

Abstract

Traditional newborn screening (NBS) is an effective and successful public health program that enables early detection of severe diseases and subsequent clinical intervention. With the development of whole-genome sequencing (WGS), a powerful technology that has the potential to detect multiple deleterious genetic variants at once, there is an interest in utilizing WGS in NBS to improve public health outcomes.

Illumina is the leading global biotechnology company, controlling 80% of the world's DNA sequencing market that operates in 17 countries across the 5 continents. Due to the rapid pace of innovation in the biotechnology sector and given its operations across the globe, Illumina must evaluate its role in genomics and create policies that ensure the ethical and economical practices of WGS technologies on a global scale. Although Illumina has already identified the financial burden of genetic sequencing and enacted a goal to decrease the price to \$100 per genome, they must continue to anticipate a nuanced approach towards governing its principles and policies on a global scale. To consider these ethical concerns, we surveyed the current landscape of tNBS, evaluated pilot programs related to WGS, and analyzed current legislation on tNBS and WGS.

Objectives

Currently, traditional newborn screening (tNBS) is a widely accepted, mandated medical test for newborn across the US. If whole-genome sequencing (WGS) were to be utilized in population-scale NBS, Illumina would need to evaluate the current studies on WGS, its ethical implications, and the resulting legal framework. Our project objective aims to:

- (1) **Survey the current tNBS landscape**
- (2) **Analyze pilot programs related to WGS implementation frameworks and/or related to tNBS**
- (3) **Curate a legal framework for WGS in NBS**

Methods

Landscape analysis: Read ethical and meta analyses studies on Whole Genome Sequencing (WGS) in newborn screening (NBS). Identified a list of some of the most pertinent and relevant ethical dilemmas and conducted targeted literature review.

Implementation analysis: Surveyed pilot programs relating to WGS implementation and/or WGS in tNBS and created a literature review. Then, generated a document summarizing and analyzing studies.

Legislative analysis: Reviewed and analyzed NBS statutes, statutes pertaining to WGS, and relevant federal legislation. Conducted follow up research on proposed legislation aimed at filling the gaps in genetic testing. Subsequently created framework document to account for these findings.

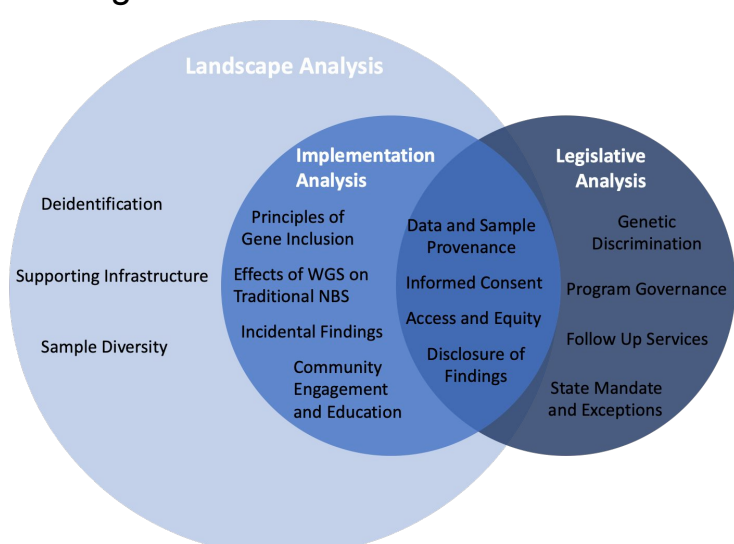


Figure 1: Ethical themes researched by project phase

Results

As a result of our project, we created two main deliverables:
(1) Document analyzing and summarizing pilot programs
(2) Legislative framework for WGS in tNBS.

In our first deliverable, we found that:

1. When pilot programs approached issues of incidental findings, they 1) incorporated parent/patient opinions and values before any testing is done, and 2) categorized gene-disease pairs based on risk of psychological harm for patients following expert, scientific advice.
2. Pilot studies incorporated genetic counseling, which allows families to be thoroughly informed on the conditions they are consenting to.
3. Due to the novel aspect of WGS in tNBS, pilot programs have not developed robust frameworks for children to re-consent, but the Newborn Genomes Programme provides children with the opportunity to withdraw consent when they reach the age of consent.
4. Introduction of WGS for NBS has the potential to decrease the widespread uptake and efficacy of NBS, as it introduces an informed consent process, while tNBS is otherwise mandated across 50 states. While referencing the BabySeq case study, we found that the analysis of control cohort (regular NBS) and test cohort (NBS + nGS) parents opinions revealed that on a Likert scale of 1 (strongly disagree) to 5 (strongly agree) parents ranked 'every newborn should receive NBS as a 4.67 in comparison to every newborn should receive genetic sequencing' at 3.60 on average.
5. Population-scale implementation of WGS in NBS incurs additional concerns such as cost, decreased uptake of tNBS, and potential data privacy risks.

