Long Title: Biobank Participant Support of Newborn Screening for Disorders with Variable Treatment and Intervention Options

Short Title: Newborn Screening Support for Variable Disorder Types

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Abstract

Purpose: We aimed to better understand biobank participant opinions of the benefits of newborn screening (NBS) for certain disorder types and how terminology used in NBS discourse might impact stakeholder opinion.

Methods: We conducted a between-subjects randomized survey of 5,840 members of the Northwestern University Biobank. The survey contained twelve scenarios, each describing a disorder and its treatment. For each scenario, we varied the terminology used to describe treatment options. One survey version used the term *intervention,* and the other *treatment.* The outcome measured for each scenario was perceived benefit (for the infant) and importance of testing (for participants). Comparisons were made between participants and between scenarios.

Results: Ratings of benefit and importance were not influenced by the use of the term *intervention* versus *treatment* within scenarios. Nuances existed in ratings of benefit to the infant and importance to participants amongst scenarios. Participants were most likely to perceive benefit and importance in screening for a disorder if treatment/intervention offered a high chance of improved outcomes.

Conclusions: While participants perceived benefit to the infant and importance to themselves in screening for most disorders, nuances in inter-scenario ratings suggest participants weighed availability and type of treatment/intervention in consideration of the benefits of NBS.

Key Words: newborn screening; benefit; treatment; intervention; biobank participants

INTRODUCTION

State-mandated newborn screening (NBS) began in the late 1960's as a public health program designed to identify newborns with rare, often genetic, disorders for which early treatment or intervention exists. In the 1990's, development of new technological methods, particularly the use of tandem mass spectrometry (MS/MS), allowed for an expansion in the number of conditions that could be included on NBS panels (Burton and Moorthie 2010).

The U.S. Department of Health and Human Services provides screening panel guidance to state programs, informed by evidence-based recommendations made by the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC). The disorders that are recommended for screening by the Advisory Committee and endorsed by the Secretary make up the recommended uniform screening panel (RUSP). States then use these recommendations to determine the screening that is mandatory for every infant born in that state. Candidate RUSP disorders are evaluated on multiple criteria such as the characteristics of the disorder, validity of screening and diagnostic measures, and the potential for treatment as compared to usual clinical identification (Calogne et al. 2010).

The Advisory Committee's role is to assess available evidence of net benefits for screening for particular disorders in newborns. The committee's process is focused on the benefits of early detection for the newborn. Alternatively, there are other NBS stakeholders, including parents and disease advocacy groups, who have called for a strong need to weigh benefits and harms to both newborns and families, and, to some extent, society, in making a final determination of the net benefits of screening for a particular disorder (Bombard et al. 2010; Burton and Moorthie 2010; Calogne et al. 2010; Petros 2011; Kemper et al. 2014).

Much research has been done to understand parental and public attitudes toward screening benefits, particularly focusing on the inclusion of conditions meeting more contentious, expanded criteria (Hasegawa 2010; Etchegary et al. 2012; Weinreich et al. 2012). Overall, the public supports screening for a wide variety of conditions, both treatable and untreatable, and accepts a wide concept of what could be considered a benefit within the NBS context (Tarini et al. 2009; Plass et al. 2010; Etchegary et al. 2012).

As a subset of the general public, biobank participants, in general, represent those individuals who have, in some manner, been recruited into a biorepository within the healthcare system in which they receive their care. A 2013 national survey of US biobanks revealed 636 such organizations and surveyed 456 of these on their general policies and procedures (Henderson et al., 2013). Public support for bio-banking is somewhat varied, thus it is reasonable to assume that those actually enrolled in a biobank are motivated in some way, though the extent of the differences between a biobank population and general public population have not been quantitatively elucidated. A 2010 qualitative study suggests that biobank participants may be more interested in research, but express similar concerns and interests as their general public counterparts (Lemke et al., 2010). Their motivation to participate in research and research-related topics makes biobank participants an important subset of the general public as far as their status as stakeholders in decisions made about newborn screening condition panels.

