

Not without my Permission: Parents' Willingness to Permit Use of Newborn Screening Samples for Research

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Key Words

Newborn screening blood spots · Public health · Research

Abstract

Background: State newborn screening (NBS) programs are considering the storage and use of NBS blood samples for research. However, no systematic assessment of parents' attitudes exists. **Methods:** We conducted an Internet-based survey of a nationally representative parent sample. We examined parents' willingness (1) to permit use of their children's NBS samples for research with/without their permission and (2) to allow NBS sample storage. Using bivariate and multinomial logistic regression, we examined the association of parent and child characteristics with parents' willingness to permit NBS sample storage and use for research, respectively. **Results:** The response rate was 49.5%. If permission is obtained, 76.2% of parents were 'very or somewhat willing' to permit use of the NBS sample for research. If permission is not obtained, only 28.2% of parents were 'very or somewhat willing'. Of parents surveyed, 78% would permit storage of their children's NBS sample. Parents who refused NBS sample storage were also less willing to permit use of the NBS sample for research. **Conclusions:** Three-quarters of parents would permit use of their children's NBS samples for re-

search – if their permission is obtained. Parents not in favor of storing NBS samples often opposed the use of NBS samples for research.

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Nearly every child born in the U.S. each year is screened through state newborn screening (NBS) programs for a number of inherited disorders that, if left untreated, can result in severe disability or death. As part of this screening process, a single drop of blood from each infant is placed on a piece of filter paper. After testing is completed, these blood samples can be stored for years. In fact, 19 states currently store blood samples for some period of time ranging from 1 to 23 years, while 8 states store their residual blood samples indefinitely [1]. States store samples for a number of reasons, including retesting of samples, evaluation of future NBS tests, forensic purposes, and research [2].

Storage of NBS blood samples provides an opportunity to conduct research on a variety of disorders includ-

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<p><i>Use of newborn screening samples for research</i></p> <p>Every infant born in the US is tested for inherited diseases. These tests are done as part of each state's newborn screening program. Blood is collected for these tests shortly after birth. After testing is completed, the DNA from these blood samples can be used for future research studies on various diseases.</p> <ul style="list-style-type: none"> - How willing are you to have your child's blood sample (from their newborn screening) used for future research studies, <i>with your permission?</i> - How willing are you to have your child's blood sample (from their newborn screening) used for future research studies, <i>without your permission?</i>
<p><i>Storage of newborn screening samples</i></p> <p>States may store newborn screening blood samples for varying amounts of time.</p> <ul style="list-style-type: none"> - How long are you willing to have your child's blood sample (from their newborn screening) be stored?

Fig. 1. Survey instrument. Text that was not provided to participants is represented in italics. The order of the questions in the first section was randomized.

ing those not related to newborn screening. Because samples are collected from every infant and stored for years, they can be used in population-based research studies (e.g., prenatal chemical exposures, genetic association studies) that would otherwise require long periods of follow-up [3–5]. A recently published study also demonstrated the feasibility of using stored newborn screening blood spots to quantify gene expression [6].

However, a number of ethical and policy challenges need to be considered prior to the use of NBS samples for research. First, these samples were originally collected as part of state public health programs that seek to identify infants with inherited diseases in order to provide timely treatment that prevents adverse health outcomes. Testing is mandatory, and in all but 3 states infants are tested without the consent of parents [7]. Therefore, when NBS samples are collected, parents have not explicitly consented for their use in activities beyond traditional screening such as research. Second, although storage of NBS samples is a routine practice in many states, the majority of states do not actively obtain parent permission to store blood samples. In some states, parents who do not want their children's samples used for research have the right to contact the state and request that their children's samples be destroyed [1]. In general though, most state programs do not actively provide parents with information regarding policies for storage and use of NBS samples, and it is unclear how many parents are aware of these storage and use policies [8].

