Diverse Parental Perspectives of the Social and Educational Needs for Expanding Newborn Screening through Genomic Sequencing

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\begin{abstract}
\textbf{Objective:} The aim of this study was to explore the parental views, attitudes, and preferences of expanded newborn screening (NBS) through genomic sequencing. \textbf{Study Design:} We conducted a semi-structured interview study with English and Spanish speaking mothers who had given birth within the USA in the past 5 years. The interviews explored opinions of expanding NBS, ethical and privacy concerns, and educational and social needs. \textbf{Results:} All participants were interested in some degree of NBS expansion. However, there were differing opinions about the characteristics of conditions that should be included with less consensus for conditions with low penetrance, those without approved treatment, or onset outside of early childhood. All parents endorsed potential medical utility but also nonmedical utility as a motivating factor including being able to prepare and not being surprised by health issues as they occurred. Most felt that it was important to have some choice about the conditions screened, and many expressed the importance of proper education to make an informed choice and a desire to receive this education in the prenatal period. Responses to the type of education and information needed to make an informed decision varied. \textbf{Conclusions:} Parents anticipate value in expanded NBS through genomic sequencing both for medical and nonmedical/personal utility. In order to successfully implement expanded NBS, prospective parents need more and earlier education about the process. These needs may differ by language and culture. Information needs to be easily accessible and to be curated by appropriate experts and stakeholders, including parents representative of the diversity of the USA.
\end{abstract}

\section*{Introduction}

Newborn screening (NBS) is the process of screening all newborns for select conditions shortly after birth. This process reduces morbidity and mortality by the detection of medically actionable conditions in presymptomatic babies. Traditionally, NBS is performed by detecting an analyte or clinical marker of disease. There have been preliminary studies exploring the potential addition of ge-
nomic sequencing (GS) as a method for NBS [1–4]. GS has had a significant impact on medicine. It has improved our ability to diagnose rare and novel genetic conditions, shortened the diagnostic odyssey, and dramatically improve health outcomes when treatable conditions are identified [5–9]. Within the context of NBS, GS can detect a wider range of diseases than traditional NBS alone [10]. GS-based NBS workflows can aid in the interpretation of borderline metabolic results with genotypic data providing an additional line of evidence to predict prognosis and need for intervention [10, 11]. GS NBS also has the capacity to identify infants with genetic conditions that would not have been detected by standard NBS and that have implications for immediate newborn care including metabolic storage disorders and inherited arrhythmias that can cause sudden infant death syndrome [3, 4].

There is medical and public support for GS NBS [12, 13]. Many parents support expanded NBS through GS and express a desire to learn about their child’s risk for health conditions, often regardless of the availability of intervention [3, 14–16]. Despite this willingness, parents have reservations about the potential for false positives, concerns about incomplete penetrance [3], concerns about the risk of discrimination, unwanted results, or impairment on children’s rights to an open future [12, 13, 17, 18]. Even without the added complexity of GS, public understanding of current traditional NBS is modest. Parents tend to be misinformed or uninformed and can feel overwhelmed by the process [12, 19–21]. The scientific community, while supportive of exploring GS for NBS, has expressed caution about the implementation of GS NBS and emphasized the importance of close examination of the full process before widespread implementation including ethical, legal, and social implications in studies of this process [22, 23].

In 2019, the Bioethics and Legal Workgroup for the Newborn Screening Translational Research Network published recommendations to guide pilot studies of NBS to generate the data needed to inform any changes to NBS [22]. They recommended systematic evaluations of the ethical, legal, and social implications of the potential screening results; resource allocation; equity and access; and public trust when exploring adding new conditions. They also recommended that studies should include diverse participants to understand the heterogeneity and complexity of parental perceptions. Guided by these recommendations, we examined the parental views, attitudes, and preferences of expanded NBS of women who had had a child in the USA in the last 5 years and therefore had experience with NBS.