While the body of work demonstrating stakeholder opinions includes numerous condition-specific support studies, it does not include many studies that allow participants to express varying levels of support for certain types of conditions over others (Campbell and Ross 2003; Lipstein et al. 2010) or allow respondents the opportunity to express varying levels of support based on condition characteristics (Plass et al. 2010; Etchegary et al. 2012; Weinreich et

al. 2012; Christie et al. 2013). To our knowledge, no research to date has looked specifically at the impact of terms like "treatable" on stakeholder perception of the potential benefits of screening for a particular disorder, or how certain terms like "treatment" and "intervention" may influence support of screening for certain types of conditions. Without such research, it is not possible to know how much, if at all, the language that is used to describe disorders is influencing public perception of net benefits and harms.

MATERIALS AND METHODS

Study Population

Enrollees in the NUgene Project, a genomic biobank sponsored by Northwestern University (Chicago, IL, https://www.nugene.org) were surveyed over a 6-week period in December 2014-January 2015 regarding their perceptions of benefit and importance in NBS for 12 distinct disorder scenarios. NUgene, is an IRB approved, HIPAA compliant biospecimen repository with longitudinal medical information from participating patients at Northwestern University-affiliated hospitals and outpatient clinics. To date, over 8,000 patients have enrolled in NUgene. Any patient, regardless of health status, is eligible to participate if the following criteria are met: (1) age 18 or older; (2) receiving health care at a Northwestern affiliated hospital or clinic; (3) able to provide informed consent.

Survey administration

Eligible participants included English-speaking members of NUgene who had agreed to be re-contacted at the time of enrollment and had a valid email address on file. An email containing the survey link was sent to all eligible members (N=5,840). The survey was created and distributed online using SurveyMonkey™. Responses were anonymized and IP addresses were not collected. The survey took participants approximately 8-12 minutes to complete. One email reminder was sent to all participants one week after the initial survey invite. The Northwestern University Institutional Review Board approved this study (Project #: STU00099674).

Survey Design

This survey assessed differences in biobank participant perception of the terms *treatment* and *intervention* within the context of benefit in NBS. The variation in these terms was designed to test a potential framing effect, which is a form of cognitive bias in which individuals react differently to a particular choice or statement depending on how it is presented (Druckman, 2001). Survey design was intended to screen for this bias in addition to eliciting information about participant support for screening for conditions with varying characteristics. Our hypotheses was that, due to prior experiences with these words, participants might rate potential benefit to the infant or to themselves differently if a disorder was described as having an associated "treatment" vs. "intervention.

The scenarios utilized in the survey were based on different disorders that are either currently screened for on the RUSP or are part of the current national NBS discourse. The scenarios described a disorder and associated treatments/interventions. These scenarios were developed by the study investigators and based on prior studies of stakeholder attitudes towards

condition-specific NBS, which utilized disorder scenarios in qualitative methodology (Campbell and Ross 2003; Lipstein et al. 2010).

The beginning of the survey included a brief explanation of NBS (Appendix 1), followed by these survey directions:

- Imagine that there are new tests that can be used to test all newborns for specific health disorders. There is a very small chance that a child will be born with one of these disorders.
- The test will use the same blood sample that is already collected from all newborns at the hospital. No extra blood sample will be required; however, there is a cost associated with each additional test that is run.
- Each of the following scenarios outlines a particular health disorder and the available interventions/treatments or lack of interventions/treatments.

Important and noteworthy decisions were made within the survey directions. For example, participants were explicitly told to assume that there is a "very small chance that a child will be born with one of these disorders." The decision to use this language was made on the grounds that the majority of disorders tested for on the newborn screen, and the majority of disorders that are proposed for inclusion are relatively rare. Participants were additionally told, "There is a cost associated with each additional test that is run." This was meant to reflect the fact that additions to the newborn screen are not free, and while the total cost would vary considerably with the disorder proposed and its associated testing platforms, there is some cost associated with the test and its result interpretation and communication. Our aim was to have participants at least aware of the concept of additional cost, though the survey was not designed in such a way to allow very nuanced interpretation of the impact of cost on newborn screening decision-making.

Linguistic influences within survey design

Eligible participants were randomized via random number generator into one of two groups, each of which received a different version of the survey. One group received a version that used the word *treatment* (n=2,864) within the disorder scenarios. The other group received a version that used the word *intervention* (n=2,976). Table 1 contains the language used for the 12 disorder scenarios. The terms *treatment* and *intervention* are bolded.

