



BabySeq Project Unearths Actionable Genetic Variants Impacting Infants, Parents

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NEW YORK – The latest results from the [BabySeq project](#) suggest that unexpected, medically actionable variants in monogenic disease genes found by newborn genome screening can have clinical implications for both infants and their family members.

"By screening apparently healthy newborns, entire families were alerted for the first time that dangerous but treatable genetic variants were present," study leader Robert Green, a physician and researcher affiliated with Mass General Brigham, Brigham and Women's Hospital, the Broad Institute, Ariadne Labs, and Harvard Medical School, said in a statement.

As they [reported](#) in the *American Journal of Human Genetics* on Monday, he and his colleagues from the BabySeq project team started with 159 infants who underwent comprehensive exome sequencing for a previous clinical trial, including 32 infants being treated in an intensive care unit and 127 seemingly healthy infants. Within that group, they picked up inherited unanticipated monogenic disease risk (uMDR) variants — including pathogenic or likely pathogenic variants classified as moderately or highly clinically actionable — in 17 babies, or nearly 10.7 percent of those tested.

"[T]hese early data on medical utilization from the BabySeq project suggest that over 10 percent of infants may carry unanticipated monogenic risks for actionable conditions that over [three to five] years will result in important medical consequences for those infants and their families," the authors reported.

The pathogenic or likely pathogenic variants turned up in 13 genes, the team noted, and included variants implicated in Lynch syndrome, breast and ovarian cancer, dilated cardiomyopathy, and other actionable adult-onset or childhood-onset conditions.

While the detected alterations helped explain known clinical phenotypes in three of the cases, the researchers wrote, the remaining 14 uMDR variants informed disease surveillance for the affected infants as they age. In at least one case, a suspicious heart disease-related uMDR variant encouraged clinical testing that uncovered a high-risk aortic narrowing in one of the seemingly healthy infants.

"The results of this study indicate that conducting thorough genetic sequencing of newborns has the potential to significantly improve health outcomes for infants and their families," coauthor Alan Beggs, BabySeq co-leader and director of Boston Children's Hospital's Manton Center for Orphan Disease Research, said in a statement.

When the team dug into follow-up data collected on the infants and their family members in the three to five years after the results were first disclosed, meanwhile, it found that the exome sequencing-based insights led to additional screening in family members of 13 of the uMDR variant-affected infants. As a result of that screening, three mothers of at-risk babies underwent prophylactic risk-reducing surgeries to dial down their own cancer risk.

"We were stunned to see that with no specific guidance from the study, newborn sequencing prompted lifesaving actions among several mothers," Green said.

He and his coauthors noted that "assessments of clinical utility and cost-effectiveness will require larger datasets." Even so, they argued that the results so far "suggest that large-scale comprehensive [DNA] sequencing of newborns will reveal numerous actionable uMDRs and precipitate substantial, and in some cases lifesaving, downstream medical care in newborns."

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