### Methods

#### Sample and Recruitment

There were two sources for recruitment of participants for this study. Mothers who had previously participated in a pilot study for spinal muscular atrophy at the Columbia University Irving Medical Center who had consented to future contact for additional research studies were selected at random and invited by email and phone. In addition, the team wanted to ensure diverse opinions particularly from marginalized communities were represented. Therefore, the team recruited mothers from the local community in which the medical center is located. This was accomplished through collaboration with a local community-based partner that serves and is trusted by those in the local community. Participants were identified from El Nido de Esperanza [24], a Washington Heights community-based organization (CBO) which serves low-income, mixed citizenship status, Spanish speaking mothers within the Northern Manhattan, New York community. For both recruitment sources, interested mothers contacted the study team; and eligibility was confirmed by phone or email, and interviews were scheduled. Eligibility criteria included

### Table 1. Demographics of participants

| Demographic Variable          | n   | %   |
|-------------------------------|-----|-----|
| Agea                          | 33  | 24–47 |
| Language of interviewb        |     |     |
| English                       | 19  | 54  |
| Spanish                       | 16  | 46  |
| Recruitment groupb            |     |     |
| NBS pilot study               | 22  | 63  |
| CBO                           | 13  | 37  |
| Parental roleb                |     |     |
| Mother                        | 35  | 100 |
| Race/ethnicity/ancestryc      |     |     |
| Hispanic/Latinx               | 17  | 50  |
| White                         | 11  | 32  |
| African-American/Black        | 4   | 12  |
| Asian                         | 1   | 3   |
| Native American               | 1   | 3   |
| Education level               |     |     |
| Less than high school         | 5   | 15  |
| High school diploma           | 6   | 18  |
| Some college/associate        | 2   | 6   |
| College                       | 9   | 26  |
| Advanced degree               | 12  | 35  |
| Insurance type                |     |     |
| Private                       | 12  | 35  |
| Medicaid                      | 18  | 53  |
| None                          | 4   | 12  |
| Employment status             |     |     |
| Employed                      | 15  | 44  |
| Not employed                  | 19  | 56  |

* a Mean and range.  
  b N = 35, includes the participant who is missing demographics for all other fields.  
  c Asked as an open-ended question.
speaking English or Spanish and having a child between the ages of 1 year and 5 years who was born in the USA and therefore had had NBS. The sample with demographics is described in Table 1.

Procedures
We conducted semi-structured qualitative phone or video interviews (participant choice) with 35 mothers. Guided by the recommendations of ELSI research in NBS, the interviews explored opinions of expanding NBS, ethical and privacy concerns, and educational and social needs. The interview began by reminding the parent of the current NBS process including when it is done, the types of conditions screened, and follow-up diagnostic testing (interview guide provided in online suppl. Materials; for all online suppl. material, see www.karger.com/doi/10.1159/000526382). Next, we provided a brief explanation of how GS technology could be used to expand NBS. The first set of questions explored how the availability of treatment, condition severity, and age of onset influence the parent’s preference for expanded screening. Next, we explored the parent’s concerns about false-positive and false-negative NBS results, issues of equity of NBS and follow-up care, generation and storage of GS data on newborns, and potential for genetic discrimination. Finally, we asked the parent about their educational needs regarding expanded NBS and scalable education options.

Interviews were conducted by a clinical/research genetic counselor (J.W.) and research assistant (G.T.T.) or bilingual research assistant (A.B.) with experience conducting semi-structured interviews. Interviews in Spanish used a culturally competent and linguistically accurate interview guide and analysis based on insights and feedback from our bilingual culturally competent interviewer to ensure thematic accuracy of insights from Spanish participants. Participants received a USD 50 gift certificate for completing the 30–60 min interview.

Analysis
Interviews were transcribed, and those in Spanish were translated and reviewed by a professional service to ensure culturally and linguistically competent translation. We used interpretative phenomenological analysis to code the interviews in NVivo [25]. Given the shared experience of these mothers as participants in the current NBS process within the state of New York and their highly personal ways of using and understanding those results, we utilized this shared experience across participants as the foundation for questioning the ways in which expanding NBS is understood and could impact these parents. This shared experience is the primary source of meaning on the topic throughout the interview, and the reflections of the participants based on this are therefore the key contents of the quotes coded throughout our analysis. First, the interview script was used to draft an initial code book. Next, the code book was applied to three interviews by two independent coders (A.M.S. and G.T.T.). New codes were developed for recurrent themes not addressed in the initial code book. Disagreement in the coding was resolved through meetings with the two independent coders and a third researcher (J.W.) who conducted the interviews. This process was repeated until a final code book was developed, and the average Kappa, a measure of coding reliability, for each of the interviews was over 0.8 with an average of 0.9 for all four interviews. The final code book was used to code the remaining interviews by a primary coder, and a secondary coder reviewing the primary coder’s work. Reverse translation by an independent native speaker was completed for all Spanish quotes used in this publication. Participants were asked open-ended questions across three categories: perceptions of expansion of NBS to include GS, privacy and ethical concerns, and social and educational needs.

