and child advocates"[27].

Even before the U.S. assumed a mantel of leadership advancing children's rights in international organizations—at least up to the point of ratification of the CRC—the U.S. had evidenced its commitment to the advancement of children's rights domestically through the promotion of public education in the 19th century, limitations on child labor in the 20th century, and the creation of welfare benefits for children during the Great Depression. Even then, the U.S.'s ambivalence towards at least some children and their rights was tragically evident in widespread discriminatory practices such as the enslavement of children, Indian boarding schools, the imprisonment of children in Japanese internment camps during World War II, and more, during these same periods. These and other examples of intentional and discriminatory treatment of some populations of children in the U.S. raise long-standing issues of access and equity now facing the pediatric medicine community.

3. Social and Economic Policies in Pediatric Medicine

Consistent with the rise of children's rights and the principles of the CRC, the pediatric community is growing increasingly attuned to issues of access and equity regarding research and clinical care. For these efforts to have a positive effect on pediatric outcomes, it is important to examine the origins of problems in pediatric medicine if we hope to understand and address the pervasive injustice, health inequities, and health disparities that have plagued the U.S. healthcare system. Clinicians, researchers, and public health professionals routinely acknowledge that genomics has a diversity problem[28]. Datasets used to conduct genome-wide association studies, produce polygenic indices, or facilitate drug development are made up mainly of human research participants with European ancestry. The risk of this reality is that any insights derived from the research will apply only (or predominantly) to the members of society with European ancestry. In a social environment where there are increasing calls for researchers and clinicians to contribute to the fight against unjust racial health disparities, there have naturally been growing calls for more diverse research cohorts and more effort invested in earning the trust of diverse communities to facilitate this inclusive mindset[29–31]. Diverse data, however, is just the first step in a very long process that ultimately delivers better health outcomes to the communities represented in that data. Decisions about which diseases are prioritized for study, which variants are deemed by private companies to offer the best return on investment, which treatments get covered by insurance providers, which clinics are equipped to provide such treatments, and who can afford to access those clinics all work towards privileging the use of the data in such a way that it benefits communities who already have more resources. Two examples provide useful insight into the magnitude of the issues and the possible solutions.

First, the comparative histories of research on sickle cell disease (SCD) and cystic fibrosis (CF) offer a powerful example of how efforts may mean well but ultimately limit, a child's right to healthcare and the best possible outcome[32,33]. Both SCD and CF inherited disorders included in newborn screening throughout the world require lifelong care and management and result in a substantial reduction in the median life span. However, there are far more people living with SCD, which has a U.S. birth rate of 1 in 365 black individuals, versus CF, which has a US birth rate of 1 in 2500 white individuals. In addition, the molecular and genetic mechanism of SCD was understood in 1910, years before the discovery and characterization of the gene for CF in 1989. SCD NBS began in 1975, and by 2006, all states, Puerto Rico, and the U.S. Virgin Islands had implemented screening[34], while CF NBS was universally adopted only in 2009[35]. African Americans were eager to participate in research to understand and treat SCD, which aided in understanding the diversity of the genotypic and phenotypic factors. And yet, historically, more research resources per patient have been devoted to CF. The biomedical research landscape used the data in such a way that it resulted in more publications pertaining to CF, more drugs approved to treat CF, and more clinics designed to care for patients with CF, meaning patients with CF had far more options for care than patients with SCD[36–38]. The recent discoveries

of gene therapies for SCD and CF are also expected to contribute to this disparity. Both CF and SCD provide useful examples of areas for improvement, and one possible solution is to focus our attention on ensuring that all conditions included in newborn screening are prioritized for the development of novel therapies and that longitudinal follow-up of diagnosed cases is in place to inform whether all children are achieving the best possible outcome[39].

Second, the economics of novel therapeutics remains an unresolved problem[40]. Life-saving treatments like Zolgensma for SMA, Zokinvy for Hutchinson-Gilford progeria syndrome, and Zynteglo for severe beta-thalassemia offer the prospect of longer and healthier lives for patients with rare genetic diseases. These pharmaceutical interventions, though, are often exorbitantly expensive. Zolgensma, Zokinvy, and Zynteglo are all priced at one to three million dollars for one-time treatments, creating access challenges for the patients who need them. To address this dilemma, advocates within the personalized medicine community have called for interventions designed to rein in costs: a streamlined federal approval process, more regulatory control over the pricing of such drugs, limits on what insurance companies can call "experimental," and novel approaches to paying for the treatments by insurance companies.

