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BRIEF REPORT

Frequency and reasons that parents decline genetic testing for critically ill neonates

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ABSTRACT

Purpose: Current literature reports strong support among parents for genetic testing for ill neonates; yet, some parents decline this testing for unknown reasons. We aimed to document the proportion of parents who decline, describe their clinical and demographic characteristics, and categorize their rationales.

Methods: We reviewed medical records to collect and compare clinical and demographic information for patients whose parents consented to and declined recommended genetic testing. We also conducted brief interviews with parents who declined testing to discover their rationales.

Results: Fifty-one of 247 parents (21%) declined recommended genetic testing. The most common reason for declining, cited by 83% of parents interviewed, was that the testing felt irrelevant to the problems they saw as most important. The second most common reason, cited by 63%, was worrying that the testing might yield unwanted information. Compared with parents who consented, those who declined were more likely to be making the decision for a child with a prenatally diagnosed condition ($P = .022$) or congenital anomaly ($P = .029$) and to have private health insurance ($P = .031$).

Conclusion: Parents who decline genetic testing for ill neonates provide an alternate appraisal of benefits and harms which should be incorporated into informing future parents considering these tests.

Introduction

Parents of critically ill neonates sometimes decline recommended clinical genetic testing, although no reports of the frequency or reasons for such declinations have been published. Since the initiation of genetic sequencing in ill neonates, critics have expressed concerns that genetic diagnoses may pose so-called informational hazards, such as interrupting nascent relationships, causing unwarranted worry, and perpetuating ableism.[1-3] In contrast, studies have reported that parents generally accept the testing, and some researchers have dismissed critics' concerns.[4,5] Notably, these

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studies have typically enrolled parents participating in genetic research studies, raising potential questions about generalizability. A few studies document that a substantial proportion of parents, 12% to 93%, decline genetic research studies for neonates in various contexts.[6,7] However, rationales reported largely relate to concerns about research, which would not explain why parents decline clinical testing.

Distinct from parents, neonatal intensivists remain apprehensive about informational hazards, citing the potential for misapplication of burgeoning genetic information and continued worries about the effects of this information on families.[8,9] Persistent trepidation is reflected in the continued practice of asking parents to consent for genetic testing, setting this testing apart from other diagnostic tests. That parents do exercise their right to refuse suggests greater ambivalence among parents than is captured in the current literature.

Here, in the context of clinical genetic testing, we document the proportion of parents who decline, describe their clinical and demographic characteristics, and categorize their rationales.

Materials and Methods

As part of a larger study, we reviewed medical records of all patients admitted to the neonatal intensive care unit (NICU) at the Children's Hospital of Philadelphia between 15 October 2023 and 15 May 2024. We recorded demographic and clinical data, including whether patients had a clinical genetics consultation and were recommended testing, and whether their parents consented or declined. Race and ethnicity are gathered by self-report in electronic our medical records. At our center, the clinical genetics service must be consulted before most genetic tests. A rapid genome-based panel is recommended as the first-line genetic test for a majority of patients in the NICU.

We compared the demographic and clinical characteristics of the cohorts for whom parents had consented and declined using t tests and χ^2 analyses.[10] We looked at each characteristic independently, although they were not mutually exclusive (eg, a patient could have a congenital anomaly and prenatal diagnosis) because our sample size was small too small to support multivariable regression.[11] We regarded a 2-tailed P value of less than .05 as significant.

We contacted parents who declined within 2 weeks of declining genetic testing. We approached parents in person if their child was still admitted, and they were present at bedside, or by phone if the child had been discharged, or the parents were not at bedside. One of 2 study members (K.P.C. or K.C.) approached whichever parent was at bedside or listed as the first contact in the medical record. If they agreed, the study member asked them 2 questions: "What were your reasons for deciding not to have the recommended genetic testing?" and "How likely would you be to have genetic testing for your child on the future? Please tell us on a scale from one to five, with one being very unlikely, 3 being neutral, and 5 being very likely." These questions were developed through interdisciplinary discussion and refined through 3 pilot interviews. The Likert scale was added to the second question after initial pilot testing produced binary yes/no answers. Follow-up probes were used after both questions when parents did not immediately volunteer the reasoning behind their answers.