Results
Participants
288 individuals who previously participated in a pilot study of SMA NBS were invited by email, 24 responded to the email, and 22 completed an interview (19 English, 3 Spanish). The remaining 13 participants, all Spanish speaking, responded to the invitation shared with the CBO members. Interviews were conducted from May 2020 to April 2021. Half of the participants identified as Latina. The average age was 33 years (24–47), and a third had a high school diploma or less. Five mothers had children with childhood onset health conditions including one whose child had deafness identified through NBS. In addition, one was diagnosed prenatally (Down syndrome). The final three had children diagnosed after presenting with symptoms (infantile seizures, DiGeorge syndrome, multiple congenital anomalies who was deceased). Based on phenomenological analysis of the interviews, the following five themes were established:

Weighing of Benefits and Risks of Expanding NBS
While all participants were interested in some degree of NBS expansion, there were differing opinions about the characteristics of conditions that should be included. All felt comfortable including conditions that have available treatment and affect children early in life. Some participants did not feel comfortable with expanding to include conditions with low penetrance, without approved treatment, onset outside of early childhood, and/or those with few symptoms/very low severity. One mother shared her reluctance to learn about conditions that had no or low penetrance:

“Is that possible to have a disease that doesn’t really have any symptoms or doesn’t really show itself in any way but would show up on a test if she was tested, then maybe I wouldn’t need her to be tested. So then I would say that doesn’t need to be on a newborn screening because it doesn’t matter anyway.” ID14

When weighing the benefits and concerns in making the hypothetical choice, many mothers expressed the benefits of both medical (treatment) and nonmedical (preparation, psychosocial support, early intervention,
and life planning) steps that could be made because of a diagnosis. One mother reflected:

“If you already have that knowledge, it’s perhaps less... Like you’re giving time to adjust to it. It’s less alarming, perhaps, than if you found out later." ID06

Universally, participants expressed concern about the potential for expanded NBS to produce anxiety including that related to the stress of waiting for confirmation testing, anticipation of symptoms after a diagnosis has been made, and potential pain from the treatment and to a lesser extent, the screen itself. Parents also shared concerns about the newness of the testing and uncertainty about what to expect. One mother reflected:

“Well maybe because I don’t know, because it’s new, so I wouldn’t know if there are risks, if there’s any kind of risk or consequences of those tests. I don’t know if – I don’t know what would happen. So, I’d be scared.” ID19

Though after stating their concern, parents often reflected on how the benefits outweighed them. For example, one mother stated:

“Well maybe as a mother you feel bad when you find out your child has some kind of fatal or physical disease, but I think it’s good, right? To be informed about what the child needs.” ID26 (Spanish-speaker)

Desire for and Challenge of Choice

Most parents felt that it was important for parents to have some degree of choice about the additional conditions screened. Many expressed the importance of proper education to make an informed choice. Some, who advocated for a choice, indicated it would be valuable to have a certain set of conditions for which a parent could not decline, such as a tiered system of conditions. One mother reflected on the importance and challenge of a choice:

“Well, it’s very difficult but I think it’s just that’s the key to it. I think it is giving people the choice to make the decision themselves, but without the proper explanation or education about it, then I don’t know how you could just – how it could just be left up to the individuals.” ID14

There was significant diversity in the information mothers felt was important in knowing when making the decision. One mother expressed a desire to have a detailed explanation of each condition:

“The extent of the disease, if it’s very advanced, if it’s minor, how long it would last, also the cost, the cost of the treatment, what type of procedure, what are the risks that come with each procedure.” ID 24 (Spanish-speaker)

Another mother advocated for grouping the condition types:

“I think if there’s less information it’s less overwhelming. I think the understanding of information is better when it’s by groups because if you see them one by one, it’s a lot of information.” ID 21 (Spanish-speaker)

A handful of mothers felt that there should not be parental choice and had concerns that the decision was too complex for them or other parents and/or other parents would choose not to test for treatable conditions and children would suffer. One mother noted:

“I think it should be something that the medical community agrees is what kids need to be screened for because... you see a lot of ignorance out there and... because somebody lacks knowledge about that aspect, you don’t want their child to suffer.” ID13

