

Parents' Decisions to Screen Newborns for *FMR1* Gene Expansions in a Pilot Research Project

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KEY WORDS

newborn screening, informed consent, patient decision making, screening tools

ABBREVIATIONS

NBS—newborn screening
FXS—fragile X syndrome
RA—research assistant
FX—fragile X (*FMR1* gene expansions)

Dr Skinner made substantial contributions to the conception and design, acquisition, analysis, and interpretation of data; and drafted the article for intellectual content. Ms Choudhury made substantial contributions to the acquisition, analysis, and interpretation of data; and helped draft article for intellectual content. Dr Sideris made substantial contributions to analysis and interpretation of data; and helped draft article for intellectual content. Ms Guarda made substantial contributions to the acquisition and interpretation of data; and helped revise the article for intellectual content. Mr Buansi made substantial contributions to the analysis of data and helped revise the article for intellectual content. Ms Roche and Drs Powell and Bailey made substantial contributions to the conception and design, analysis and interpretation of data; and helped draft the article for intellectual content. All authors read and approved the manuscript submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2010-3078

doi:10.1542/peds.2010-3078

Accepted for publication Feb 10, 2011

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*

Funded by the National Institutes of Health (NIH).

COMPANION PAPER: A companion to this article can be found on page 1593 and online at www.pediatrics.org/cgi/doi/10.1542/peds.2011-0677.



WHAT'S KNOWN ON THIS SUBJECT: Fragile X syndrome is not diagnosed until patients are aged 3 years or older. Although parents of affected children support newborn screening, public acceptance of a screening test that would identify both affected children and carriers is unknown.



WHAT THIS STUDY ADDS: In the context of a prospective, longitudinal study in which parents are offered voluntary newborn screening for *FMR1* gene expansions, this article reports uptake rates of parents offered screening shortly after birth and their reasons for accepting or declining.

abstract



OBJECTIVE: The goal of this study was to document rates of parental consent in a pilot study of newborn screening for *FMR1* gene expansions, examine demographic characteristics of mothers who consented or declined, describe the reasons for their decision, and discuss ethical and social aspects of the consent process.

METHODS: A brief survey was used to record basic demographic data from mothers and an open-ended question was used to elicit parents' reasons for accepting or declining screening. A descriptive analysis was conducted on the number of mothers who consented to or declined screening, and a logistic regression model predicted mothers' likelihood to agree to screening based on demographic characteristics. Reasons for decisions were analyzed using content analysis. The study was conducted at University of North Carolina Hospitals. A total of 2137 mothers were approached.

RESULTS: The uptake rate for couples was 63%. Acceptance rates varied by race/ethnicity, with black respondents being less likely to accept screening. Primary reasons for accepting were "to know," "belief in research," and "the test was minimal/no risk." Reasons for declining included not wanting to know or worry, not being a good time, and issues with testing children or with genetic tests.

CONCLUSIONS: Findings demonstrate that a majority of parents accepted newborn screening for *FMR1* gene expansions, but decision rates and reasons for accepting or declining varied in part as a function of race/ethnicity and in part as a function of what parents most valued or feared in their assessment of risks and benefits. *Pediatrics* 2011;127:e1455–e1463

State newborn screening (NBS) programs are currently the focus of public debate and scrutiny regarding which conditions should be added to screening panels and whether parental consent should be obtained for screening and the retention of blood spots.^{1–3} Recent expansions of NBS and the potential for adding tests for more conditions in the future have raised several concerns, including the ethical, legal, and social implications of including conditions for which there are no medical treatments; labeling infants as asymptomatic carriers or “at-risk” individuals; and disclosing findings of uncertain medical significance, carrier status, or susceptibility to adult-onset disorders.^{4–9} Given these concerns, screening for conditions that do not meet current NBS criteria should only be conducted as part of a research protocol with a rigorous consent process clearly discussing the risks and benefits of a positive result.^{10–12}