In response to these concerns, we evaluated the current legislative statutes governing tNBS and genomic data and compiled proposed legislative frameworks in our second deliverable. We found many articles of proposed legislation aimed at addressing diagnostic reporting and a streamlined informed consent process through funding of genetic counselors, such as Access to Genetic Counselor Services Act of 2021. Other proposed legislation has been advocating for increased expansion of WGS through Medicaid funding, such as the Expanded Genetic Screening Act of 2021, the Precision Medicine for Kids Today Act, and the Ending Diagnostic Odyssey Act of 2021. Lastly, there are statutes related to NBS sample provenance, focused on regulating research studies on newborn blood spots, such as the Newborn Screening Saves Lives Act 2021.

	Relevant Legislation	Gaps	Legislative Proposals
Genetic Discrimination	<ul style="list-style-type: none"> GINA HIPAA ADA 	<ul style="list-style-type: none"> Life insurance long-term care insurance Disability insurance housing decisions 	<ul style="list-style-type: none"> Comprehensive federal legislation Expanded protection from private institutions Broadened inclusion of genetic technologies and information
Informed Consent	<ul style="list-style-type: none"> Patchwork of state statutes on genetic screening State NBS statutes 	<ul style="list-style-type: none"> Lack of consensus on large-scale mandate Feasibility of informed consent at a large scale 	<ul style="list-style-type: none"> Evaluate possibility of large-scale genetic counselling to dictate what patient must consent to
Program Governance	<ul style="list-style-type: none"> State NBS statutes 	<ul style="list-style-type: none"> N/A 	<ul style="list-style-type: none"> Adapt state committees to govern WGS in NBS Appoint expert organization to classify and recommend disease inclusion
Sample Provenance	<ul style="list-style-type: none"> State NBS statutes State Statutes on genetic testing, discrimination, and use in insurance settings 	<ul style="list-style-type: none"> N/A 	<ul style="list-style-type: none"> Apply universally concept that genetic samples should be destroyed after intended use
Disclosure of Results and Genetic Confidentiality	<ul style="list-style-type: none"> State NBS statutes 	<ul style="list-style-type: none"> Closely tied to issues of informed consent: disclosure dependent on availability of genetic counselling Balancing patients' right to know with their right to non-maleficence with respect to reporting 	<ul style="list-style-type: none"> Newborn Screening Saves Lives Act of 2021 seeks to align blood-spots in NBS with confidentiality constraints for human subjects Evaluate possibility of large-scale genetic counselling to dictate which results to be mandatory
Access and Equity (Cost)	<ul style="list-style-type: none"> State NBS statutes State statutes of genetic testing 	<ul style="list-style-type: none"> States differentially cover the cost of genetic testing for minors States differentially cover the cost of newborn screening 	<ul style="list-style-type: none"> Ending Diagnostic Odyssey Act of 2021, Precision Medicine for Kids Today Act, and Expanded Genetic Screening Act of 2022 seek to expand Medicaid coverage of genetic screening and testing in select populations

Figure 2: Chart summarizing our findings for the legislative framework

Conclusion

WGS has the potential to accelerate innovations in precision medicine and public health efforts, such as in newborn screening. In response to this emerging interest in utilizing WGS in NBS, there are a variety of ethical concerns and legislative actions that must be considered in order to build the healthcare infrastructure needed to support population-scale incorporation of WGS in NBS. We took two approaches to addressing these considerations, evaluating pilot programs implementations of WGS and assessing current and potential legislation concerning WGS and NBS. In our analysis of pilot programs, we found patterns indicating that it is imperative for WGS programs to incorporate parent values before testing; in order to do this, many pilot programs worked towards making sure their participants were adequately informed on incidental findings and the consent process. Nonetheless, as WGS for NBS is an emerging innovation, there are still many legislative actions necessary to support the development of such initiatives.

We concluded that that is it necessary to expand current community engagement models and education surrounding genetic testing so that community members are educated on the implications and their rights as pertaining to genetic testing. As shown through our pilot program study and legislative framework, the incorporation of genetic counselors throughout the entire genetic testing process can bolster patient/parent comprehension and autonomy. The incorporation of genetic counselors in the return of test results is especially effective, and therefore, essential. Moreover, we show that potential future areas of focus rest on funding for program, genetic data privacy risks, and its implications for tNBS.



Link to the catalog of our implementation analysis of whole-genome sequencing pilot programs in newborn screening

References

For a compiled list of our references:

Pilot program analysis –

https://docs.google.com/spreadsheets/d/1-8UhtXUck2HK6ihpAMPB7H-MisDeZiEubrBCF07Dttk/edit?usp=drive_link

Literature review matrix –

https://docs.google.com/spreadsheets/d/1_nYRcAYTuShNR72HdJEQh9OI4PWsVnqafnPJ1vqmRvo/edit?usp=drive_link

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