Perceived Nonmedical Utility

All parents expressed some type of nonmedical utility as a motivating factor in choosing to have expanded NBS. Most indicated the utility of being able to prepare both themselves and potentially the child for the condition and not being surprised by health issues as they occurred. As one mother reflected:

“I think it’s good to do those kinds of tests on babies because that way you know about anything, if there’s any kind of anomaly. As a parent, you can start to prepare and find help.” ID33 (Spanish-speaker)

Less common nonmedical utility referenced by the parents included: the ability to rule out tested diagnoses within potential future health emergencies, psychological support, connecting with other parents of children with the same condition, preparing the child for the condition and its symptoms and impacts on the child’s life, planning the educational services and schooling options for the child, planning for the financial impacts of a child with special needs, including insurance concerns, family planning and informing other family members, preparing the home for possible equipment needs, and preparing needed behavioral interventions as a result of symptoms or social isolation. Mothers who had children with special needs were especially aware of these types of issues. One of the mothers reflected:

“I think regardless of treatment if knowing ahead of time could get a family access to, you know, support, right, or better understanding of what they’re about to go through, right, I think that’s a win.” ID01 (mother of a child with Down syndrome)

Several reflected on the altruistic potential that identifying children through screening could advance our understanding of these conditions, while it may not be immediately helpful to their own family.
Confidentiality and Privacy Concerns for NBS Information
Participants were asked an open-ended question about concerns related to the privacy and confidentiality of participating in a study of expanded NBS and the storage of genomic data. Several participants expressed concern about the confidentiality of their child’s data, acknowledging the potential for breach of confidentiality but also trusting that the data would be appropriately protected. As one mother stated:

“Well I actually feel really safe…that everything’s confidential and maybe it really doesn’t affect me too much that – that’s not really a problem for me.” ID22 (Spanish-speaker)

Some participants had difficulty understanding this question and the concept of genomic data storage and how this was different from standard medical records. One mother shared:

“…because it’s not like it’s your credit card information. It’s not that kind of stuff. No one’s going to steal your identity unless, I don’t know. Unless they’re going to clone people. I’m not sure…But I just feel like, in this day and age, more and more people would be kind of freaked out about that.” ID06

All parents were in favor of storing the data for future clinical use if the child presented with symptoms of a genetic condition. Some participants shared it would be helpful to have some choice in how or if the data was stored. As one mother reflected:

“I think it should be a choice as well, like do you allow us to keep the information, or you don’t want to keep the information.” ID17

Earlier and Expanded Education for NBS
All parents expressed interest in education regarding NBS beyond the current education. A majority expressed a desire for education on routine screening and optional screening to occur during pregnancy with several specifically referencing the 2nd or 3rd trimester as a preferred time frame for education. Mothers shared that early education was important as decision-making in the postpartum period is challenging. One mother stated:

“Maybe at the beginning of the third trimester just because once you have a baby, you feel like you got hit by a truck so you’re not even thinking about anything else. You’re – especially if it’s a first child – your life is completely changed…you make decisions in survival mode, but…you could give people the opportunity to do some research or read up more about something.” ID13

While discussing educational needs, some mothers noted that they did not know much about the standard NBS process. Several reflected how when their baby had standard NBS they were uncertain what was happening, and this produced anxiety. In reflecting on her own experience with her baby, one mother recommended more explanation of the process:

“It’s better that they do it and sometimes it’s also better that they explain why they’re doing it to the parents. Because a lot of us don’t understand.” ID25 (Spanish-speaker)

Mothers described that education could be accomplished through several modalities including brochures, pamphlets, websites, and a clinician prompting a discussion. For several participants, all who had experience with parenting support previously, raised the idea of having social groups with classes for peer support and in-person education in a relaxed community setting.

Discussion
We present semi-structured interviews about expanded NBS with a small and diverse sample of Spanish and English speaking mothers. Our experience adds to the growing literature that parents support the expansion of NBS but desire greater education and control in this process than the current standard NBS process. However, there was less consensus about the specific conditions they would want to be included on the screen and how or if this should be offered as a choice.