Fragile X syndrome (FXS), the most common inherited cause of intellectual disability, is an X-linked genetic condition that exemplifies these issues. FXS is caused by a CGG trinucleotide repeat expansion (>200 repeats) of the *FMR1* gene that, when methylated, causes the reduction or absence of a protein (FMRP) necessary for normal brain development and functioning. Absence of FMRP leads to the overactivation of mGluR5, a metabotropic glutamate receptor affecting synaptic plasticity.¹³ Males with FXS typically have moderate intellectual disability and a variety of co-occurring conditions, the most common being anxiety, inattention, hyperactivity, and autism or autistic symptoms.¹⁴ Intellectual functioning in females can range from typical cognitive abilities to moderate impairment, a spectrum largely due to X inactivation. It is estimated that ~1 per 4000

males and 1 per 6000 females have the full mutation.^{15,16}

The *FMR1* full mutation leading to FXS is maternally inherited either from a carrier of a premutation (55–200 CGG repeats) or a full mutation. The prevalence of the premutation is common, estimated at 1 per 290 to 800 in males and 1 per 129 to 259 in females.^{15,16} Female carriers have an elevated risk for primary ovarian insufficiency and early menopause¹⁷; males and, to a lesser extent females, have an increased risk for fragile X tremor ataxia syndrome, a debilitating neurologic impairment occurring after 50 years of age.¹⁸ Recent animal and human studies have demonstrated that some carriers may have other neurologic or emotional problems, suggesting a broader range of risk and disability than has been previously assumed.^{14,19–22}

The rationale for FXS NBS includes a persistently delayed age of diagnosis²³; the strong support by parents of affected children²⁴; and possible benefits for families such as prevention of the “diagnostic odyssey” and its financial and emotional costs; and the early availability of information about FXS, parents’ reproductive risks, and appropriate services for the child’s special needs.²⁵ After weighing these and other benefits, an American College of Medical Genetics task force did not recommend FXS for inclusion in state NBS,²⁶ however, primarily due to the lack of a cost-effective screening test and the absence of data on possible benefits from identification of newborns. DNA-based screening for a CGG expansion also identifies carriers, evoking a wide range of ethical, legal, and social concerns. Besides the current lack of a medical treatment for children identified with the full mutation, perhaps the most fundamental concern is triggered by the ambiguity of the risk for carriers to have develop-

mental problems or adult-onset disorders such as fragile X tremor ataxia syndrome and primary ovarian insufficiency. Presymptomatic identification of children could lead to a range of adverse outcomes, such as elevated rates of postpartum depression, parents’ ongoing anxiety and worry about their child’s future, and possible disruptions to the parent-child relationship.^{2,4,11,27}

Most of these risks and benefits are not unique to FXS and apply to a wide range of other genetic conditions likely to be considered for inclusion on NBS panels. Determining whether these hypothesized risks and benefits are valid can only be accomplished by examining them in a prospective screening study. After careful deliberation of the ethical and social implications⁴ and based on our previous research with families of children with FXS,^{24,28} we designed a research project at the University of North Carolina Hospitals that offers, through a voluntary consent process, NBS for *FMR1* gene expansions. Our rationale for the study was that there are multiple concerns and speculations about the risks and benefits of expanded screening but very little empirical investigation. The study uses FXS as a prototype for studying issues such as public willingness to accept screening for conditions that are not medically treatable or those that would identify newborns as carriers and/or at risk for late-onset conditions, and how families adapt to genetic information and to their identified child.⁴

We initiated the pilot study in February 2009, once a cost-effective screening test was available.²⁹ The screening test identifies both the premutation and full mutation in males and females. The study’s long-term aim was to follow-up identified and matched comparison families to assess family adaptation and child development. In this article,

we report findings on rates of parental consent, examine demographic characteristics of parents who consented or declined, describe the reasons parents gave for their decisions, and discuss ethical and social aspects of the consent process. For the sake of brevity and clarity, we use the term fragile X (FX) to include both carriers (CGG repeat length of 55–200) and individuals with fragile X syndrome (FXS) (CGG repeat length >200).