We audio recorded and transcribed responses. We iteratively developed a code book, capturing reasons that parents reported for refusing testing.[12] Two investigators (K.P.C. and K.C.) independently coded each transcript to assign these reasons. We resolved discrepancies, which were few, through triangulation with a third investigator (R.M.).

Table 1 Characteristics of participants

Characteristic	Consent (N = 196)	Decline (N = 51)	P Value
Prenatally Diagnosed Anomaly	101 (54%)	36 (72%)	.022
Reason for consult			
Congenital anomaly	135 (69%)	43 (84.3%)	.029
Dysmorphic features	28 (14%)	4 (8%)	.22
Neurological symptoms	10 (5%)	2 (4%)	.73
Suspected metabolic disease	4 (2%)	1 (2%)	.97
Unexplained illness	52 (27%)	6 (12%)	.027
Atypical response to therapy	1 (1%)	0 (0%)	.61
Other	9 (5%)	2 (4%)	.84
Type of genetic test			
Single gene testing	9 (5%)	3 (6%)	.70
Panel testing	4 (2%)	3 (6%)	.14
Microarray	12 (6%)	1 (2%)	.24
Exome sequencing	44 (22%)	16 (31%)	.19
Genome sequencing	14 (7%)	1 (2%)	.17
Rapid genome-based panel	157 (80%)	42 (82%)	.72
Other	22 (11%)	4 (8%)	.48
Race			
Asian	5 (3%)	0 (0%)	.21
Black or African American	37 (19%)	8 (16%)	
Pacific Islander	1 (1%)	0 (0%)	
White	101 (52%)	31 (62%)	
Mixed race	4 (2%)	3 (6%)	
Other	24 (12%)	7 (14%)	
Unknown	22 (11%)	1 (2%)	
Ethnicity			
Not Hispanic or Latino	140 (81%)	44 (88%)	.22
Hispanic or Latino	34 (20%)	6 (12%)	
Non-English Speaking	9 (5%)	0 (0%)	.11
Private Insurance	86 (58%)	36 (75%)	.032

Characteristics that differed between parents who consented and declined are italicized.

Results

Genetic testing was recommended for 247 of 467 patients whose records we reviewed. Parents declined recommended testing for 51 patients (21%) (Supplemental Figure 1). Compared with parents who consented, those who declined were more likely to have a child with a prenatally diagnosed condition (Table 1, P = .022) or with a congenital anomaly (P = .029) and less likely to have a child with an unexplained

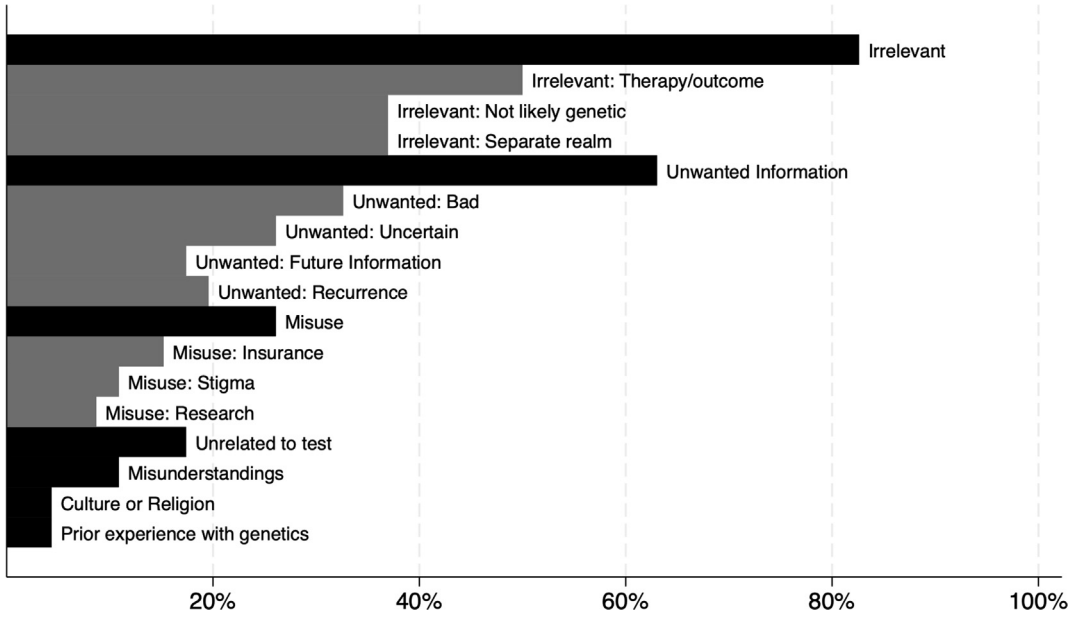

Figure 1 **Frequency of reasons to decline.** Black bars represent categories of reasons to refuse, and gray bars represent subcategories.