General survey presentation

Participants were presented with the twelve disorder scenarios in random order (Table 1) followed by these questions:

- In your opinion, how beneficial *to the* infant is testing for the following disorders at birth?
- How important is it *to you* that all infants are tested for the following disorders at birth?

Participants were asked to rate their perceptions of benefit and importance respectively using seven-point Likert scales of (1) *not beneficial* to (7) *definitely beneficial* and (1) *not important* to (7) *definitely important*. Only the ends of the scale were defined. The order of the scenarios and the response questions was randomized with participants receiving the two questions in a random order and all 12 scenarios in random order.

Participants were asked about demographic information including: gender, age, level of education, ethnicity, and income. They were also asked, "Do you have children?" and "Do you have a child with a chronic illness or disability?" The decision to assess this demographic factor

is supported by literature suggesting that parents with/without a child with a chronic illness or disability may feel differently about the actual and potential benefits of newborn screening (Detmar et al., 2008).

Statistical analysis

Data was compiled, cleaned, and statistically analyzed using IBM SPSS version 22.0 (Statistical Package for the Social Sciences). Descriptive statistics were reported for each question. The *intervention* and *treatment* group ratings were treated as continuous variables and were compared using an Independent Samples t-test and the Mann-Whitney U test to determine if any significant differences existed between these two groups on the ordinal Likert scale data (Hart 2001). Mann-Whitney U and Kruskal-Wallis tests were used to compare the distribution of responses between different groups of participants to determine if any significant differences were present (Lehman 2006). The Wilcoxon Signed Ranks test was used to assess for differences in participant rating between questions and for different scenarios. Missing responses were excluded from the data analysis. Analysis was performed post-hoc without basis in any prior hypotheses. P-value ≤ 0.05 was considered statistically significant across all analyses. A regression was run to determine if selected demographic variables shown to be significant predictors of the participants' rating of benefit and/or importance in testing (e.g. having children) were still significant after controlling for covariates (e.g. having a child with a chronic illness or disability).

RESULTS

Survey participant characteristics

The overall response rate for this study was 9.5% (555/5840). Of the 555 total respondents, the majority was white non-Hispanic (86%), female (65%), and had at least a college education (89%). Most were > 30 years old (76%) and reported having a child (62%), A small subset (9% of total) reported having a child with a chronic illness or disability. The majority of participants reported a household income of greater than $50,000 (89%). There were no statistically significant differences between respondents and the biobank population as a whole. Table 2 summarizes the demographic characteristics for all participants. There were no statistically significant differences in demographic characteristics between the randomized groups. In general, response rates for biobank studies are lower than other subsets of the general public (Lemke et al. 2010; Holm et al. 2015; Ryu et al. 2015). For the NU Gene biobank population, in particular, unpublished surveys have results in a between a 5-22% response rate.

Linguistic influence of terms *treatment* vs. *intervention*

No statistically significant differences were found between the group of participants that received the survey version with scenarios using the term *intervention* vs. the group of participants whose scenarios used the term *treatment* when comparing Likert scale rating responses, treated as a continuous variable, to questions 1 and 2 (defined above and Table 3) for each of the 12 scenarios. As no statistically significant differences existed between the two groups, and because the two survey versions were identical on all measures besides the use of *intervention* vs. *treatment*, all subsequent analysis was performed on the combined group of 555 participants (294 respondents to the *intervention* version and 261 to the *treatment* version).

Disorder scenario ratings

Overall, ratings of importance and benefit in testing were 5 or above (indicating high perceptions of benefit/importance) for the majority of scenarios. The highest ratings were given for scenario #1, (see Figures 1 & 2) which described a condition like phenylketonuria (PKU) that included a highly effective dietary intervention that must be begun early to be effective. There was a high perception of benefit and importance given for scenario #4 (see Figures 1 & 2), which described a disorder that had an associated educational intervention that could help with downstream mental abilities. Participants gave high positive, though lower than in prior scenarios, ratings to Scenario #8, which describes a disorder with no guaranteed treatment or intervention options but with a possibility for research involvement (see Figures 1 & 2).