While these proposals could address some of the issues, the fundamental economic problem posed by the novel therapeutics needs to be explored further. Genomic medicine has been marketed since the Human Genome Project as an opportunity to provide the "right treatment, for the right patient, at the right time" rather than providing "one-size-fits-all" healthcare[41]. However, the division of patient populations into smaller and smaller groups based on molecular-genetic profiles, with different groups getting different treatments, will cause pharmaceutical companies to develop treatments with drastically increased prices in order to offset the smaller pool of consumers. Thus, it will take a collective effort to fundamentally rethink how these interventions are developed and compensated [42].

These issues of diversity and access are not confined to pediatric applications. Instead, they are problems facing medicine in general, which impact pediatric populations just the same. They nevertheless serve as a critical reminder that the aspirational replacement of "one-size-fits-all" healthcare with "the right treatment, for the right patient, at the right time," no matter the population, does not automatically solve the problems of cost and equity in healthcare. Focusing on the care of children and their rights, however, opens the door to reflect on resources organized around the widespread acknowledgment of our collective responsibility to provide equitable and accessible care for all children, according to the principles of the CRC, and to improve pediatric outcomes. The NBS system represents one of the main initiatives launched in the U.S. to achieve these goals, and a renewed focus on determining the health outcomes for newborns with a screened condition would be helpful.

4. Does Newborn Screening Help Fulfill the Principles and Goals of the Convention on the Rights of the Child?

For sixty years, NBS has enabled the early identification and treatment of a variety of

diseases – both rare and common[43–45]. Importantly, NBS is meant to be a system that includes screening, diagnosis, treatment, and lifelong disease management to ensure that all diagnosed newborns achieve the best possible outcome[46]. The NBS community is beginning to gather data on the impact of NBS, timely diagnosis, and the effects of social determinants on the health outcomes of diagnosed newborns[47]. In this way, and agreement with the CRC, the NBS system could provide a roadmap to help advance healthcare equity and access to pediatric medicine through children's rights principles. The first CRC principle is the right of the child to the "highest attainable standard of health"[4] (CRC, Art. 26). By implementing NBS programs as part of public health, societies ensure that every child has an equal opportunity to enjoy the highest attainable standard of health, including early identification of potential health risks.

NBS also plays a crucial role in safeguarding the child's right to life and survival[4] (CRC, Art. 6). By identifying serious, life-threatening conditions early on, such as metabolic disorders or specific genetic abnormalities, NBS allows for timely interventions and medical care. This early detection can significantly improve outcomes, preventing severe disability and even saving lives. NBS programs also uphold the rights of all children to non-discrimination[4] (CRC, Art. 2) by operating on a non-discriminatory basis, screening all infants regardless of their social, economic, or cultural background. This approach ensures that every child, regardless of their circumstances, has an equal opportunity for early detection and treatment, thereby reducing health disparities. NBS programs recognize the right of every child to privacy[4] (CRC, Art. 16). Thus, while the screening process involves collecting a blood sample from the newborn, strict protocols are in place to protect the privacy and confidentiality of the child and their family. These measures help safeguard the child's right to privacy, ensuring that their personal health information is handled with care and confidentiality.

NBS can also fulfill the child's right to an adequate standard of living[4] (CRC, Art. 27). Early detection through NBS enables timely diagnosis and access to medical care. This can prevent or reduce the severity of health conditions, potentially avoiding long-term disability and the associated economic burden, including lost income and earning opportunities, as well as potential healthcare costs resulting from conditions not treated early. By ensuring access to early diagnosis and possibly intervention, NBS supports the right to an adequate standard of living by minimizing the economic and social consequences of undetected conditions. Early identification and treatment of conditions through NBS help realize the child's right to development[4] (CRC, Art. 6). By promptly addressing health issues, children can reach their full potential physically, cognitively, and emotionally. NBS helps protect and support the right to development for all children. All children also possess a right to an inclusive society[4] (CRC, Art. 23). Specifically, Art. 23 of the CRC provides that disabled children are entitled to "enjoy a full and decent life" and special care, including health care and rehabilitation services. By identifying conditions that may require additional support or accommodation and optimizing the potential of each child to be an active and productive member of society, NBS helps ensure that disabled children are recognized early so that

their families and providers can advocate for the support they need and are entitled to to be fully integrated members of society.