Much of the policy discussion surrounding the storage and use of NBS samples for research has occurred without a systematic assessment of parents' attitudes. An evaluation of parents' opinions about these issues is critical. For example, a Minnesota advocacy group recently called for stored NBS samples to be destroyed, claiming these samples had been stored without parental consent [9]. Such a public backlash could lead to the destruction of decades of samples which are a potentially valuable public health resource. Given the absence of a systematic assessment of parents' attitudes about the storage and use of NBS blood samples for research, we conducted a national survey to explore these issues.

Methods

Study Design

In April 2008 we conducted an Internet-based survey. This study was approved by the University of Michigan Institutional Review Board.

Study Population

We fielded 3,935 surveys to individuals ≥ 18 years old who were randomly sampled from a larger nationally representative panel of adults. This panel is maintained by the survey research firm Knowledge Networks (Menlo Park, Calif.). The process by which the panel was created has been described previously [10]. The survey was administered to both parents and non-parents, with parents over-sampled. In this sample, a parent was defined as an individual who was the parent or legal guardian of one or more children ≤ 17 years of age living in the same household. For the analyses presented here we focused on the parent respondents only.

Survey Instrument

Our survey instrument sought to examine parents' attitudes about the use of children's NBS samples for research studies and the storage of children's NBS samples by state NBS programs. Prior to receiving questions, all parents were provided with a brief description about newborn screening (fig. 1). In order to evaluate whether the ordering of questions influenced parental responses, we randomized the order in which parents received questions related to permission and use of NBS samples for research.

Outcome

Use of NBS Samples for Research. We asked parents to indicate their willingness to have their children's newborn screening samples used for research using a 4-point Likert scale: 'very willing/somewhat willing/somewhat unwilling/very unwilling'. We considered that parents who were 'very willing' or 'very unwilling' would be most likely to allow or not allow their children's NBS samples to be used for research, respectively. Parents who were 'somewhat willing' or 'somewhat unwilling' were considered to be more hesitant – and potentially uncertain – about allowing their children's NBS samples to be used for research. Given this conceptual framework, we felt it would be most useful to explore de-

Table 1. Parent and child characteristics (1,508 respondents)

Characteristics	Weighted estimate
Age, mean (years)	38.1
Female	57.0%
Race/ethnicity	
White, non-Hispanic	67.3%
Black, non-Hispanic	11.0%
Hispanic	14.8%
Other, non-Hispanic	6.9%
Education	
High school or less	39.6%
More than high school	60.4%
Household income (USD)	
<15,000	9.8%
15,000–30,000	13.6%
30,000–60,000	28.5%
60,000–100,000	29.9%
>100,000	18.2%
Number of children (median)	2
Age of children, mean (years)	
First child	11.9
Second child	9.5
Child health status	
Any child in poor/fair/good health	12.2%
All children in excellent or very good health	87.8%

mographic factors of parents who were more hesitant about allowing their children's NBS samples to be used for research (e.g., parents who were 'somewhat unwilling').

Storage of Newborn Screening Samples. Parents indicated ('yes' or 'no') whether they would permit the state to store their children's newborn screening samples. Parents who would permit the storage of their children's samples were asked the length of time that they would allow the samples to be stored. Parents were able to specify either a discrete number of years from 1 to 18 or that they would permit the state to store the newborn screening sample for an indefinite period of time.

Parent Demographics and Child Characteristics

We collected the following information about parents: age, education, race/ethnicity, and household income. We also collected information on the number of children in the household, each child's age, and parental report of each child's health status ('excellent/very good/good/fair/poor'). Because we did not ask parents about their attitudes toward a specific child's NBS sample, we constructed a dichotomous variable that took into account the health status of all children in the household: all children in excellent or very good health vs. other (e.g., any child in poor, fair, or good health).

Statistical Analysis

Research on NBS Samples. Univariate analyses were used to determine the proportion of parents willing to have their chil-

dren's newborn screening samples stored with and without their permission. For bivariate analyses, we used χ^2 tests to examine the effect of the question order on parental responses. We used multinomial logistic regression to examine associations between parent (age as continuous variable) and child characteristics associated with parents who were 'somewhat unwilling' to have their children's NBS samples used for research purposes by comparing them to parents who were 'very willing' or 'somewhat willing', respectively. We chose this comparison scheme because we wanted to determine how parents who were 'somewhat unwilling' differed from parents who were more likely to permit use of the NBS sample for research.