Ratings of importance and benefit were mixed for scenarios #2 and #3. Both described a disorder with no intervention or treatment that could begin prior to development of signs of the disorder. Significantly lower ratings of benefit and importance were given for scenarios #9 and #10, which described a disorder with a treatment/intervention option that could respectively add 6 months to 3 years of time (spent in and out of the hospital) to the child's life.

Scenario comparisons

Certain pairs of scenarios were initially designed to allow for useful inter-scenario comparison. The goal of comparison was to elucidate any significant differences in the ways that participants perceived and rated benefit and importance in screening based on the specifics of the presented scenario. All data for these comparisons can be found in Table 3, including scenario wording, means for questions 1 and 2 for each scenario, and p-values associated with the

comparisons.

Scenario #2 vs. #3 (Timing of diagnosis with no available intervention/treatment)

Scenario #2 and #3 differed only in the inclusion of the statement "*the child's family will know of the diagnosis much sooner"* within scenario #3. Both scenarios otherwise described a disorder with no available early treatment/intervention. The goal of this comparison was to understand if participant ratings were affected by the explicit reminder that, although no treatment existed for this particular disorder, the family would be alerted of the diagnosis at an earlier time than would otherwise be possible. When scenario #2 responses were compared to scenario #3, it was found that participants more highly rated both benefit to the infant for scenario #3 vs. #2 ($P< 0.0005$) and also more highly rated importance to themselves ($P< 0.0005$) that infants be tested for disorder scenario #3 vs. #2.

Scenario #9 vs. #10 (Adding limited time to lifespan)

Scenarios #9 and #10 both described a disorder with a treatment or intervention that could add only limited time to the lifespan, time that was described as being spent "in and out of the hospital." The goal of this comparison was to elucidate any differences in participant rating that were due to the extension in lifetime, and whether participants would support even a very small increase in overall lifespan. Scenario #9 described a disorder with a treatment/intervention that would add 6 months of life and scenario #10 offered 3 years of life. While ratings of benefit to the infant and importance to oneself that infants be tested were low in both cases, participants more highly rated scenario #10, which offered greater total increase in lifespan (Q#1: $P< 0.0005$; Q#2: $P< 0.0005$).

Scenario #11 vs. #12 (Alleviation of physical vs. mental symptoms)

A comparison was also made between scenarios #11 and #12, which respectively described a disorder that had a treatment/intervention that could alleviate physical but not mental symptoms and a disorder that had a treatment/intervention that could alleviate mental but not physical symptoms. The goal of this comparison was to understand if any differences in rating existed based on the potential type of benefit, physical or mental, that existed for the child. Participants more highly rated both questions for scenario #12, which states potential for improvement of mental, but not physical, abilities (Q#1: $P< 0.0005$; Q#2: $P< 0.0005$).

Demographic factors affecting ratings of benefit and importance

A variety of demographic factors were assessed for impact on participant perception including gender, age, level of education, ethnicity, and income, whether participants had children, and whether they had a child with a chronic illness or disability. Females rated benefit and importance as higher for questions #1 and #2 for four of the 12 scenarios (#4, 7, 11 and 12) ($P< 0.0005$, $P=0.030$, $P=0.030$, $P=0.025$). Having a child with a chronic illness or disability was a significant factor in influencing ratings. Participants with a child with a chronic illness or disability gave significantly higher ratings for question #2 for 8 of the 12 disorder scenarios (#1, 3, 4, 5, 6, 7, 11, 12) ($P=0.019$, $P=0.021$, $P=0.022$, $P=0.001$, $P<0.0005$, $P=0.019$, $P=0.002$, $P=0.010$). Question #2 asked: *How important is it <u>to you</u> that all infants are tested for the following disorders at birth?* When the effect of having a child with a chronic illness or disability was controlled for within the cohort of individuals who reported having a child, parental status alone was not a significant predictor of ratings.

DISCUSSION

Nuanced support for newborn screening

The results of our study suggest that, in general, participants perceived benefit and importance in screening for most disorder types. This finding is consistent with the current body of literature, which suggests that parents and the public support NBS in a wide variety of contexts (Quinlivan and Suriadi 2006; Tarini et al. 2009; Lipstein et al. 2010; Goldenberg et al. 2013). However, our participants were not asked whether or not they perceived benefit and importance in screening but were instead asked to rate the *amount* of benefit and importance they perceived.