Despite the close alignment between NBS and some of the core principles of children's rights, there remain some limitations in the current NBS system. Research suggests that screening without follow-up care can lead to health inequities and highlights how access to healthcare is critical for NBS to have a positive effect on children. Some studies have emphasized financial constraints in ensuring appropriate follow-up after NBS. In contrast, others have pointed to unequal outcomes following NBS among different ethnic groups for specific diseases such as hearing deficits or CF[48–50]. Moreover, an analysis of the effect of NBS on infant health outcomes and mortality in the 1960s, 1970s, and 1980s, as state-mandated NBS programs were being implemented for the first time across the U.S., showed that screening programs did not affect infant mortality while leading to more significant within-state health inequities[51,52]. Instead, infant mortality improved, and inequities decreased only when healthcare access increased as Medicaid programs started to be implemented in each state in association with NBS[52,53].

These outcomes suggest how the shortcomings of the U.S. healthcare system can conflict with the children's rights framework developed by the international community, including the U.S.[1]. For example, Article 24 of the CRC recognizes every child's right to enjoy "the highest attainable standard of health" and to access "facilities for the treatment of illness and rehabilitation of health." These rights are in addition to but overlap with the obligations of parties to ensure prenatal and post-natal helthcare and reduce infant and child mortality[4] (CRC, Art. 24.2). When children do not have access to healthcare for financial or other related reasons, it "regenerates" and compounds structural inequities that disproportionally impact already vulnerable populations of children.

Article 23, which focuses specifically on one of these populations of children—the disabled—expressly obligates parties to "ensure that the disabled child has effective access to and receives…health care services, rehabilitation services, preparation for employment and recreation opportunities in a manner conducive to the child's achieving the fullest possible social integration and individual development, including his or her cultural and spiritual development." Assistance to meet the special needs of a disabled child "shall be provided free of charge, whenever possible"[4] (CRC, Art. 23.3). In short, the international community recognizes that disabled children have an additional right to special care and assistance and that they and their families should not be expected to bear the costs of that special care.

In summary, with the necessary attention and support, the NBS system could provide a model that recognizes and upholds fundamental human rights of every child by realizing the child's right to health, life, non-discrimination, privacy, adequate standard of living, development, and an inclusive society. By facilitating early detection and access to medical care, NBS could promote equitable healthcare and reduce disparities, benefiting all children, regardless of their background or circumstances, providing a model for the implementation of pediatric personalized medicine. However, in order to ensure that NBS does not compound structural inequities, it is critical that every child has access

to all appropriate follow-up care consistent with their rights.

5. Conclusion

The CRC emphasizes the importance of ensuring appropriate prenatal and post-natal healthcare for infants and mothers, as well as applying technological advances to combat disease[4] (CRC, Art. 24). Over the last few years, and there has been increasing interest in the potential for g-NBS to help achieve these goals[20,21,54,55]. The hope is that screening every single newborn through sequencing will ensure equity. In considering the further implementation of g-NBS, it is, however, important to remember those reports demonstrating that screening without follow-up care can exacerbate health inequities and that access to healthcare is critical for universal NBS to have a positive effect on infant mortality[52,53]. Therefore, the question for the pediatric medicine community is how NBS and g-NBS could provide a model that recognizes and upholds the fundamental human rights of every child while advancing health outcomes for all children rather than just introducing a new node for inequity to take hold. How could it ensure the right to health, life, non-discrimination, privacy, adequate standard of living, development, and inclusive society? By facilitating early detection and access to medical care, how could NBS and g-NBS promote equitable healthcare and reduce disparities, benefiting all children, regardless of their background or circumstances?

As the pediatric medicine community contemplates establishing a roadmap for folding genome sequencing into NBS, we must explore the questions of access to healthcare and advocate for health equity for all children. We must use the knowledge of our history of science, research, and policy to propel us forward to realize the rights of all children. Technological innovations in rapid testing and new gene-based treatments are critical first steps; however, they are one component of the puzzle to save children's lives and improve population outcomes. The other essential component is ensuring healthcare access for all children. Providing capacity-building resources, such as increasing workforce development, education, and training at the intersection of social determinants of health and genomic medicine, could help decrease health inequities and disparities and improve health outcomes[56]. However, other measures are likely to be needed to deliver on the promises of personalized medicine.