METHODS

Participants and Design

A research assistant (RA) employed by the study approached mothers on the postpartum unit within 24 hours of their giving birth. Parents were given a study brochure and consent form describing the purpose of the study, the experimental screening test that detects infants with FX, information about the range of features expected in those who screen positive, a detailed list of the risks and benefits of a positive result, and follow-up procedures including confirmatory testing and genetic evaluation and counseling. (The information given to parents can be found at www.fpg.unc.edu/~fxnewborn/. The specific risks and benefits communicated to parents are listed in the Appendix.) RAs were trained to communicate this information in a consistent manner to all families, and were available to discuss the study in detail and answer questions. In most cases, parents had several hours to consider the study before deciding. All materials were available in Spanish, and an RA fluent in Spanish approached Spanish-speaking families. Mothers were not approached if younger than age 15 years, were experiencing stressful medical or personal circumstances, had infants in critical care for life-threatening conditions or relinquished for adoption, or if not proficient in either English or Spanish. The institu-

tional review board approved this study under 45 CFR 46.406, requiring consent from both parents “unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.” For consented newborns, an extra blood spot obtained at the same time as the regular NBS was placed on a separate card and sent to a Clinical Laboratory Improvement Amendments–approved laboratory to conduct the screening test. No additional heel stick was done for this study. Parents were informed they would receive notice of the results within 8 weeks, by letter if screened negative, and by a phone call from the medical geneticist on the research team if positive.

Survey and Data Collection

After deciding whether to enroll, parents were asked to respond to a brief survey with basic demographic data: mother’s age, ethnicity/race, education, primary language, and number of previous births. An open-ended question elicited parents’ reasons for their decision to accept or decline screening. Parents were not prompted to give >1 reason, although many did so. The RA recorded their responses verbatim.

Data Analysis

A descriptive analysis was conducted on the number of mothers who consented to or declined screening according to age, education, race/ethnicity, whether English was the primary language, and number of previous births. These variables were used to run logistic regression models to predict the mother’s likelihood to agree to screening. Open-ended reasons for accepting or declining were entered into NVivo8, a software program that facilitates analysis of textual data (QSR International.com). Following established procedures for content analy-

sis,^{30–32} the first and second author independently read the first 1000 responses, and devised codes subsuming each response. This coding scheme was refined through comparison, discussion, and application of codes in an iterative process, and the final codes were then used to categorize all responses. Two coders independently coded responses and compared coding. Any discrepancies in coding were reconciled through reviewing the responses, discussion, and consensus.

RESULTS

Consent Rates

Between February 2009 and April 2010, study recruiters approached 2137 mothers. Of these, 2045 (95.7%) were willing to hear about the study. About two thirds (67.5%) of the 2045 consented to have their newborn screened. Because some fathers actively declined screening ($n = 16$) or failed to return a signed consent form ($n = 76$) after the mother consented, the rate of consent for couples dropped to 63%. Of the 2045 mothers, 1930 filled out the brief survey, providing basic demographic information for 1381 acceptors and 549 decliners (Table 1). Of the 115 who did not fill out the brief survey, 114 were decliners.

The project was conducted at a university research and teaching hospital serving a diverse population, including lower-income families and Latino immigrants as well as university faculty and students. Of the mothers, 37% were Latino/Hispanic, almost all of whom were Spanish speakers; 43.7% were white; and 13.4% black. As for education, 44.2% had a high school education or less while 21.1% had postgraduate or professional degrees.

When looking at screening decisions by race/ethnicity alone, black mothers were less likely to agree to screening

TABLE 1 Demographic Features of Mothers

| Feature | Acceptors (n = 1381) | Decliners (n = 549) | Test of Difference |
|---------------------------------------|-------------------------|------------------------|----------------------|
| Mean age, y | 28.4 | 28.7 | <i>t</i> = .88 |
| Marital status, % | | | $\chi^2_2 = 1.59$ |
| Single, never married | 39.5 | 38.1 | |
| Married | 57.6 | 59.9 | |
| Previously married | 2.8 | 2.0 | |
| Education, % | | | $\chi^2_4 = 3.74$ |
| <High school | 28.2 | 30.8 | |
| High school degree | 15.4 | 14.6 | |
| Some college | 17.1 | 17.9 | |
| College degree | 17.0 | 18.2 | |
| Postgraduate degree | 22.1 | 18.6 | |
| Race/ethnicity, % | | | $\chi^2_3 = 16.39^a$ |
| Black | 11.8 | 17.3 | |
| Latino/Hispanic | 37.0 | 37.0 | |
| White | 45.9 | 37.9 | |
| Other | 5.3 | 7.8 | |
| Language, % | | | $\chi^2_2 = 9.85^a$ |
| English | 63.6 | 59.0 | |
| Spanish | 32.8 | 34.1 | |
| Other | 3.6 | 6.9 | |
| Gender of newborn, % | | | $\chi^2_1 = .90$ |
| Male | 51.7 | 49.3 | |
| Female | 48.3 | 50.7 | |
| No. of live births, including newborn | | | <i>t</i> = .63 |
| 1 | 38.9 | 38.8 | |
| 2 | 34.4 | 32.2 | |
| 3 | 16.5 | 17.7 | |
| 4 | 6.4 | 5.8 | |
| >5 | 3.8 | 5.0 | |

^a *P* < .01.

