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Parents seen as critical stakeholders in expanding newborn screening

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Parents must be considered when states decide to expand genetic screening programs for newborns, according to a new study that looked at mandatory testing panels and political pressure by advocacy groups.

Nearly all infants in the United States undergo a heel prick within days of birth for a simple blood test to detect rare genetic disorders. For decades, state-based mandatory newborn screening programs have focused on disorders such as phenylketonuria (PKU) or hypothyroidism in which a prompt diagnosis and treatment could prevent disability or even death.

In recent years, advocacy groups have been pushing to expand newborn screening to include lysosomal storage diseases (LSDs), a group of rare metabolic disorders, despite the lack of consensus on which children should be treated or the effectiveness of available therapies. With the high degree of uncertainty around LSDs, many medical ethicists as well as some genetic health professionals and public health officials are questioning the clinical value and the morality of screening mandates.

In an article published by The Journal of Pediatrics, researchers from the University of Chicago Medicine argue that parents should be critical stakeholders in the expansion of newborn screening. Despite federal recommendations against the addition of these conditions, LSDs have been tacked on to the screening panels in several states and strong lobby efforts are under way across the nation with little or no consideration for parental consent or even notification.

"A problem with incorporating LSD screening into state screening programs is the 'all-or-nothing' constraint," said co-author Lainie Friedman Ross, MD, PhD, professor of pediatrics, medicine and surgery, and assistant director of the MacLean Center for Clinical Medical Ethics at the University of Chicago. "Parents cannot say that they want their child to be tested for some conditions and not others. There is simply not enough available information on many LSDs to justify overriding the ethical standard of parental informed consent."

The push for more widespread screening for once little-known diseases is largely the result of impassioned campaigns led by parents of children affected by these conditions. Among the most notable advocates is former Buffalo Bills quarterback Jim Kelly, whose son died of complications from Krabbe disease, a rare genetic disorder of the nervous system. In 2006, Kelly successfully lobbied the New York State Department of Health for the inclusion of Krabbe disease in its mandatory newborn screening program. Since then Missouri and New Mexico have passed legislation to screen for a broader array of LSDs.

Similarly, in Illinois, seven LSDs have been mandated to the newborn screening program due to the efforts of the Evanosky Foundation, formed by parents of three children diagnosed with metachromatic leukodystrophy (MLD).

Ross says that while such stories are heartbreaking, this trend is worrisome because arguments from parent advocacy groups tend to be based on anecdotal experience rather than scientific, peer-reviewed evidence — and they represent only one side of the coin.

"There are many parents whose voices are not being heard: parents who have experienced the distress of a false positive or who have children identified with conditions that may not present until adulthood, if ever," Ross said. "There are also parent advocacy groups around the country

worried that their children's blood spots are being used for research without their permission, even without their awareness."

Another concern for ethicists is the funding advocacy groups often receive from pharmaceutical companies that have a vested interest in the promotion of treatments for the disorders the group represents. Studies have confirmed that many of these groups fail to disclose conflicts of interest on their websites, promotional brochures and lobbying activities.

Ross and co-author Darrel Waggoner, MD, associate professor of human genetics and pediatrics and medical director of human genetics at the University of Chicago Medicine, join a chorus of experts calling for expansion of newborn screenings to be initially conducted within research protocols, including oversight from a human-subject protection committee known as an institutional review board (IRB).

"By placing such conditions under an IRB protocol, it acknowledges that there is much still to be learned," Waggoner said. "It acknowledges that we need parents to be co-adventurers. It also means that additional reviews will be necessary before these conditions become entrenched in mandatory newborn screening programs."

Watchers of New York's adoption of Krabbe disease screening are closely tracking the outcomes. In the state's first four years of testing for LSD, hundreds of children were called back for further testing. Of those, 29 tested positive for Krabbe and only four were diagnosed with the infant-onset form of the disease. Another 25 children were classified as moderate to high risk for developing a later onset form of the disease, but none has developed any symptoms. New York does not follow the psychological impact on parents of these "patients in waiting."

"What we've learned from New York's Krabbe screening program is how incompletely we understand the natural history of the disease and

that late onset of symptoms is likely to be more common than previously diagnosed clinically," Ross said.

LSD screening pilots in Taiwan and Italy, both of which employed research protocols including parental consent and IRB review, have provided key insights. One of the most fundamental findings, say the researchers, is that when given an option, more than 98 percent of parents elected to move forward with testing.

The observation helps strengthen the case for a proposed two-tiered screening program in Illinois. The first tier could include mandatory screening for conditions with established therapies and consensus on when treatment is necessary. A second tier, designated to less understood diseases, could be offered under a research protocol with active parental consent. This model was adopted by the Massachusetts Department of Public Health with the expansion of its newborn screening program in the 1990s.

Waggoner and Ross acknowledge that large-scale screening initiatives are needed to uncover the many unknowns regarding LSDs, yet they strongly oppose policies that allow research studies to operate under the guise of public health programs.

"The development of enzyme replacement and other innovative therapies for many LSDs is exciting and motivate the pursuit of IRB-approved research on populations that may benefit from early identification and treatment," Ross said. "But infants are vulnerable and need their guardians to determine whether participation is in their best interest. Let's give voice to all parents by requiring their permission for the enrollment of their children in experimental newborn screening protocols."

More information: The article, "Parents: Critical Stakeholders in

Expanding Newborn Screening," has been published by *The Journal of Pediatrics*, DOI 10.1016/j.jpeds.2012.04.035