In addition to policy efforts such as working for U.S. ratification of the CRC to advance our ability to protect all children, future studies and analysis of NBS and g-NBS, in line with the principles enunciated in the CRC, should dissect the effects on outcomes of the screening test that includes the diagnosis, care, and long-term management of disease. We believe there is good reason to think that these approaches would increase our understanding of the role of social determinants of health and could help advance child health in the U.S. and abroad. This is how the pediatric medicine community could chart a course forward, leading the way in fulfilling children's rights and advancing children's health and wellbeing by using genomics in equitable and non-discriminatory ways. The evolving recognition of children's rights, the foundational rights to healthcare and non-discrimination, and the incorporation of genomics into newborn screening presents a useful case study to recognize and uphold the rights of every child.

Author Contributions:

Conceptualization included: L.B., K.C., J.T., W.B., and A.B.; writing—original draft preparation, L.B., K.C., J.T., W.B., and A.B.; writing—review and editing, L.B., K.C., J.T., W.B., and A.B. All authors have read and agreed to the published version of the manuscript.

Funding Statement:

This work was funded by federal funds from the NICHD, National Institutes of Health, Department of Health and Human Services, under Contract No. HHSN275201800005C

Institutional Review Board Statement:

Not applicable.

Informed Consent Statement:

Not applicable.

Data Availability Statement:

No new data were created, and thus, this statement is not applicable.

Acknowledgement Statement:

None

Conflict of Interest Statement:

The authors declare no conflicts of interest and the funders had no role in the design of the study, in the collection, analyses, or interpretation of data, in the writing of the manuscript, or in the decision to publish the results.

References:

1. Binford WWH. School Lessons in War: Children at Tuol Sleng & the Rise of International Protection for Children in War. *Willamette J Int'l L & Dis Res*. 2008;16:28.

2. *Geneva Declaration of the Rights of the Child, Sept. 26, 1924, League of Nations, O.J. Spec. Supp. 21 at 43 (1924).*

3. *Declaration of the Rights of the Child, G.A. Res. 1386 (XIV), GAOR 14th Sess., Supp. No. 16, U.N. Doc. A/4249 (Nov. 20, 1959).*

4. *Convention on the Rights of the Child, Opened for Signature Nov. 20, 1989, 1577 U.N.T.S. 3.*

5. McGough M, Telesford I, Rakshit S, Wager E, Amin K, Cox C. PETERSON-KFF health system tracker. *How does health spending in the US compare to other countries?* https://www.healthsystemtracker.org/chart-collection/health-spending-u-s-compare-coun tries/.

6. Isaacs JB, Lou C, Hahn H, Lauderback E, Quakenbush C, Steuerle CE. Kids' Share 2019: Report on Federal Expenditures on Children through 2018 and Future Projections. *Urban Institute*. 2019.

7. Thakrar AP, Forrest AD, Maltenfort MG, Forrest CB. Child mortality in the US and 19 OECD comparator nations: a 50-year time-trend analysis. *Health Affairs*. 2018;37(1):140-149.

8. Adamson P. Child Well-Being in Rich Countries: A Comparative Overview. Innocenti Report Card 11. *UNICEF*. 2013.

9. Clark H, Coll-Seck AM, Banerjee A, et al. A future for the world's children? A WHO–UNICEF–Lancet Commission. *The Lancet*. 2020;395(10224):605-658.

10. Council NR, Population C on. US health in international perspective: Shorter lives, poorer health. 2013.

11. Schneider EC, Shah A, Doty MM, et al. Reflecting Poorly: Health Care in the US Compared to Other High-Income Countries. *New York: The Commonwealth Fund*. 2021.

12. Adler NE, Cutler DM, Fielding JE, et al. Addressing Social Determinants of Health and Health Disparities: A Vital Direction for Health and Health Care. *NAM Perspectives*. 2016; 6(9). doi:10.31478/201609t

13. Gibbs RA. The human genome project changed everything. *Nature Reviews Genetics*. 2020;21(10):575-576.

14. Singu S, Acharya A, Challagundla K, Byrareddy SN. Impact of social determinants of health on the emerging COVID-19 pandemic in the United States. *Frontiers in public health*. 2020;8:406.

15. Tabery J. *Tyranny of the Gene: Personalized Medicine and Its Threat to Public Health*. Knopf; 2023.

16. Collins FS, Green ED, Guttmacher AE, Guyer MS, Institute UNHGR. A vision for the future of genomics research. *nature*. 2003;422(6934):835-847.