Mothers appreciated the potential risks of expanded newborns screening to cause anxiety about the potential health threats for their child, but ultimately all felt the utility of the information outweighs these risks as all stated interest in some degree of NBS expansion. Even when there was no treatment for the condition, many felt that the ability to prepare socially and financially, find support, and support potential for future treatment was the trade-off for the potential negatives of this knowledge in advance. This risk-benefit trade-off is a common theme among individuals, reflecting on expanded NBS [26–29]. Parents often reflect on the nonmedical utility of potential results and the benefits of knowledge for the sake of knowledge as was notable in our study as well [15, 18, 30, 31]. Parents may have unrealistic expectations of the impact of the conditions detected and therefore potential utility [32]. While we observed parental interest in NBS due to this medical and nonmedical utility, the tendency to overestimate the utility of genetic testing has been documented for other predictive genetic tests [33–35].

Standard NBS is performed without explicit parental consent and not infrequently parents are unaware of the
screen until they are notified of an abnormal result [21]. Given the nature of GS and the potential types of results, whether and how to engage parents in the decision-making process should be reexamined [36, 37]. Parents have expressed a desire to more actively engage in the NBS process, ideally in the prenatal period when they are more receptive to new information [30, 31, 38, 39]. In our study, 31.4% of mothers recounted poor experiences with the standard NBS process and wanted to have more and earlier education particularly during pregnancy and especially if they were being asked to make decisions about the screening for their child. Parents had very diverse opinions about the information they felt they might need, complicating the development and delivery of education for a diverse population.

We found most mothers desired a choice regarding the conditions screened, though many reflected on the challenge of this choice. Some felt that they or others did not have the necessary knowledge to make the choice and parental choice could be a risk to the child. Others voiced concern around having a choice and the potential fear that parents would opt out of screening for treatable conditions [38].

When considering expanded NBS, how parents make the choice of what conditions are screened and the factors they consider are numerous and likely influenced by diverse lived experiences [26, 30, 40]. This lends to the challenge of how to provide an informed choice. One hypothetical study of parental choice found that the penetrance of the condition was the most important characteristic in their decision, and options to improve the quality of life did not significantly influence choice [40]. A pilot study of expanded NBS found that nearly 3/4 of parents elected to receive some additional results and 90% elected to receive all possible results but of those who did not want all possible conditions there was little consistency in what they did and did not want to learn [3]. Mothers in our study reflected on the challenges to provide sufficient education to make this choice and varied in what information they desired. Some binned conditions together, though others desired a detailed understanding of the phenotype and treatment options for all conditions screened – likely an option that is not feasible. Research exploring the best way to offer choice potentially through the use of decision aids to facilitate an informed decision consistent with personal values and based upon realistic expectations will further inform this process [40].

Our exploration of parental views about storage of data for future clinical use revealed that all parents supported this option and several advocated for having a choice in the decision. In our study, the conversation was focused around the use of the data if a child presented with symptoms, though others have documented a parental preference to have the data stored for the future in the context of delaying disclosure of results that are not relevant in the neonatal period [38]. Similarly, in our study, some mothers asked about tiered disclosure of results over their child’s lifespan as results become relevant. These options are not feasible within the current NBS infrastructure, and alternatives that allow for storage and future use of data should be explored to ensure the full potential of GS NBS is realized.

Limitations

The participants in our study were from a single institution, though we were able to recruit a sample that was diverse in race/ethnicity, insurance status, and educational attainment. Though we reached saturation of the themes from participants, the sample is still relatively small. Additionally, more than half of the participants had previously participated in a pilot study of spinal muscular atrophy NBS, and the others received parental support from a CBO. Their views may differ from mothers who had not had these experiences or had declined participation in the pilot study. While the study was open to fathers, none participated in our study, and their views may differ from those reported by mothers. Our interviews discussed the hypothetical choice of expanded NBS through GS, and consequently, opinions and views may differ in real life scenarios. These studies were conducted during the COVID-19 pandemic, and this experience may have influenced mothers’ opinions.

Practice Recommendations

In order to successfully implement expanded NBS through GS, it is critical to educate prospective parents in the prenatal period. We recommend developing education infrastructure through an easily accessible web interface that allows parents to use it to access information and reflect on benefits and concerns about participating in the expanded screening. Information needs to be curated by appropriate experts and stakeholders, including parents, to ensure that it delivers the information they want and need but does not overwhelm them. It should be accessible to variable literacy levels through the inclusion of culturally appropriate infographics and bilingual videos. It is important to provide information that describes what is involved in the screening process including when to expect results, the types of results, and the potential for false positives and false negatives. Our study and others have demonstrated the value parents place on potential
nonmedical/personal utility; therefore, it is important
that the resources provide realistic expectations [15, 18,
30, 31]. When a diagnosis is made, parents need practical
next steps – especially with conditions that lack medical
actionability – and need the support to find and take ad-
vantage of services that may be helpful for their baby. The
impact of NBS may be lifelong and therefore requires
thoughtful consideration of parental needs.