Storage of NBS Samples. We used univariate analyses to determine the proportion of parents who would allow their children's NBS samples to be stored for some length of time and those who would not allow storage. For bivariate analyses, we conducted logistic regression analyses to examine associations between parent (age as continuous variable) and child characteristics with parents' refusal to store their children's NBS samples.

We also examined willingness to have a child's NBS blood sample used for research among parents who would not permit storage of the NBS blood sample.

All analyses were conducted with STATA 10 software (Stata Corporation, College Station, Tex.) using sample weights provided by the survey vendor to draw nationally representative inferences.

Results

We obtained a response rate of 49.5%. In total, 1,508 parents completed the survey while 1,539 parents failed to complete the fielded survey during the study window. Fifty-five parents who agreed to take the survey were unable to open the survey due to malfunction of the survey link; we did not include these individuals in the response rate calculation. Characteristics of respondents are presented in table 1. Non-respondents were more likely to be female, non-white, have a lower education, and a lower household income (data not shown).

Willingness to Permit Use of Newborn Screening Blood Samples for Research

If parental permission was obtained, most parents reported that they would be either 'very willing' (38.8%) or 'somewhat willing' (37.4%) to permit use of their children's newborn screening samples for future research studies. Meanwhile, 13.7% of parents were 'somewhat unwilling' and 10.1% were 'very unwilling' to permit use of samples. If parental permission was not obtained, substantially fewer parents reported that they would be either 'very willing' (11.3%) or 'somewhat willing' (16.9%) to permit use of the NBS sample for research. Moreover, over half of parents (55.7%) would be 'very unwilling' to

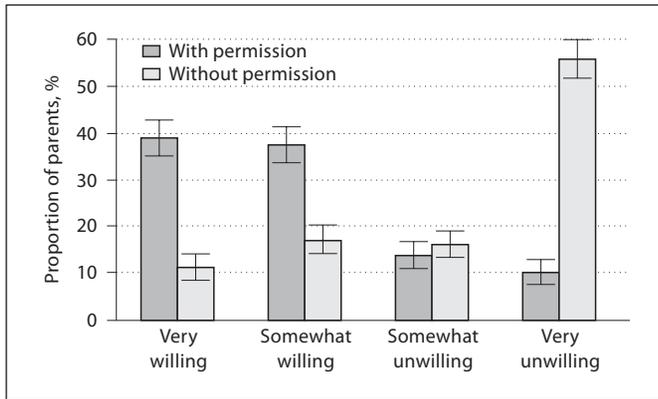


Fig. 2. Parents' willingness to have child(ren)'s newborn screening sample used for research with or without parental permission.

permit the use of their child's newborn screening sample for research purposes (fig. 2). We found no effect of question order on the distribution of parental responses about use of NBS blood samples for research ($p = 0.17$).

When we presented the scenario in which parental permission was obtained, parents who were 'somewhat unwilling' to permit use of their child(ren)'s newborn screening blood sample for research were more likely to be older (vs. very willing: OR: 1.03, 95% CI: 1.0–1.06; vs. somewhat willing: OR: 1.03, 95% CI: 1.0–1.06) and to report all their children to be in excellent or very good health (vs. very willing: OR: 2.1, 95% CI: 1.2–3.9; vs. somewhat willing [not significant]: OR: 1.8, 95% CI: 0.9–3.5).

There was no significant association between parent gender, race/ethnicity, education, household income, number of children, age of 1st child, or age of 2nd child with parents' report of being 'somewhat unwilling' to permit use of their children's NBS samples for research.

Willingness to Permit Storage of Newborn Screening Blood Samples

Of parents surveyed, 77.9% would permit their child(ren)'s NBS sample to be stored for at least some length of time, with 38.5% allowing the state to store the samples indefinitely.