17. Green ED, Gunter C, Biesecker LG, et al. Strategic vision for improving human health at The Forefront of Genomics. *Nature*. 2020; 586(7831):683-692.

18. Allan KM, Farrow N, Donnelley M, Jaffe A, Waters SA. Treatment of Cystic Fibrosis: From Gene- to Cell-Based Therapies. *Front Pharmacol*. 2021;12:639475. doi:10.3389/fphar.2021.639475

19. Ogbonmide T, Rathore R, Rangrej SB, et al. Gene Therapy for Spinal Muscular Atrophy

(SMA): A Review of Current Challenges and Safety Considerations for Onasemnogene Abeparvovec (Zolgensma). *Cureus*. 2023;15 (3):e36197. doi:10.7759/cureus.36197

20. Dimmock D, Caylor S, Waldman B, et al. Project Baby Bear: Rapid precision care incorporating rWGS in 5 California children's hospitals demonstrates improved clinical outcomes and reduced costs of care. *The American Journal of Human Genetics*. 2021; 108(7):1231-1238. doi:10.1016/j.ajhg.2021.05.008

21. Kingsmore SF, Smith LD, Kunard CM, et al. A genome sequencing system for universal newborn screening, diagnosis, and precision medicine for severe genetic diseases. *Am J Hum Genet*. 2022;109(9):1605-1619. doi:10.1016/j.ajhg.2022.08.003

22. Berg JS, Agrawal PB, Bailey DB, et al. Newborn Sequencing in Genomic Medicine and Public Health. *Pediatrics*. 2017;139(2): e20162252. doi:10.1542/peds.2016-2252

23. The BabySeq Project Team, Holm IA, Agrawal PB, et al. The BabySeq project: implementing genomic sequencing in newborns. *BMC Pediatr*. 2018;18(1):225. doi:10.1186/s12887-018-1200-1

24. Adhikari AN, Gallagher RC, Wang Y, et al. The role of exome sequencing in newborn screening for inborn errors of metabolism. *Nat Med*. 2020;26(9):1392-1397. doi:10.1038/s41591-020-0966-5

25. *Office of the United Nations High Commissioner for Human Rights, Legislative History of the Convention on the Rights of the Child, Vol. 1, at Iii, U.N. Doc. HR/PUB/07/1 (2007); Cynthia Price Cohen, Role of the United States in Drafting the Convention on the Rights of the Child: Creating A New World For Children, 4 Loy. Poverty L.J. 9 (1998).*

26. Haggerty RJ. The Convention on the Rights of the Child: it's time for the United States to ratify. *Pediatrics*. 1994;94(5):746-747.

27. Granado-Villar DC, Brown JM, Cotton WH, et al. Policy statement-health equity and children's rights. *Pediatrics*. 2010;125(4):838-849.

28. Edwards TL, Breeyear J, Piekos JA, Edwards DRV. Equity in health: consideration of race and ethnicity in precision medicine. *Trends in Genetics*. 2020;36(11):807-809.

29. Landry LG, Ali N, Williams DR, Rehm HL, Bonham VL. Lack Of Diversity In Genomic Databases Is A Barrier To Translating Precision Medicine Research Into Practice. *Health Affairs*. 2018;37(5):780-785. doi:10.1377/hlthaff.2017.1595

30. Cooke Bailey JN, Bush WS, Crawford DC. Editorial: The Importance of Diversity in Precision Medicine Research. *Front Genet*. 2020;11:875. doi:10.3389/fgene.2020.00875

31. Keck School News. *The Path to Personalized Medicine for Everyone*. June 2021. https://keck.usc.edu/the-path-to-personalized-medicine-for-everyone/. Accessed November 10, 2023.

32. Wailoo K, Pemberton S. *The Troubled Dream of Genetic Medicine: Ethnicity and Innovation in Tay-Sachs, Cystic Fibrosis, and Sickle Cell Disease*. JHU Press; 2006.

33. Wailoo K. *Dying in the City of the Blues: Sickle Cell Anemia and the Politics of Race and Health*. UNC Press Books; 2014.

34. Benson JM, Therrell Jr BL. History and current status of newborn screening for hemoglobinopathies. In: *Seminars in Perinatology*. Vol 34. Elsevier; 2010:134-144.

35. Sontag MK, Miller JI, McKasson S, et al. Newborn screening for cystic fibrosis: a qualitative study of successes and challenges from universal screening in the United States. *International Journal of Neonatal Screening*. 2022;8(3):38.