TABLE 2 Relationship Between Selected Maternal Demographic Variables and Acceptance of FXS NBS

| Variable | OR (SE) | CI | χ^2 |
|---------------------------------------|-------------|--------------|--------------------|
| Asian vs black | 1.27 (0.37) | 0.72 to 2.24 | 0.67 |
| Asian vs Hispanic | 0.69 (0.20) | 0.39 to 1.22 | 1.59 |
| Asian vs other | 1.99 (0.87) | 0.85 to 4.68 | 2.49 |
| Asian vs white | 0.66 (0.17) | 0.40 to 1.08 | 2.69 |
| Black vs Hispanic | 0.55 (0.10) | 0.38 to 0.78 | 10.71 ^a |
| Black vs other | 1.57 (0.61) | 0.74 to 3.35 | 1.36 |
| Black vs white | 0.52 (0.09) | 0.38 to 0.72 | 15.51 ^b |
| Hispanic vs other | 2.88 (1.12) | 1.34 to 6.18 | 7.34 ^a |
| Hispanic vs white | 0.95 (0.16) | 0.69 to 1.31 | 0.09 |
| Other vs white | 0.33 (0.12) | 0.16 to 0.68 | 8.89 ^a |
| Single vs married | 1.27 (0.16) | 0.98 to 1.64 | 3.34 |
| Single vs previously married | 0.78 (0.28) | 0.38 to 1.59 | 0.48 |
| Married vs previously married | 0.61 (0.22) | 0.30 to 1.24 | 1.84 |
| <high school vs high school degree | 0.77 (0.14) | 0.54 to 1.09 | 2.17 |
| <high school vs some college | 0.74 (0.14) | 0.51 to 1.08 | 2.49 |
| <high school vs college degree | 0.71 (0.16) | 0.46 to 1.09 | 2.45 |
| <high school vs graduate degree | 0.53 (0.13) | 0.33 to 0.84 | 7.16 ^a |
| High school degree vs some college | 0.96 (0.18) | 0.67 to 1.39 | 0.04 |
| High school degree vs college degree | 0.92 (0.19) | 0.61 to 1.39 | 0.16 |
| High school degree vs graduate degree | 0.69 (0.15) | 0.44 to 1.06 | 2.82 |
| Some college vs college degree | 0.96 (0.18) | 0.66 to 1.38 | 0.06 |
| Some college vs graduate degree | 0.71 (0.14) | 0.48 to 1.06 | 2.83 |
| College degree vs graduate degree | 0.75 (0.13) | 0.53 to 1.04 | 2.91 |
| Mother's age | 0.99 (1.01) | 0.97 to 1.01 | .69 |
| No. of live births | 0.97 (1.05) | 0.89 to 1.06 | 0.41 |

OR indicates odds ratio; CI, confidence interval.

^a *P* < .01.

^b *P* < .001.

(63.7%) than Hispanic (71.6%) or white (75.4%) mothers. A logistic regression model to predict a mother's likelihood to agree to screening used maternal variables of ethnicity/race, marital status, education, age, and number of previous births. Results are reported in Table 2. In this model, black respondents were about half as likely to agree as either Hispanic (odds ratio: 0.55) or white (odds ratio: 0.52) respondents. Those classified as "other" were about one third as likely to agree as white respondents. Education was measured as a categorical variable with 5 levels: less than high school, high school, some college, college degree, and graduate degree. In general, education was positively related to willingness to participate; as education increased, so did willingness. However, only 1 of the pairwise comparisons between levels was significant: those with graduate degrees were more likely to agree to participate than those with less than a high school diploma.