illness as the reason for genetics consult ($P = .027$). Those who declined were also more likely to have private health insurance ($P = .031$). There were no differences between groups in terms of race, ethnicity, or genetic test recommended. Of the 9 non-English speaking parents offered testing, none declined.

Forty-six of 51 eligible parents who declined genetic testing consented for interviews (90% consent rate). For 3 children, 2 parents were present on initial contact, and both participated in the interview. For statistical analysis, we counted these pairs of parents as a single respondent because they corresponded to the same child. Our final code book included 7 categories of reasons to decline, some with subcategories (Supplemental Table 1).

The most common reason, cited by 83% of parents, was that the testing felt irrelevant to the problems they saw as most important (Figure 1). Typically, this was because parents believed the testing was unlikely to change their child's current treatment or ultimate outcome because they felt their child's illness was not likely to be genetic or because they perceived genetic testing as a realm separate from regular clinical care. There is "nothing that we can do or even the doctors currently can do to change genetics. So, for me, I just feel like it's pointless," stated one parent. "Right now, we need to have our minds on things that are way more important," explained another.

The second most common reason to decline, cited by 63%, was worrying that the testing may yield unwanted information. "Sometimes, you know, ignorance is bliss," explained one parent. Parents expressed concerns about receiving additional bad news, uncertain information, information relating to the future but not the present, and information on recurrence risk. One parent summarized many of these statements explaining, "we had gotten bad news after bad news with [our baby] and we just wanted to feel a little normal. And not have to worry about potential future problems that may or may not happen." Objections to receiving information on recurrence risk reflected feeling that parents' or children's fitness was being judged. One parent demonstrated this in saying, "we don't want to be afraid of the potential of having future kids just because you guys have the genetic markers or your offspring might have the genetic markers of this and this and this and this, so don't have any more kids because all of them will be awful and abnormal." Parents also expressed concerns about misuse of genetic information, which could exclude children from insurance coverage (15%) or expose them to stigma (11%). One mother explains, "I want to see first what he can do himself before we go ahead and label him and say, well, this is what you have and this is how we're going to treat you."

Less common reasons for refusing, cited by 4% to 26% of parents, were misunderstandings about genetic testing, cultural or religious beliefs, prior experiences with genetic testing, and reasons unrelated to genetic testing. Most of the reasons unrelated to genetic testing related to the overall stress of having a child admitted to the NICU. "Everything was such a blur," recalled one parent.

When asked how likely they would be to have genetic testing for their child in the future, on a Likert scale, parents' average response score was 2.52 (SD 1.38), corresponding to midway between neutral and unlikely. Parents explained what would lead them to pursue testing: changes in their child's medical situation or the expected benefits of testing, feeling less overwhelmed, or their children reaching adulthood and being able to decide about testing themselves.

Discussion

In this study, 1 in 5 parents declined recommended genetic testing. Their stated rationales reflected an appraisal of harms and benefits that extended beyond standard

considerations, with many parents expressing skepticism about the benefit of genetic tests. Parents were ambivalent about pursuing genetic testing in the future.