Parents were more likely to prohibit storage of their children's NBS samples if they had a high school education or less (OR: 1.6, 95% CI: 1.07–2.5) or report all children who were in excellent or very good health (OR: 2.1, 95% CI: 1.3–3.6). There was no association between a parent's refusal to permit storage and parent's age, gender, self-reported race/ethnicity, household income, number of children, age of the 1st child, or age of the 2nd child.

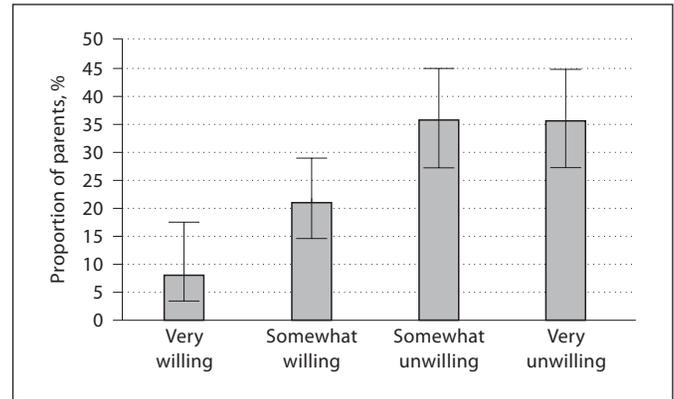


Fig. 3. Willingness to permit use of newborn screening sample for research among parents who oppose NBS sample storage.

Of note, proportionately more parents were more likely to refuse storage of the NBS sample as their willingness to permit use of the NBS sample for research decreased (fig. 3).

Discussion

In this survey of a nationally representative sample of parents, we found that over three-quarters of parents would be willing to permit the use of their children's NBS samples for research purposes if their permission was obtained prior to such use. However, if permission was not obtained prior to the use of these NBS samples for research purposes, more than half of parents would be 'very unwilling' to permit use of their child's sample. These findings indicate the importance of considering parental permission in future plans to use NBS samples for research purposes.

Even in cases in which parental permission is obtained, 14% of parents were 'somewhat unwilling' to permit the use of their children's NBS samples for research. There are a number of potential explanations for this unwillingness. It may be due to a lack of parental understanding about how these samples will be used for research. For example, these parents were more likely to have children in very good or excellent health, and so they may believe that use of NBS samples for research is unlikely to directly improve their children's health. In a previous survey of post-partum women's attitudes towards participation in a pediatric biobank, two-thirds of new mothers believed that the research would benefit their individual child [11]. Alternatively, parents may fail

to consider the potential for research to benefit the general health of children at a population level.

Parents' unwillingness to permit use of their children's NBS samples for research may also stem from a lack of trust in the state to safeguard private health information from these samples [11]. We did not ask parents directly about issues of trust or specific privacy concerns. However, the finding that parents who oppose NBS sample storage were also less willing to permit use of a NBS sample for research prompts us to wonder whether these parents are concerned about the state having any sustained access to their children's blood samples. If this is true, then structuring a system with privacy safeguards that are uniform across states and that meet standards for privacy in other sensitive arenas both within and outside of the healthcare system may help to alleviate such privacy concerns. The Danish Newborn Biobank has provided an example of NBS blood spot storage in which explicit detailed regulations and guidelines have been created to provide opportunities for research with NBS blood samples while simultaneously protecting individual rights [12].

Despite the fact that some states have been storing newborn screening samples since the start of the screening programs in the 1960s, there has been little examination of parents' attitudes about this storage, independent of their use for research purposes. While we found that the vast majority of parents were willing to permit the state to store their children's NBS samples, 22% of parents were not willing to permit storage of their children's NBS samples. Non-participation of this magnitude could create problems in using the NBS blood samples either for ongoing program evaluation (e.g., NBS candidate test validity studies) or for future research studies that rely on the population representation of this sample collection [4].