Reasons for Accepting or Declining

The content analysis including categories, frequencies, and representative comments for the reasons parents gave for their decisions is reported in Table 3. The most prevalent reason, by far, given by acceptors was "to know" (71.6%). Parents indicated they wanted to know to monitor their child's health and development, and to plan ahead. Most comments were similar to the parent who said, "Cause I believe that every test can help. I'd rather know more than less. It can give us a jump start if something is wrong, to help her get better." Almost one third cited a belief in research as a reason for consenting. For example, 1 mother wanted to participate "to further knowledge, to help with research." Another mother viewed participation as a social responsibility, saying "You can't find cures for dis-

TABLE 3 Couples' Reasons for Accepting/Declining NBS

| | <i>n</i> (%) ^a | Representative Responses |
|---|---------------------------|--|
| Reasons for accepting (<i>n</i> = 1288) | | |
| Knowing is good/there is benefit to knowing/knowing earlier is better | 922 (71.6) | "More information is always a bonus. I'd rather know about stuff." "I believe in early intervention kind of stuff. No better way to prepare your future than to know up front." |
| To contribute to research | 412 (32.0) | "We're happy to do it if it benefits research." "I want to support research." |
| The test is minimal risk/noninvasive/just an additional test | 354 (27.5) | "It's non-intrusive; an additional drop of blood is not much." "There are no risks; he's being pricked already." |
| Participating cannot hurt/nothing to lose | 108 (8.4) | "Figured it would be a good thing to do. Not much reason not to." "I don't see any reason why I wouldn't do it." |
| My family has a history of problems | 76 (5.9) | "In our family we have these types of problems." "I have a cousin like this with mental retardation." |
| The screening is free | 60 (4.7) | "Extra screening is always a bonus, especially if it's free." "It is good to get a free test. You won't hurt the child and it's free." |
| Just curious | 27 (2.1) | "Just curious. Better safe than sorry." "Curiosity is a big factor for me." |
| Spouse/partner convinced me | 27 (2.1) | "Main reason is my husband is a scientist and he knows it is important. I agree with him and believe him." |
| Because the screen was offered | 18 (1.4) | "Because it was offered. We have the opportunity." "Why not if it's something that's offered. He'll be tested for 50 other conditions." |
| To provide reproductive risk information | 8 (0.6) | "We think it would be good for him to know for when he has children." "To decide whether to have more children in the future." |
| Reasons for declining (<i>n</i> = 565) | | |
| Logistics (the context, the timing is not good) | 121 (21.4) | "Not right now. I'm participating in lots of studies. The traffic in and out (of the room) has been non-stop." "We're not too comfortable with it at this time. We're bombarded with a lot right now." |
| Do not want to worry | 121 (21.4) | "Because I want to believe that everything is OK; I don't want to worry." "At this stage, we feel information would cause more stress than be helpful." |
| Issues regarding testing | 109 (19.3) | "The baby is tested for enough things already. Too much testing can make one paranoid." "I'm not interested in extra testing. I had no prenatal testing either." |
| Do not want to know | 100 (17.7) | "At this point I don't really want to know if there's anything and I don't want to know if I passed it." "I don't want to because I don't want to know if he has a problem." |
| Do not want to be in study/not interested | 84 (14.9) | "I'm not the study participant type." "I'm not interested." |
| It is not necessary | 78 (13.8) | "No, I think the regular screening you are talking about is enough. We don't think the other is necessary." |
| Little chance of having it/no family history | 70 (12.4) | "It's not something we're worried about. No genetic predisposition. We already have a healthy child. There's no one in our family with mental retardation." "Neither us nor the family has this type of syndrome; we don't think she can inherit it." |
| Spouse/partner declined or disagreed | 65 (11.5) | "I would have liked to have done it, to know and be prepared in case he has it, but my husband doesn't want to." |
| My baby is fine/healthy | 62 (11.0) | "I think God made her a healthy baby. I believe she will be perfectly fine." "She looks pretty healthy to me; I know nothing is wrong." |
| I would rather wait for symptoms to appear | 53 (9.4) | "I would rather not know since I don't know when it will kick in. I'd rather not know and find out later when it happens." "If he's going to have mental retardation, then we'll deal with it when it happens. There's no point in knowing now." |
| There is no cure or treatment | 30 (5.3) | "Not interested because there's no cure." |

^a Based on number of couples providing reasons for their decisions. Some families' gave >1 reason, thus percentages total >100%.

eases without doing these things. It's your social responsibility. Try to help out all you can." The only other predominant reason, given by more than one fourth of the acceptors, was that the study was noninvasive, posing minimal or no risk to the child.