In general, NBS is indicated in situations in which early detection and intervention can lead to improved health outcomes when compared to traditional clinical diagnosis. This study found that while participants perceived benefit and importance in screening for disorders that did not meet these criteria, there was substantially less agreement in ratings of benefit and importance for these types of scenarios, as compared to those for which screening has historically been accepted. This result suggests that when study methods allow, participants are able to express important differences in the perceived benefits of screening across disorders with varied characteristics (Campbell and Ross 2003; Lipstein et al. 2010)

Expanded concepts of benefit and beneficiaries

Despite the increasing technological capacity for NBS disorder inclusion, the basic tenets of NBS programs remain focused on screening in contexts of potential benefit to the infant. The

results of this study indicate that the biobank participants, a research-interested subset of the general public, understands a very wide definition of what benefit entails, though differentiates between benefit types as evidenced by higher perceptions of benefit and importance in screening for certain types of disorders over others. For example, participants perceived benefit and importance in screening for a disorder described as having only an educational intervention and with one described as having no intervention other than additional state services and support. Though participants perceived both benefit and importance in screening for these disorders, they indicated higher levels of perceived benefit in screening for a disorder with a more typical dietary intervention/treatment. These results are helpful in adding to the discussion about NBS for disorders like fragile X, for which some of the proposed interventions are educational in nature or may involve increased access to additional state services in addition to offering reproductive information to parents and extended families (Bailey 2004; Skinner et al. 2011; Christie et al. 2013).

Within this discourse surrounding benefit, the availability of treatments and/or interventions is a commonly raised consideration (Bailey 2006). To understand the link between treatment/intervention availability and benefit, a distinction between the terms *treatment* and *benefit* must be delineated. Bailey et al. (2006) clearly defines *treatment* as the intervention or service that is provided, whereas *benefit* refers to the results achieved by the early identification or treatment. This particular definition highlights the status of *treatment* and *benefit* as separate, though related, concepts. This idea frames what Bailey (2009) refers to as the "blurred distinction between treatable and untreatable conditions in newborn screening," alluding to difficulties inherent in defining the boundaries of treatment and resulting benefits and impacts.

Expanded concepts of benefit can include a broadening of what constitutes an actual

benefit, but can also include an expanded conception of potential beneficiaries. Participants in this study gave high ratings for scenarios #5 and #8, which described disorders in which screening would offer reproductive benefit and research benefit respectively. What is most noteworthy is that participants rated greater importance to themselves that all infants be screened, as compared to perceived benefit for the infant in question. By asking participants to consider both benefit to the infant and importance to themselves, this study suggests that participants are not always in support of screening because they perceive benefit to the infant, but may support screening for a wide variety of reasons outside of direct infant benefit. This is important because if NBS programs aim to remain focused on the infant him or herself, elucidating why stakeholders support screening for certain conditions will be critical in making decisions about what types of conditions merit inclusion on state NBS panels.

Risky interventions and uncertain gains

As NBS programs expand to include disorders like lysosomal storage disorders (LSDs), which have been recently considered, and in some states implemented either through pilots or full-scale screening, it is increasingly important to understand how the public perceives the benefits of testing when the risk of adverse events from the intervention is high and/or when the potential outcomes of treatment include only a minimal increase in lifespan for the infant in question (Ross 2012). The results of this study suggest that biobank participants are skeptical about the benefits of testing when treatment risk is high and lifespan or quality of life is minimally increased, though further research into perceived lifespan benefits is necessary to understand the factors and boundaries at play in this judgment. The skepticism noted here is consistent with the opinion of major policymakers in the field who have suggested that NBS for

LSDs does not meet currently accepted NBS criteria and thus LSDs are not ready for inclusion in universal NBS panels (Petros 2011; Ross 2012). However studies of the general public have characterized support for screening for Pompe disease through a vignette-style survey, particularly focusing on the difficulties of screening given different phenotypes and onset ages (Weinreich et al. 2012). This is somewhat at odds with our findings of skepticism about screening for disorders like Pompe, however our LSD-based vignettes (#9 & #10) were not meant to be all-encompassing of the disorders, and instead focused on the low-success of treatment aspect, showing that parents care about the added time of life that a treatment can provide. This perspective, the policymaker perspectives and the perspective of our participants as a subset of the public will be important to continually contemplate as LSD testing moves forward in pilot programs and is considered for and/or adapted for universal inclusion in some states.

