Researchers assess impact of exome sequencing on newborns and their families

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Early results from the BabySeq Project, a Boston-based study exploring the impact of whole-exome sequencing (WES) on newborn infants and their families, suggest some utility in genetically sequencing these infants and offer new insights into parental attitudes toward the procedure and results. Findings were presented at the American Society of Human Genetics (ASHG) 2016 Annual Meeting in Vancouver, B.C.

Led by Robert C. Green, MD, MPH, of Brigham and Women's Hospital, Harvard Medical School, and the Broad Institute; and Alan H. Beggs, PhD, of the Manton Center for Orphan Disease Research at Boston Children's Hospital and Harvard Medical School; the project has recruited more than 100 families to date. Infants are enrolled from the neonatal intensive care units at Boston Children's Hospital and Brigham and Women's Hospital as well as the well-baby nursery at Brigham and Women's Hospital. Half of each group is randomized to receive WES - genetic sequencing of all protein-coding genes, with analysis of about 1,800 genes implicated in childhood health - and follow-up counseling. Data are collected from participating families at enrollment, when receiving their sequencing results, three months after sequencing, and ten months after sequencing.

"This is the first randomized trial to sequence healthy infants with interpretation and return of the information," Dr. Green said. "We faced enormous early challenges in creating processes for informed consent, accurate sequencing and interpretation, choosing which genes to report, clearly reporting results to families and their providers, and measuring

potential benefits and harms."

"Having created these processes, we are now collecting data from medical record reviews and parental surveys, in order to measure medical benefits, harms, and costs, as well as parents' understanding of genetic sequencing, their attitudes and anxieties about it, and any actions they may have taken based on the results," said Shawn Fayer, MSc, MS, Project Manager of the BabySeq Project.

So far, the researchers have identified potentially harmful variants in two healthy infants who were sequenced - variants that would not have been detected otherwise - suggesting some value in sequencing infants with no family history of genetic disease. It is not yet known how this knowledge will affect the families' medical actions or the infants' eventual health outcomes.

In some cases, challenges during the recruitment process led to unexpected insights. Before enrolling, parents had the opportunity to meet with a genetic counselor to discuss the study. Those who declined to participate after learning about the study expressed concerns about receiving unfavorable or uncertain results, insurance discrimination, and confidentiality and privacy. These findings reflect current societal attitudes about genetic testing, which are likely to affect its clinical implementation.

In the coming months, the researchers hope to enroll several hundred additional infants and families. In addition to measuring parental attitudes about sequencing newborns, they plan to assess the usefulness of WES information over time, including how it is used in later medical decisionmaking.

"This is the first rigorously designed study to examine the often-cited vision that humans will benefit from having genomic information from

the very first days of life," said Dr. Green. "While it will take many years of follow-up to determine the ultimate benefits and harms, we are already learning a tremendous amount about creating the process for returning genomic information in newborns, parental hopes and concerns, and the kinds of results that are emerging."

More information: Presentation: Dr. Green will present his research on Wednesday, October 19, 2016, from 9:45-10:00 a.m., in Room 109 of the Vancouver Convention Centre.

Provided by American Society of Human Genetics