Reasons for declining were more equally distributed and included not wanting to worry about the test result (21.4%), negative feelings about testing children or genetic testing in general (19.3%), and not wanting to know (17.7%). About one fourth noted that the timing or context for deciding was not good. Decliners voiced the same concerns that bioethicists and others have raised about NBS. One mother said, "Knowing can cause anxiety. The chances of it happening are very small; don't know how it will unfold. Not knowing will not make you treat your child a certain way." Another mother declined "because I don't feel comfortable. I would rather not know since I don't know when it will kick in. I don't want to stress over the test results. I'd rather not know and find out later when it happens." Those who indicated a distrust of or opposition to tests in general made comments like, "I just didn't want an extra test because we didn't do any extra tests with the pregnancy," "The infant is tested for enough things already," and "Too much testing can make one paranoid."

Both an advantage and a risk of screening for FX, depending on one's perspective, is that identifying a newborn with an altered *FRM1* gene provides information to parents that one of them has a substantially increased risk for having children who are either carriers or have FXS. Although this knowledge was presented as both a benefit and risk in the consent form, only 8 parents noted "to provide reproductive risk information" as a reason for accepting.

DISCUSSION

This pilot project was not designed to maximize uptake but rather to examine the extent to which parents accept or decline screening within the context of a written consent process that explicitly stresses the risks and benefits specific to learning whether their newborn has an expanded *FMR1* gene. The acceptance rate of 63% is considerably lower than those reported in other NBS pilot projects^{33–35} and lower than the 79% rate reported in a pilot study that offered FX screening for male newborns in South Carolina.³⁶ Acceptance rates are likely to vary depending on the timing, content, and extent of the consent process, whether consent is oral or written or opt in or opt out, the type of disorder, and whether treatments exist.³⁵ In this study, the acceptance rate is not surprising considering that the screening test detects a condition with no cure, discloses carrier status for which predictive information is equivocal, and is preceded by a rigorous consent process, generally requiring both parents' consent, conducted in the hospital within 24 hours of birth. One concern about pilot studies offering informed consent for NBS is that parents may begin to question or choose to opt out of state NBS. There were no cases of that happening in this study.

In a previous article, we examined possible challenges to an informed consent process in screening for FX in the neonatal setting.⁴ These challenges included the ability to adequately explain the potential consequences of having FXS or of being a premutation carrier, and the possible ramifications of a positive diagnosis for the family, including confirmatory testing and genetic counseling. Although we designed educational and consent materials to convey this information, and RAs were trained to explain and discuss the study and FX in more de-

tail, the reasons some parents gave, or did not give, indicate that they may not have fully understood the study or FX and its personal, familial, and social consequences. For example, the mother who indicated she consented to the screening to help to find cures for diseases may have misunderstood the purpose of the study. Parents who gave as a reason for consenting "to help my child get better" may have not understood that there is no cure or standard medical treatment or they may have been referring to early-intervention services. Those who declined the study because the infant looked healthy or there were no problems in their family may not have understood how FX is inherited or manifests, but they may also have not wanted to consider that something could be wrong with their newborn. The lack of responses about a positive result providing information on reproductive risk or possible medical conditions in adult carriers is likely due to parents at this time focusing more on the implications of a positive diagnosis for the newborn and not what this information would mean for others. About one fourth of those who declined also indicated that the timing and context of consent were not optimal, raising the issue of the most appropriate time for consent and screening. Parents' opinions about these issues warrant additional study. We are currently conducting interviews with a subset of decliners and negatively screened acceptors to examine in more detail their evaluations of the consent process, understanding of the information presented, and reasons for their decision. We are also assessing the positive screened families to ascertain their responses and experiences related to the diagnosis.