Finally, it is critical to consider the role of choice in
considering the expansion of NBS. If NBS expands be-
yond conditions with treatment required in the neonatal
period, choice is preferred among many parents. This
likely will require substantial education and further re-
sources in the prenatal period rather than limited consent
in the postnatal period as is currently practiced.

Conclusion

The perspective of these mothers of diverse racial/eth-
nic and educational backgrounds adds to the growing
consensus that parents support the expansion of NBS
through GS. Furthermore, they desire earlier education
and greater participation in the process. Studies imple-
menting GS with prenatal education interventions, par-
ticipant choices, and follow-up support will provide fur-
ther evidence and guidance as to how to effectively imple-
ment NBS using GS into practice.

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Statement of Ethics

This study was approved by the Columbia University Irving
Medical Center Institutional Review Board (AAS8851) who
waived the need for written consent from participants. This study
design was approved allowing each participant to provide verbal
informed consent to minimize potential risk.

Conflict of Interest Statement

None of the authors has a financial or other conflict of interest.

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lia Wynn, MS, MS, and Wendy K. Chung, MD, PhD, reviewed and
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Data Availability Statement

The data that support the findings of this study are not pub-
licly available due to their containing information that could com-
promise the privacy of research participants but are available from
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References

1. Ruiz-Schultz N, Sant D, Norcross S, Dan-
sithong W, Hart K, Asay B, et al. Methods and
feasibility study for exome sequencing as a
universal second-tier test in newborn screen-
ing. Genet Med. 2021;23(4):767–76.
2. Ceyhan-Birsoy O, Murry JR, Machini K, Lebo
MS, Yu TW, Fayer S, et al. Interpretation of
genomic sequencing results in healthy and ill
newborns: results from the BabySeq Project.
Am J Hum Genet. 2019;104(1):76–93.
3. Roman TS, Crowley SB, Roche MI, Foreman
AKM, O’Daniel JM, Seifert BA, et al. Genom-
ic sequencing for newborn screening: results
of the NC NEXUS Project. Am J Hum Genet.
2020;107(4):596–611.
4. Wojcik MH, Zhang T, Ceyhan-Birsoy O, Ge-
netti CA, Lebo MS, Yu TW, et al. Discordant
results between conventional newborn screen-
ing and genomic sequencing in the BabySeq
Project. Genet Med. 2021;23(7):1372–5.
5. Yang Y, Muzny DM, Reid JG, Bainbridge
MN, Willis A, Ward PA, et al. Clinical whole-
exome sequencing for the diagnosis of men-
delian disorders. N Engl J Med. 2013;369(16):
1502–11.
6 Splinter K, Adams DR, Bacino CA, Bellen HJ, Bernstein JA, Cheattle-Jarvela AM, et al. Effect of genetic diagnosis on patients with previously undiagnosed disease. *N Engl J Med*. 2018;379(22):2131–9.

7 Retterer K, Juusola J, Cho MT, Vitazka P, Mallan F, Gibellini F, et al. Clinical application of whole-exome sequencing across clinical indications. *Genet Med*. 2016;18(7):696–704.

8 Petritkin JE, Dakic IA, Clark MM, Willig K, Sweeney NM, Farrow EG, et al. The NSIGHT1-randomized controlled trial: rapid whole-genome sequencing for accelerated etiologic diagnosis in critically ill infants. *NPJ Genom Med*. 2018;3:6.

9 Lord J, McMullan DJ, Eberhardt RY, Rinck G, Hamilton SJ, Quinlan-Jones E, et al. Next-generation sequencing in newborn screening evaluations. Pediatrics. 2011;128(1):53–61.

10 Bodian DL, Klein E, Iyer RK, Wong WSW, Kohiyial P, Staufer D, et al. Utility of whole-genome sequencing for detection of newborn screening disorders in a population cohort of 1,696 neonates. *Genet Med*. 2016;18(3):221–30.