Parents assessments of both harms and benefits warrant discussion. First, a substantial proportion of these parents were concerned about informational hazards, such as interfering with bonding, which are concerns previously reported to be uncommon.[4,5,13] Additionally, parents' concerns extended beyond what clinicians traditionally consider harms, for example the harm of receiving information about the future. Such effects are not typically discussed in testing consent procedures.[14,15]

Parents who declined were skeptical about benefits of testing. These concerns were not as prominent in studies of why parents decline research-based genetic tests, perhaps because in a research context, inclusion criteria would be more clear cut, and clinical benefit may not be the expectation.[7] Although genetic results may lead to targeted treatments with clear benefit, many respondents in our study concluded that the likelihood of such results was low (and do so correctly[16]). We do not have data on how beneficial clinicians expected genetic testing would be in these cases. However, parents' perceptions deserve at least equal weighting in determining true benefit, apart from rare cases in which targeted therapy is likely. Perhaps parents of children with congenital anomalies were more likely to decline testing because a genetic etiology was, as some pointed out, unlikely to change the surgical corrections their children required. Or, alternately, these parents may have declined because the congenital defect they could see provided sufficient explanation of why their children were sick, and they were not convinced a genetic etiology of the visible problem would meaningfully add to their understanding. Additionally, certain consequences of genetic testing typically considered benefits, such as information about recurrence risk, for some parents constitute unwelcome or harmful bad news or at least do not constitute benefits sufficient to warrant testing.

Parents ability to clearly articulate their reasoning and their willingness to share their rationales, as reflected in a high consent rate for this study, suggest that declining reflects thoughtful analysis rather than misunderstanding. The finding that parents were more likely to decline testing if they had private insurance (which generally correlates with better health literacy[17]), is further evidence that declining is unlikely to result from misunderstanding. Concerns about future insurance ramifications may also have contributed to this trend, although worries about test payment were less likely because our hospital currently covers out-of-pocket expenses for first-line genetic tests. Additionally, if declining testing were the result of misunderstanding, one might expect those not fluent in English to be more likely to decline. These findings contrast with general sentiment in the field that parents' understanding is a major barrier to acceptance of genetic testing.[18]

Some of the reported benefits and harms of genetic tests are likely to change over time, perhaps explaining parents' ambivalence about future testing. If patients stabilize and are discharged from the NICU, parents will likely feel less overwhelmed and have fewer reasons to decline additional tests. As children age, their medical or developmental problems will likely be demarcated more clearly, and perhaps the relevance of genetic testing will become clearer to parents.

Taken in sum, these findings pose an important question: should informed consent for genetic testing incorporate the perceptions and values of parents who have declined? Typically, informed consent for genetic tests (and most medical procedures or advanced testing) centers on the harms and benefits identified by experts.[19,20] Our findings suggest that parents' considerations may be poorly aligned with expert perspectives and guidance. Parents could alternately be informed about the reasons that other similarly positioned parents choose to pursue or decline testing and how these rationales may apply to their child's particular case. Parents could also be engaged in discussions about how benefits and harms of genetic tests might change as a child gets older. Lastly, these findings suggest that rigorous, systematic assessment of genetic testing's benefits and harms (equivalent to measuring the testing's utility and disutility) should likewise account for the diversity of perception and values incorporated into appraisals of outcomes.

Data Availability

Redacted transcripts will be available on request to the corresponding author.

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Author Contributions

Katharine Press Callahan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conceptualization: K.P.C., C.F.; Data Curation: K.P.C.; Formal Analysis: K.P.C., C.F., K.C., R.M.; Funding Acquisition: K.P.C., S.J.; Investigation: K.P.C., R.M., K.C., K.B., D.M., S.J., C.F.; Methodology: K.P.C., C.F.; Project Administration: K.P.C., K.C.; Supervision: K.P.C., C.F.; Visualization: K.P.C., C.F.; Writing-original draft: K.P.C.; Writing-review and editing: K.P.C., R.M., K.C., K.B., D.M., S.J., C.F.; Acquisition, analysis, or interpretation of data: K.P.C., R.M., K.C., K.B., D.M., S.J., C.F.

Ethics Declaration

This study was approved by the Children's Hospital of Philadelphia Institutional Review Board. Consent was obtained from all parents who participated in interviews. Informed consent was not required for the chart review portion of this study. All data have been deidentified. All research was conducted in accordance with the Declaration of Helsinki.

Conflict of Interest

Steven Joffe is a paid member of a data monitoring committee for CSL Behring. Kyle Brothers receives in-kind research support from Invitae.All other authors have no conflicts of interest to disclose.

Additional Information

The online version of this article (https://doi.org/10.1016/j.gimo.2024.101896) contains supplemental material, which is available to authorized users.

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