For the most part, the reasons given by the vast majority of parents for accepting or declining suggest that they were

assessing many of the risks and benefits of the study and were making decisions based on what they most valued, or perhaps most feared. Although acceptance rates were lower than other NBS pilot studies, almost two thirds of families consented, indicating more parental support for testing for *FMR1* gene expansions in the newborn period than reported among pediatricians or genetic counselors.^{37,38} This is consistent with studies that indicate parents may view the benefits of expanded screening more broadly than defined by current criteria for NBS and are supportive of such screening with informed consent.³⁹ Our findings also indicate some difference in acceptance rates according to race/ethnicity, with black respondents somewhat less likely to consent to screening. This may be due to mistrust rising from the historical legacy of medical and genetic research in the United States with blacks^{40–42} or to a different valuing of the benefits and risks of screening. We cannot answer this question from our data but acknowledge that the role of race/ethnicity versus cultural differences in medical decision making is complex and requires additional investigation.

During the course of this pilot project, studies that could fundamentally change the rationale and need for NBS have been reported. These include studies showing that compounds reducing excess glutamate signaling substantially improve functioning in *fmr1* knockout mice⁴³ and *Drosophila*.⁴⁴ In addition, human clinical trials with adolescents and adults with FXS are now testing the effects of medications known to reduce mGluR-activated translation.^{45–48} Because FXS affects neurologic processes necessary for normal development and learning in the early years, these treatments (if shown to be safe and effective for young children) would likely be

most effective if given early. However, the fact that carriers would be identified suggests that parent consent for screening for FXS will still be required. In anticipation of this scenario, more research is needed comparing and contrasting alternative strategies and times for informing families so that they can make informed decisions about having their child screened.

CONCLUSIONS

Our findings contribute empirical data on public willingness to participate in NBS for *FMR1* gene expansions. Results indicate that almost two thirds of parents support FXS screening in the neonatal context, and parents' reasons for accepting or declining suggest some understanding of the benefits and risks of the study. As for most research projects, we cannot determine if truly informed consent was obtained but have demonstrated that although not the ideal time or place, it is possible to obtain informed consent in a neonatal context. Alternative consent strategies need to be considered but of ultimate importance will be the impact of the information on families who receive a positive diagnosis, including those individuals who may be asymptomatic carriers.

APPENDIX: RISKS AND BENEFITS LISTED IN CONSENT FORM AND BROCHURE

Benefits to Infants Identified as Having FXS or Being a Carrier May Include:

The diagnostic testing, genetic counseling, clinical evaluation, and referrals provided by the study.

Eligibility for certain learning and therapeutic services that may be helpful to the infant.

Alerting parents to the future health or learning problems the infant may have.

Preparing parents to raise a child with special needs.

Benefits to Parents of Infants Identified as Having FXS or Being a Carrier May Include

Saving financial and emotional costs of many trips to physicians to find out the cause of their child's problems.

Getting the early-intervention services the child may need.

Information that they and their relatives may be at risk for having children with FXS.

Getting support services that may be helpful to them.

Risks of Being in the Study

There may be a small emotional risk; you might worry about whether the infant's screening in the study will show a need for more testing.

Learning that one's infant has FXS may bring about feelings of grief, a sense of loss, worry, or anxiety. It may cause some stress in the family.

Learning that one's infant has FXS may cause parents to worry about what the condition will mean for the infant and family.

If an infant has the gene change for FXS, it means that one of the parents also has the gene change. Parents may feel bad about passing on that gene change. They may worry that other children or family members need testing.

There may be some stigma associated with learning there is an inherited genetic condition in one's family.

Although there are laws to protect genetic information, you may worry about how others could use this information. Discrimination against your family or child by insurance companies, employers, or schools could be possible.

Finally, although unlikely, the study screening test result could be wrong. It

may show that infants need more testing when they do not or it may not find infants with FXS. If your infant has health or developmental problems later, he or she may need diagnostic testing for FXS.

ACKNOWLEDGMENTS

The Fragile X Newborn Screening Study is supported by the Eunice Kennedy Shriver National Institute for

Child Health and Human Development (P30 HD003110-S1); the National Human Genome Research Institute's Ethical, Legal, and Social Implications Research Program (5P50HG004488); Centers for Disease Control and Prevention in conjunction with the Association for Prevention Teaching and Research (Cooperative Agreement No. U50/CCU300860, Project TS-1470); the National New-

born Screening and Genetics Resource Center, a cooperative agreement between the Maternal and Child Health Bureau, Genetic Services Branch and the Department of Pediatrics, University of Texas Health Science Center at San Antonio; Health Resources and Services Administration (U32-MC00148); and the National Center of Research Resources, National Institutes of Health (UL1RR025747).

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