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New study raises questions about genetic testing of newborns

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Mandatory genetic screening of newborns for rare diseases is creating unexpected upheaval for families whose infants test positive for risk factors but show no immediate signs of the diseases, a new UCLA study warns.

"Although newborn screening undoubtedly saves lives, some families are thrown on a journey of great uncertainty," said UCLA sociology professor Stefan Timmermans, the study's lead author. "Rather than providing clear-cut diagnoses, screening of an entire population has created ambiguity about whether infants truly have a disease — and even what the disease is."

The study, which appears in the December issue of the *Journal of Health and Social Behavior*, describes these families as "the collateral damage of newborn screening," an unanticipated consequence of the expansion of mandatory screening for a wide range of conditions in 2005.

"Basically you're telling families of a newborn, 'Congratulations, but your child may have a rare genetic condition. We just don't know, and we don't know when we'll know,'" Timmermans said.

Conducted with Mara Buchbinder, who earned a doctorate in anthropology at UCLA and is now an assistant professor of social medicine at the University of North Carolina–Chapel Hill, the study paints a picture of families caught in limbo as they wait months for conclusive evidence that their children are out of the woods for

conditions that have been associated with schizophrenia, mental retardation, heart and lung disease, coma and sudden death.

In many cases, the medical results never come; the children slowly age out of having risk factors for up to 29 metabolic, endocrine or hemoglobin conditions. But by that time, some families are so traumatized that they follow unwarranted and complicated regimens for years afterward, including waking their children up in the middle of the night, enforcing restrictive diets and limiting contact with other people. "Years after everything appears to be fine, parents are still very worried," Timmermans said.

For three years, Timmermans and Buchbinder followed 75 California families whose newborns received screenings that sent up red flags for diseases characterized by an inability to digest food containing fat, proteins or sugars. Of the total, 40 of the infants became what the researchers describe as "patients-in-waiting" — children who have not developed symptoms but whose genetic tests raise flags.

"The parents don't know whether their child is a false positive or they're a true positive," Timmermans said.

In one particularly poignant case of a patient-in-waiting, a father refused to allow anyone but the infant's mother to care in any way for the boy, fearing contamination that might aggravate his potential condition. More than a year after the baby's birth, the mother had not been apart from the baby. Her dream, she confessed to the researchers, was to be able one day to go on a date with her husband.

Parents of another patient-in-waiting were afraid to pursue an out-of-state job opportunity because they were uncertain about the quality of medical care that would be available for their child with potential medium-chain acyl-coenzyme A dehydrogenase deficiency (MCADD), a

condition that prevents babies from being able to turn fat into energy. Without treatment, MCADD babies can experience seizures, extreme sleepiness or comas, and even die. And several parents decided either to give up a job or not return to a job in the hopes of keeping a closer eye on their children in case symptoms of the rare diseases did eventually surface.

"When the test results ultimately suggest the risk is nothing or not as significant as with patients who are symptomatic, the physicians are ready to let go of preventative measures," Timmermans said. "But the parents are reluctant to give them up because they come to believe that they're keeping their child disease-free. Over and over again, we saw parents and doctors at odds."

The genetic testing of newborns dates back four decades, when the approach showed promise in identifying phenylketonuria (PKU), a genetic disorder characterized by the body's inability to utilize an essential amino acid, phenylalanine. The disorder causes a build-up of phenylalanine in the blood, which can result in mental retardation, brain damage, seizures and other problems. But if PKU sufferers are identified early enough, they can avoid these problems through diet and medication.

The advent of new screening technologies in the late 1990s vastly increased the number of potential diseases that could be detected with a blood sample easily obtained by pricking the heel of a newborn. Genetic testing of newborns got another shot in the arm in 2005 when the American College of Medical Genetics called for mandatory screening of 29 conditions and 24 sub-conditions. By 2009, all 50 U.S. states and the District of Columbia screened for at least 21 of the 29 recommended conditions, and the full recommendations had been adopted by 44 states, including California.

Other countries have since adopted genetic screening, but they test for fewer conditions and add new conditions more slowly than the U.S. The study findings cast doubt on the medical efficacy of the battery of screenings administered widely in America, the researchers said.

"Expanded newborn screening has called into question whether screening targets correspond to actual diseases or just benign forms of human variation," Buchbinder said.

"There are many more positive screenings than were anticipated based on the incidence of the diseases in the general population," Timmermans added.

Nobody knows the number of families who fall into the patient-in-waiting category, but it is assumed to be a relatively small number. Still, the number is much larger than was anticipated when screening for a wide range of conditions began in 2005, the study argues.

The researchers also suggest the need for increasing the speed with which follow-up tests are administered so that parents of patients-in-waiting spend less time wringing their hands.

"When the American College of Medical Genetics advocated for the expansion of newborn screening, they argued that the societal benefit of newborn screening would be the avoidance of diagnostic odysseys in which parents of kids with rare diseases travel from doctor to doctor in an attempt to find out what is wrong with them," Timmermans said. "Our study shows that, in fact, the expansion of newborn screening has created a new population on diagnostic odysseys — the parents of these patients-in-waiting. Now we need to figure out how to dramatically shorten or eliminate this unexpected and stressful journey."