36. Strouse JJ, Lobner K, Lanzkron S, Haywood Jr C. NIH and national foundation expenditures for sickle cell disease and cystic fibrosis are associated with PubMed publications and FDA approvals. *Blood*. 2013;122(21): 1739.

37. Farooq F, Strouse JJ. Disparities in foundation and Federal Support and development of new therapeutics for sickle cell disease and cystic fibrosis. 2018.

38. Farooq F, Mogayzel PJ, Lanzkron S, Haywood C, Strouse JJ. Comparison of US federal and foundation funding of research for sickle cell disease and cystic fibrosis and factors associated with research productivity. *JAMA network open*. 2020;3(3):e201737-e201737.

39. Geneviève LD, Martani A, Shaw D, Elger BS, Wangmo T. Structural racism in precision medicine: leaving no one behind. *BMC Medical Ethics*. 2020;21:1-13.

40. Konkel L. WHO will benefit from precision medicine. *UCSF Magazine Winter*. 2020:1-19.

41. Marcus MB. Precision Medicine Initiative Aims to Revolutionize Health Care. February 2016. https://www.cbsnews.com/news/presidents-precision-medicine-initiative-is-propelling-forward.

42. Lu CY, Terry V, Thomas DM. Precision medicine: affording the successes of science. *NPJ Precision Oncology*. 2023;7(1):3.

43. Grosse SD, Hannon WH. Using tandem mass spectrometry for metabolic disease screening among newborns; a report of a Work Group. 2001.

44. Bick D, Ahmed A, Deen D, et al. Newborn Screening by Genomic Sequencing: Opportunities and Challenges. *Int J Neonatal Screen*. 2022;8(3). doi:10.3390/ijns8030040

45. Guthrie R, Susi A. A simple phenylalanine method for detecting phenylketonuria in large populations of newborn infants. *Pediatrics*. 1963;32(3):338-343.

46. Watson MS, Lloyd-Puryear MA, Howell RR. The Progress and Future of US Newborn Screening. *Int J Neonatal Screen*. 2022;8(3). doi:10.3390/ijns8030041

47. Sontag MK, Yusuf C, Grosse SD, et al. Infants with Congenital Disorders Identified Through Newborn Screening - United States, 2015-2017. *MMWR Morb Mortal Wkly Rep*. 2020;69(36):1265-1268. doi:10.15585/mmwr.mm6936a6

48. Holte L, Walker E, Oleson J, et al. Factors Influencing Follow-Up to Newborn Hearing Screening for Infants Who Are Hard of Hearing. *Am J Audiol*. 2012;21(2):163-174. doi:10.1044/1059-0889(2012/12-0016)

49. McColley SA, Martiniano SL, Ren CL, et al. Disparities in first evaluation of infants with cystic fibrosis since implementation of newborn screening. *Journal of Cystic Fibrosis*. 2023;22 (1):89-97. doi:10.1016/j.jcf.2022.07.010

50. Hoff T, Hoyt A, Therrell B, Ayoob M. Exploring barriers to long-term follow-up in newborn screening programs. *Genetics in Medicine*. 2006;8(9):563-570. doi:10.1097/01.gim.0000237790.54074.3d

51. Brosco JP, Grosse SD, Ross LF. Universal State Newborn Screening Programs Can Reduce Health Disparities. *JAMA Pediatr*.

2015;169(1):7. doi:10.1001/jamapediatrics.2014.2465

52. Sohn H, Timmermans S. Inequities in newborn screening: Race and the role of medicaid☆. *SSM - Population Health*. 2019;9:100496. doi:10.1016/j.ssmph.2019.100496

53. Brunelli L, Sohn H, Brower A. Newborn sequencing is only part of the solution for better child health. *The Lancet Regional Health–Americas*. 2023;25.

54. Seydel C. Baby's first genome. *Nat Biotechnol*. 2022;40(5):636-640. doi:10.1038/s41587-022-01306-1

55. Kaiser J. Sequencing projects will screen 200,000 newborns for disease. *Science*. 2022;378(6625):1159-1159. doi:10.1126/science.adg2858

56. Khoury MJ, Bowen S, Dotson WD, et al. Health equity in the implementation of genomics and precision medicine: A public health imperative. *Genetics in Medicine*. 2022;24(8):1630-1639.