11 Remec ZI, Trebusak Podkrajsek K, Repic Lampret B, Kovac J, Grošelj U, Tesovnik T, et al. Next-generation sequencing in newborn screening: a review of current state. *Front Genet*. 2021;12:662254.

12 DeLuca JM, Kearney MH, Norton SA, Arnold GL. Parents’ experiences of expanded newborn screening evaluations. *Pediatrics*. 2011;128(1):53–61.

13 Miller FA, Hayeems RZ, Bombard Y, Cress-Adhikari AN, Gallagher RC, Wang Y, Currier RJ, Amatuni G, Bassaganyas L, et al. The role of exome sequencing in newborn screening for inborn errors of metabolism. *Nat Med*. 2020;26(9):1392–7.

15 DeLuca JM. Public attitudes toward expanded newborn screening. *J Pediatr Nurs*. 2018;38:e19–25.

16 Miller FA, Hayeems RZ, Bombard Y, Cress-Adhikari AN, Gallagher RC, Wang Y, Currier RJ, Amatuni G, Bassaganyas L, et al. The role of exome sequencing in newborn screening for inborn errors of metabolism. *Nat Med*. 2020;26(9):1392–7.

17 Pereira S, Robinson JO, Gutierrez AM, Petersen DK, Hsu RL, Lee CH, et al. Perceived benefits, risks, and utility of newborn genomic sequencing in the BabySeq project. *Pediatrics*. 2019;143(Suppl 1):S6–13.

18 Campbell ED, Ross LF. Incorporating newborn screening into prenatal care. *Am J Obstet Gynecol*. 2004;190(4):876–7.

19 Campbell E, Ross LF. Parental attitudes regarding newborn screening of PKU and DMD. *Am J Med Genet*. 2003;120A(2):209–14.

20 Berg JS, Powell CM, et al. Parental views on expanded newborn screening using new technologies. *Public Health Genomics*. 2011;14(4–5):298–306.

21 Davis TC, Humiston SG, Arnold CL, Bocchi-ni JA Jr, Bass PF 3rd, Kennen EM, et al. Recommendations for effective newborn screening communication: results of focus groups with parents, providers, and experts. *Pediatrics*. 2006;117(5 Pt 2):S326–40.

22 Moultrie RR, Paquin R, Rini C, Roche MJ, Berg JS, Powell CM, et al. Parental views on newborn next generation sequencing: implications for decision support. *Matern Child Health J*. 2020;24(7):856–64.

23 Amendola LM, Lautenbach D, Scollon S, Bernhardt B, Biswas S, East K, et al. Illustrative case studies in the return of exome and genome sequencing results. *Per Med*. 2015;12(3):283–95.

24 Wynn J, Lewis K, Amendola LM, Bernhardt BA, Biswas S, Jochi M, et al. Clinical providers’ experiences with returning results from genomic sequencing: an interview study. *BMC Med Genomics*. 2018;11(1):45.

25 Wynn J, Martinez J, Bulafka J, Duong J, Zhang Y, Chiuzan C, et al. Impact of receiving secondary results from genomic research: a 12-Month Longitudinal Study. *J Genet Couns*. 2018;27(3):709–22.

26 Berg JS, Agrawal PB, Bailey DB Jr, Bergs AH, Brenner SE, Brown AM, et al. Newborn sequencing in genomic medicine and public health. *Pediatrics*. 2017;139(2):e20162252.

27 Berg JS, Powell CM. Potential uses and inher-challenges of using genome-scale sequencing to augment current newborn screening. *Cold Spring Harb Perspect Med*. 2015;5(12):a023150.

28 Joseph G, Chen F, Harris-Wai J, Puck JM, Young C, Koenig BA. Parental views on expanded newborn screening using whole-genome sequencing. *Pediatrics*. 2016;137(Suppl 1):S36–46.

29 Lipstein EA, Nabi E, Perrin JM, Huff D, Browning MF, Kuhlthau KA. Parents’ decision-making in newborn screening: opinions, choices, and information needs. *Pediatrics*. 2010;126(4):696–704.

30 Lewis MA, Paquin RS, Roche MJ, Furberg RD, Rini C, Berg JS, et al. Supporting parental decisions about genomic sequencing for newborn screening: The NC NEXUS Decision Aid. *Pediatrics*. 2016;137(Suppl 1):S16–23.