VIEWPOINT

Parental Consent for the Use of Residual Newborn Screening Bloodspots

Respecting Individual Liberty vs Ensuring Public Health

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On December 18, 2014, the Newborn Screening Saves Lives Reauthorization Act of 2014 was signed into law, renewing federal funding for the state-run newborn screening programs[1] that have proven to be extraordinarily effective at saving children from lifelong disability.[2] The bill included a last-minute amendment, however, that has generated immense concern among state newborn screening program officials and biomedical researchers. The amendment, which remains in effect until an updated Common Rule is released, stipulates that research on deidentified newborn dried bloodspots must be classified as research involving human subjects, thus requiring explicit parental informed consent. Public health officials' major concern is that requiring explicit consent from parents may reduce the number of samples available for research and could even negatively affect newborn screening participation overall.[3]

This shift represents a significant departure from long-standing practice; dried bloodspots research has traditionally been outside of the human subjects research regulations. The Common Rule currently defines *human subjects research* as activities in which either the research investigator obtains samples through direct interaction with living individuals or the samples are linked to individually identifiable private information. Dried bloodspots are deidentified before use by researchers, which is why research on dried bloodspots was interpreted not to be human subjects research until this new law. In this Viewpoint, we explore the implications of the law's approach, highlighting the effects of requiring explicit informed consent for dried bloodspots research.

Emerging Public Concern About Dried Bloodspots Research

Given emerging views, it is not surprising that this change was introduced. Recently, advocates have demanded that parents be asked to give permission for storage and research use of their child's dried bloodspots. Research on parental opinions about the use of dried bloodspots for research also supports the conclusion that most parents want to be asked before dried bloodspots are used in research[4] and support an opt-in process for obtaining consent over the current opt-out approach, which presumes consent unless parents actively choose otherwise.[5]

Furthermore, 2 cases brought against the departments of health in Texas in 2009 and Minnesota in 2011 exemplify increasing concern over retaining and using dried bloodspots for research without parental consent. In Texas, the Western District Court preliminarily held that it is plausible to argue that storing and using residual dried bloodspots without parental consent constitutes a violation of Fourteenth Amendment liberty and privacy rights. The case was ultimately settled, resulting in the destruction of 5.3 million dried bloodspots samples in February 2011. In Minnesota, the state supreme court held that because dried bloodspots contain genetic information, state laws pertaining to retention and use of genetic materials applied. In November 2014, Minnesota completed the destruction of all newborn screening samples collected before November 16, 2011. These cases suggest that there is a basis for legal challenges to the use of dried bloodspots without parental permission, which could undermine, or potentially improve, public trust that undergirds the almost universal participation in newborn screening.

A Threat to the Public's Health

At a meeting in late March, the Secretary's Advisory Committee on Human Research Protections, which advises the US Secretary of Health and Human Services, discussed a number of issues related to the Newborn Screening Saves Lives Act. First, the committee noted that the definition of what constitutes research on dried bloodspots remains unclear. In particular, *research* broadly construed could include any activity from laboratory quality assurance to program evaluation and public health practice, which would not be considered research under the current Common Rule.[6] The committee was also concerned that obtaining and documenting consent for each research project would be a significant burden that could seriously hinder research. But sensitive to the need for respecting parental preferences, the committee recommended a simplified consent process involving the use of one-time broad consent and pointed out that institutional review boards may grant waivers of consent documentation for dried bloodspot research.

Even if a simplified parental consent process were implemented, there remain concerns that requiring explicit parental permission will reduce the number of available samples for research. Michigan's BioTrust for Health provides a model for whether requiring informed consent will likely precipitate the consequences anticipated by public health officials. As of April 30, 2010, Michigan implemented an opt-in process for obtaining parental consent for dried

bloodspots research. (A separate opt-out process is still in place for clinical newborn screening.) After the birth of their child, parents are asked if they want their child's residual bloodspots to be stored indefinitely and made available for future medical research. Parents are provided with a brochure that outlines the steps taken by the BioTrust to ensure the confidentiality of the sample, the ability of parents to withdraw their child's sample at any time, and examples of research uses. Parents are then given a consent card that allows them to select "Yes, my baby's bloodspot may be used for health research" or "No, my baby's bloodspot may not be used for health research." According to the most recent available data, the Michigan program screened 99.5% of the live births occurring in Michigan in 2013, indicating that the opt-in process has not caused an increased number of parental refusals for clinical newborn screening. However, parental consent for research use of dried bloodspots through the BioTrust was obtained from only 60% of parents.[7] Thus although surveys have predicted that as many as 78% of parents would, if asked, consent to retention and research use of dried bloodspots, fewer parents in Michigan have in fact consented through the state's opt-in process. Concerns that the number of samples available for research involving dried bloodspots will be significantly reduced if an opt-in consent process is implemented therefore appear to be well-founded.

Recurring Tension Between Public Health and Individual Liberty

The issue over whether and how to obtain parental consent for health research on residual dried bloodspots represents a tension between respecting individual liberties and ensuring public health. From a privacy perspective, there are justifiable concerns about researchers' ability to irreversibly deidentify data containing genetic information. Although the likelihood of samples being reidentified is remote, the risk of reidentification has led to a reexamination of previous assumptions about when explicit research consent should be required. Notably, one of the proposed major changes to the Common Rule is to require consent for all biospecimen research.

From a public health perspective, state dried bloodspots repositories are extremely valuable resources for biomedical research that are free of selection bias. Public health research using stored samples has contributed to important advances such as diagnosing childhood leukemia; testing mercury levels in bloodspots to determine if pregnant mothers are eating safe amounts of fish; and, depending on how *research* is defined, improving newborn screening methods and developing additional screening tests. Population-level dried bloodspot research is particularly important for the health of those with rare diseases, because data from many patients are needed to generate sufficient samples sizes to conduct rare-disease research. Autonomy is a vital principle of medical and research ethics, but the benefits of public health research on dried bloodspots should be weighed against parental desire for the opportunity to consent to dried bloodspot research.

There are good reasons to be cautious about abandoning the current opt-out approach to obtaining consent. First, an opt-out system continues to allow parents a choice in whether to include their child's dried bloodspot in a research database, particularly if coupled with robust efforts to educate parents on deidentification of samples, the kinds of research conducted, and the option to opt out. Second, changing the current legal status quo on when to require consent for human tissues research requires more deliberation. A broader conversation is needed about changing consent norms in an era of genomic medicine, and it is not appropriate to single out dried bloodspot research. Third, while Michigan provides one model of an opt-in system, it is still possible that other states could implement systems that reduce participation in newborn screening or result in even lower consent rates. Finally, Michigan's example demonstrates that requiring explicit consent will most likely reduce dried bloodspot samples available for research population level, which could hinder public health research. Ultimately, the importance of biomedical research for public health purposes is too great, particularly for those with rare disease, to risk seriously adversely affecting the number of samples available for research.

ARTICLE INFORMATION

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