Genetic testing could save babies' lives — if insurance actually pays for it

By Ariane Lange
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Rapid whole-genome sequencing as a first-line test can save babies' lives and reduce health care costs by thousands of dollars per patient, a paper published Friday says.

"It saves money, and it saves kids lives, and it improves outcomes, and it makes parents happier and docs happier," said David Dimmock, senior medical director of Rady Children's Institute for Genomic Medicine and the lead author of the *American Journal of Human Genetics* paper. "It's something which is a win all-round."

The pilot project was ordered by the California legislature to evaluate possible implementation of the sequencing statewide; a bill is currently under consideration. The researchers looked at acutely ill babies less than 1 year old admitted to five regional intensive care units throughout the state; the babies' symptoms had unclear causes and thus might have been due to a genetic abnormality. Every baby in the study was insured by Medi-Cal, the state's Medicaid program. The 184 infants were admitted between November 2018 and May 2020, and providers synthesized their genomes either within one week of their

stay in the ICU or shortly after they developed an adverse response to their current treatment.

The intervention was remarkably effective: Of the 184 babies enrolled, 74 received a diagnosis of a rare genetic disease that explained their illness in a median of three days; doctors changed the medical care of 58 babies based on the results of the test.

Although the cost of testing was $1.7 million overall, the changes in care led to savings of $2.2 million to $2.9 million, mostly through reduced hospital stays. The cost of rapid whole-genome sequencing and precision medicine was $9,492 per baby; conservatively, it saved $12,041 to $15,786 per baby, on average.

However, Dimmock is concerned that the bill making its way through the California legislature is not strong enough to actually ensure that hospitals get paid.

"It's one thing having an insurance company say they're going to cover testing," he said. "It is another thing for the nuts and bolts of this to happen, such that the hospitals get reimbursed for the testing, even though it's covered." As of early June, legislators had removed the section of the bill that specified a payment structure.

The paper was focused on one state, but the findings have widespread relevance. Each year, 4 million infants are born in the U.S., and around 7% to 10% of them will be admitted to a neonatal intensive care unit because of an acute illness. Some studies have shown that significant

minorities of babies admitted to high acuity units have genetic disorders and malformations.

Although the testing saved money, "The nonmonetary benefits clearly hugely, hugely outweigh the monetary benefits," Dimmock said. One child, he recalled, was brought to the hospital with multiple bone fractures, and doctors, as mandated reporters, called child protective services, who removed the critically ill infant from the parents' custody.

"We did rapid testing on this child and diagnosed the child with a genetic disorder that leads to bone fractures with minimal to no trauma," Dimmock said. "The child was returned to the family. Unfortunately, the condition is not compatible with long-term life, and the child passed a couple of months after we made the diagnosis, but those couple of months were spent at home, with parents, with the parents getting to enjoy their child and not worrying about fighting with CPS, the courts or anyone else about child abuse. ... Not something you could say that this saved any money, or this changed the child's outcome. It just dramatically changed the experience of care for the family."

It also, according to the supplemental case reports, did save money: Doctors estimated that it would have taken a week to get alternative test results coming to the same conclusion about the child's condition, so the baby spent seven fewer days in the hospital.

There was no "control" group of untreated babies — notably, many of these children had incredibly rare problems — so researchers estimated the cost savings of the treatment through a three-part expert elicitation process. First, the doctors who cared for the children would fill out a report explaining how they would have treated the child, what tests or surgeries they would have ordered and how long it would have taken to get results in the absence of the genome sequencing; then, a panel at the hospital would evaluate the reports and make their own determination; then, Dimmock and co-author Lauge Farnaes, also at Rady Children's Institute for Genomic Medicine, would review these reports and make their own determination.

"The thing that was expected to have the least benefit to the child and the least favorable economic profile of those three was the one that was selected for what would have happened," Dimmock said. "We probably hugely underestimated both the clinical benefit and the economic benefit of doing the testing. But we felt like we really wanted to be in a place where I could go to Sacramento and swear in front of the committee that this was the absolute minimum benefit that we would see."

If anything, the potential savings were likely much larger, because doctors, with a limited number of tests, appeared to save the tests for the babies they believed were more likely to have a genetic abnormality. Some rarer babies who had a totally unsuspected abnormality likely slipped through the cracks, Dimmock said.

"If you make a diagnosis in a kid that nobody suspects has a genetic disorder, that actually has a much bigger impact on the way we care for that child than if you were just refining what you already suspect a child has," Dimmock said.

Of the 58 children whose medical care changed, 27 altered care plans had no substantial effect on cost. There were 30 babies whose length of stay changed, and somewhere between 457 and 592 collective ICU days were avoided. The researchers estimated that 89% to 93% of cost savings came from shorter hospital stays.

Dimmock said that even no diagnosis could have a positive impact on a family. The analysis ruled out genetic issues for multiple children enrolled, and both parents and doctors could move forward with better information. He mentioned one baby in particular, who was admitted with seizures that weren't responding to typical treatments. The baby's doctor ordered genome sequencing, but the pattern looked familiar to Dimmock, and he and his colleagues were "very, very excited" for testing, thinking the results would likely make "a dramatic difference." When they found nothing that would make a difference, they were crestfallen.

But, he continued, the family had been in anguish over their decision: They hated the baby's current quality of life, but they didn't want to miss an opportunity for some kind of treatment or cure. Once they had the results of the genome sequencing, "it made a huge difference to the

family in feeling comfortable that the right decision for their child was actually to stop the aggressive care," he said. "Hugely powerful for the family, not making a diagnosis."

The paper, "Project Baby Bear: Rapid precision care incorporating rWGS in 5 California children's hospitals demonstrates improved clinical outcomes and reduced costs of care," published June 4 in the American Journal of Human Genetics, was authored by David Dimmock, Sara Caylor, Bryce Waldman, Wendy Benson, Shimul Chowdhury, Katarzyna Ellsworth, Charlotte Hobbs, Stephen F. Kingsmore, Kristen Wigby and Lauge Farnaes, Rady Children's Institute for Genomic Medicine; Christina Ashburner, Jason L. Carmichael, Carolina I. Galarreta, Maries Joseph, Aaina Kochhar, Jolie Limon, Rosanna Spicer and Mario Augusto Rojas, Valley Children's Hospital; Jeanne Carroll and A. Doshi, Rady Children's Institute for Genomic Medicine and University of California, San Diego; Elaine Cham, Arthur D'Harlingue, Kathleen Houtchens and Priscilla Joe, University of California, San Francisco, Benioff Children's Hospital Oakland; John Cleary, Juliette Hunt, Jason Knight, Adam Schwarz, Ofelia Vargas-Shiraishi and Neda Zadeh, Children's Hospital of Orange County; Robert H. Kaplan, Torrey Pines Health Group Inc.; Richard G. Kronick, Torrey Pines Health Group Inc. and University of California, San Diego; and Madelena Martin, Katherine A. Rauen and Suma P. Shankar, University of California, Davis, and Davis Children's Hospital.