Effects of terminology on benefit perception

The lack of significant differences in rating between the *treatment* and *intervention* survey versions suggests that participants were not influenced by differential use of these terms. Instead, participants may be more focused on the particulars of what type of care has the potential to alleviate symptoms or increase positive outcomes via screening. Continued exploration of potential terminology influencers will be particularly necessary as NBS programs consider the possibility of including expanded NBS panels that require parental consent.

Importance of public opinion in informing newborn screening

The public is a typically considered stakeholder in the decisions made regarding newborn screening. However, the Advisory Committee ultimately makes newborn screening decisions.

While public opinion does not directly translate to changes in newborn screening protocol, an understanding of the opinions of the general public, including parents and advocacy groups, is still uniquely important in informing discussions on potential benefits and harms of newborn screening. Classifying and categorizing the public opinion of potential newborn screening benefits is critical in conversations about potential expansion of screening for certain types of disorders. As a subset of the general public likely to support research and genetic testing, classifying biobank participants opinion adds to the body of knowledge about potential public sentiment.

Demographic comparisons

Our study indicates that significant differences exist in the way that certain subgroups of the population perceive both benefit and importance in NBS. As the public is often construed as a single major stakeholder, these findings are particularly relevant to the NBS decision-making process. This study showed that females were more likely to perceive benefit and importance in testing for the majority of disorders. The reason for this is not clear, but could be due to female perception of caregiver responsibility. Further research should assess the effect of caregiver status, independent of gender, on perceived benefit and importance in NBS. Interestingly, females rated both benefit to the infant and importance to themselves significantly higher than males. The general body of NBS literature has focused on maternal attitudes with regard to current and expanded NBS practices, but there is a lack of consensus regarding the effect of gender, as a separate effector than maternal status (Davey 2006; Christie et al. 2013; Newcomb 2013).

Our data also demonstrate that participants with a child with a chronic illness or disability

found it highly important that all infants be tested for the disorders presented, and for most scenarios (Campbell and Ross 2003; Tarini et al. 2009; Bombard et al. 2010; Burton and Moorthie 2010; Hasegawa 2010; Petros 2011; Etchegary et al. 2012; Kemper et al. 2014) rated statistically significantly higher benefit to the infant in question. Within NBS literature, it has been documented that participants with children are more in support of screening (Plass et al. 2010). However, without assessing for the health status of these children, the potential effect of having a child with a chronic illness or disability versus simply parental status cannot be known. Our finding that parents of a child with a chronic illness are more in support of screening and outspoken about their opinions is consistent with other literature (Detmar et al., 2008), including a recent study by Goldenberg et al. (2013), which demonstrated that participants whose youngest child had two or more health conditions were statistically significantly more likely ($p < 0.01$) to support whole genome sequencing through NBS. In future studies of NBS support, it will be important to assess not only parental status, but also the effect of the health status of these children to better understand nuances in parental support of screening based on this effect.

This study offers a nuanced look at the types of characteristics that biobank participants perceive as beneficial in considering screening for certain disorders. Much literature surrounding the topic of NBS focuses specifically on particular disorders, (fragile X, cystic fibrosis, LSDs etc.) giving little opportunity for nuanced comparison of condition characteristics. This hinders any attempts to understand what characteristics of a disorder are being privileged throughout decision-making surrounding screening support.

This study's aims are similar to a qualitative, focus-group study by Lipstein et al. (2010) which explored parental opinions surrounding scenarios about disorders with a variety of characteristics including those that are treatable vs. untreatable, those with treatments associated

with high morbidity, and those associated with a highly versus less accurate screening test. Similar to the results of this study, their study detected nuances in parental support of testing for certain types of disorders, showing that although parents were in support of screening for many disorders there was less consensus about disorders that were not clearly treatable (Lipstein et al. 2010).