Our finding that parents who refused storage were more likely to have a lower education level and to have children in excellent or very good health suggests that parents may not understand the rationale behind storage of the NBS sample. Educational outreach programs that inform parents about the population-oriented goals of the NBS storage program may help alleviate any underlying concerns or confusion that make parents hesitant to permit storage. It is also important that, as we continue to explore public concerns about NBS sample storage, we engage the public in a transparent and informative discussion that also provides parents a forum in which to voice their concerns.

Our study has additional limitations that should be noted. The first set of limitations relate to the population

studied. As with any survey, there may have been a response bias. We attempted to evaluate this by comparing demographic characteristics between respondents and non-respondents. Given that non-respondents were more likely to have less education and that there was a direct relationship between education and support of NBS sample storage, we may have underestimated the proportion of parents who would be unwilling to permit NBS sample storage.

As we noted previously, the study population was randomly selected from a nationally representative Web-enabled panel. Some level of participation bias may result from a person's desire to participate when initially contacted by panel management through random-digit-dialing methods. However, since participants enrolled in the panel without knowledge of the content of surveys, we believe that it is unlikely that participation bias affected our results in a meaningful way. Moreover, surveys using nationally representative Web-enabled panels have been used to explore important population-based health questions on a wide range of topics [13–15].

In addition, participants in our survey are not actually providing permission for the use of a newborn screening sample for research purposes; so in this sense, our survey questions are hypothetical. We recognize the importance of assessing attitudes of parents who are faced with the decision about whether or not to allow the use of their child's sample for research. However, in this survey, the participants are parents and therefore assume the responsibility of making decisions for their child's participation in research. Second, the children of these parents may have blood spots already in storage in their state. For these parents consideration of the use of their children's blood spots for research purposes is not entirely hypothetical.

The other set of study limitations relate to the concepts presented in the survey instrument. First, we acknowledge that parents can operationalize the concept of 'permission' in a number of ways. The issue of the flexibility of informed consent is one that is being actively debated with regard to the addition of new tests onto state newborn screening panels [16]. We are not assuming that parents expect or require a formal informed consent process prior to the use of newborn blood spots for any research. In fact, it is quite possible that some parents may prefer a more general means of being informed that NBS samples will be used for research purposes (e.g., through brochures or a public health campaign) or that consent can be waived in certain circumstances. While the structure of the consent process is beyond the scope of this paper, both parental attitudes and formal human subjects pro-

tection regulations need to be considered when assessing issues of consent or parental permission in the future.

In addition, parents' opinions about the use of NBS samples for research may be influenced by a state's research protocol on the identifiability of specimens. For example, parents may be willing to forego a formal permission process if the research were to involve de-identified samples. On the contrary, other parents would be more willing to permit use of the NBS sample for research if the studies had a direct health benefit for their children. These salient issues are beyond the scope of this study but are ones which we will examine as part of a larger national survey.

Finally, some may be concerned that parents were alarmed by our use of the term DNA in our survey instrument (e.g. 'the DNA from these blood samples can be used for future research studies') and from our generic use of the term research. However, the potential research uses of the DNA from these samples is openly acknowledged and discussed among researchers in this field [6, 17, 18]. We would also like to highlight that despite the use of both 'DNA' and 'research', over three-quarters of parents still expressed some degree of willingness to permit the use of their child's NBS blood sample for research.

While we recognize these study limitations, we believe that our study represents an important first step in understanding, on a national level, parents' attitudes towards the storage and use of NBS samples for research. Addressing parental concerns is critical from both a public policy and a public health standpoint. NBS samples represent a public health resource that has the potential to provide meaningful information about the health of children as well as the larger population. However, precisely because NBS samples are a public health resource, we also have the responsibility of engaging the public in discussions about policies and procedures for their use.

Acknowledgements

This research was conducted as part of the C.S. Mott Children's Hospital National Poll on Children's Health (<http://www.med.umich.edu/mott/npch>). The project was funded by the Clinical Science Scholars Program at the University of Michigan (B.A.T.). The funder had no role in any of the following: the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript. There are no conflicts of interests for any of the authors.

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