Limitations

Limitations in this study's methodology and data warrant consideration. The population surveyed included enrollees in a university biobank. Though enrollment criteria for this biobank are broad, participants were at least familiar with and open to the utilization of genetic information on a basic level. While over 550 individuals responded to this survey, response rate was low (9.5%). However, this response rate is not atypical for biobank population surveys of this nature, thus it is reasonable to interpret these data as representative of the opinions of a university biobank population. Though demographically the populations of responders and recipients were not significantly different, it is possible that the responders were those who were particularly motivated because of an interest in this particular topic. This is typical of biobank populations in general. The vast majority of our participants were located in or within 100 miles of the city of Chicago, which potentially limits the generalizability of this study to other, particularly rural, populations.

The survey was developed for the purposes of this study and was not validated. Although the disorder scenarios were informed by actual NBS conditions, the study was hypothetical in nature. Some of the conditions presented are not under consideration for screening inclusion and/or do not precisely reflect an existing disorder. In addition, it is likely that participants had

disparate interpretations of how medically, mentally and/or physically serious each disorder actually was, and this interpretation could affect the way that benefit and importance in screening was rated. Despite these limitations, for the broad aims of elucidating a platform of information about benefit perception in testing for disorders with certain characteristics over others, the format of the survey allowed for meaningful comparisons between disorder characteristics and participant ratings.

Finally, the specific aims of this study were to assess biobank participant perceptions of benefit in NBS for disorders with certain characteristics as compared to others. In this study, as in many others that assess perceived support for NBS, is a lack of consideration about the harms of screening both in current and expanded protocols. While this study mentioned the additional costs associated with the addition of new disorders within the background of the survey, harms were not explicitly noted within the scenarios, most of which would carry specific harms if added to a screening panel. Thus, the perceived benefits and screening importance noted by participants in the study must be interpreted in light of what is known about potential harms, which, if reliably assessed, would be expected to temper the broad perceptions of benefit noted here and in other studies of NBS support and decision-making.

CONCLUSIONS

While the body of prior research on the topic of support for NBS demonstrates that the majority of stakeholders is in favor of screening for many different disorder types, our data indicates a substantial degree of nuance in how these stakeholders perceive benefit in testing for disorders with certain characteristics over others. In general, stakeholder see benefit in screening for most types of disorders, but perceive much greater benefit when an intervention is available

(Campbell and Ross 2003; Tarini et al. 2009; Skinner et al. 2011; Etchegary et al. 2012a; Etchegary et al. 2012b; Weinreich et al. 2012). This study highlights a lack of stakeholder consensus regarding the benefits and importance of screening for disorders that do not meet traditional NBS criteria. These results provide a more detailed look at the types of conditions that the public perceives as having the greatest benefit and importance within a screening paradigm.

NBS programs, limited by public health resources, potential harms of false positive results and logistic concerns, should not screen for every possible condition. Rather, NBS as a public health program, must consider the resources available with the goal of screening for conditions in which the most benefit, balanced with associated harms, can be gained. This study supports such an approach, highlighting that although biobank participants, as a subset of the general public, supports screening in many scenarios, there is a lack of consensus about the benefits associated with screening for disorders without clear treatment or intervention options, or in which potential treatments may be risky or associated with only a minimal increase in lifespan.

It is impossible to separate the decisions made regarding newborn screening practices from the stakeholders who ultimate experience the effects of any decisions made in this realm. The Advisory Committee is officially tasked with recommending certain disorder for inclusion, yet their decisions have a direct impact upon the general public, in particular, parents, who bear the benefits and harms of any decisions made. This necessitates a consideration of the opinions of these stakeholders, most importantly how they perceive these potential benefits and harms in screening for certain types of disorders as compared to others. Bailey (2009) summarized a wider concept of the place of benefit in NBS, arguing that the primary standard for NBS should not focus on whether a treatment is available, but instead on whether benefit accrues as a result of

early identification of the disorder in question (Bailey 2009). This survey adds to the body of knowledge surrounding the accrual of benefit in less traditional ways. As NBS programs consider expanded inclusion of certain disorders, these results will be important as part of a thorough consideration of the opinions of all major stakeholders including the general public and the parents who would be key recipients of the benefits and risks of expansion.

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COMPLIANCE WITH ETHICAL GUIDELINES

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all patients for being included in the study.

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