Dec. 1, 2021 -- Even before their baby is born, parents face some tough questions: Home birth or hospital? Cloth or disposable **diapers**? Breast, bottle, or both? But advances in genetic sequencing technology mean that parents will soon face yet another choice: whether to sequence their newborn's DNA for an overview of the baby's entire genome.

Genetic testing has been used for decades to diagnose conditions even before birth. But DNA sequencing technologies, once expensive and tough to access, are now rapid and cheap enough that doctors could order genomic screening for any **infant**, regardless of health status.

The possibility has raised many questions about the ethical, legal, and social repercussions of doing so. One of the biggest sticking points of sequencing newborns is the potential psychosocial fallout for families of such wide-scale use of genetic screening.

"There's a narrative of catastrophic

distress," says Robert Green, MD, a geneticist at Harvard Medical School and lead investigator on the **BabySeq study**, which is evaluating the medical, social, and economic consequences of **newborn** genetic screening. The concern is that parents learning that their child carries a gene variant related to cancer or heart disease will become "incredibly anxious and distressed," he says. "And it's not an unreasonable speculation."

But Green's team found no evidence of such **anxiety** in the results from a randomized trial it conducted, **published in *JAMA Pediatrics***. In the meantime, Genomics England announced it would begin a pilot study involving **whole-genome sequencing of up to 200,000 babies**. The first goal is to identify severe disease that starts in childhood, but the information would also be stored and used to detect drug sensitivities and conditions that come up later in life.

The large U.K. project is a bold move, according to David Amor, PhD, a pediatric geneticist at Murdoch Children's Research Institute in Australia, who says its time has

come. Geneticists have been accused of thinking their field involves unique pitfalls, compared with the rest of medicine, he points out, and that doctors need to protect patients and families from the potential harm **genetic testing** poses.

“But it is becoming apparent that that’s not really the case,” he says, and “maybe there’s not a whole lot special about genetics -- it’s just medicine.”

When a first-draft copy of the human genome was published in 2001, scientists and doctors hailed the start of a new era of precision medicine. Knowing our genome sequence was expected to lead to a better grasp on our individual disease risks. Yet even as technologies advanced, clinical genetics remained focused on diagnosis rather than screening, according to Lilian Downie, a clinical genetics PhD candidate at the University of Melbourne in Australia. She calls the difference subtle but important.

Diagnostic genetic testing confirms whether a person has a specific condition, whereas genetic screening tests evaluate someone’s risk of getting an illness. Both

approaches use sequencing, but they answer different questions, explains Downie.

Diagnosing Disease vs. Predicting Future Illness

Genetic testing is on the upswing for both purposes, whether clinically for diagnosis or through direct-to-consumer screening-oriented services like 23andMe. Scientists began to note that many people carried disease-related genetic variants without having signs of disease. In some cases, a variant that is mathematically linked to a disease simply doesn't cause it. In other cases, though, even if the gene variant contributes to a disease, not everyone who carries the genetic change will get the condition.

This potential disconnect between having a variant and developing the condition is a big problem, says Katie Stoll, a genetic counselor and executive director of the Genetic Support Foundation in Olympia, WA.

"It's more complicated than just looking at one gene variant and one outcome," she

says. Without a sure link between the two, this information could unnecessarily entail "some pretty big emotional and financial costs."

Stoll and others in the genetics field who share similar concerns are one reason the BabySeq project was first funded back in 2015. Although the overall aim of the initiative is to answer questions about the value of genomic sequencing in newborn screening, the media and scientific attention has focused on the psychosocial impact of healthy newborn sequencing, says Green. In the study published in *JAMA Pediatrics*, his group focused on these issues, too.

For that randomized trial, they enrolled 325 families, 257 with healthy babies and 68 whose babies had spent time in neonatal intensive care. Enrolled infants were randomly given standard care alone or standard care with genomic sequencing added on. The genomic sequencing report contained information about the presence of genetic variants associated with disease that start in childhood. Parents also could choose whether to learn about genetic risks

for conditions that start in adulthood, such as cancer.

Boston-based Tina Moniz was one of those parents. When her first daughter was born in January 2016, someone from the BabySeq study asked her and her husband if they would like to take part. The decision was simple for the couple.

“I didn’t hesitate,” she says. “To me, knowledge is power.”

Using screening tools for parental and marital distress and parent-child bonding, the research evaluated BabySeq families at 3 and 10 months after parents received the sequencing results. The investigators found no significant differences in any of these measures between screened and unscreened families. Moniz learned that her daughter’s only concerning result was being a carrier for **cystic fibrosis**. Rather than finding this information anxiety-provoking, Moniz considered it to be reassuring.

“My mom brain worries about so many things, but at least I know I don’t have to add genetic disease to the list,” she says.

But Stoll, who wasn’t involved in the

BabySeq study, isn't as convinced. She says that less than 10% of the families approached about the trial ultimately agreed to take part, suggesting potential bias in the selection process. Most participants were white, well-educated, and well-off, making it hard to generalize the study's results.

What's more, the standard care involved meeting with a genetic counselor and giving a detailed family history, neither of which is routinely offered to new parents, Stoll says. These study features leave her unconvinced that **healthy newborn** genetic screening is beneficial.

"We can't assume these psychosocial consequences will be true for everyone," she says.

Follow-Up and Treatment Needed

Traditional newborn screening relies on blood biochemical tests to detect and diagnose metabolic diseases. This approach still outperforms **DNA** sequencing in trials, says Cynthia Powell, MD, a pediatric geneticist at the University of North Carolina at Chapel Hill, who wasn't

involved with the BabySeq study. Despite the enthusiasm for genomics, this kind of screening won't replace newborn biochemical screening anytime soon, she says.

"There are some states that have only one geneticist available, so should we really be doing this if we can't provide the necessary follow-up and treatment for these babies?" she asks.

Still, Powell says, the BabySeq study helps advance understanding of what the infrastructure needs are for widespread use of DNA sequencing in newborns. She says those needs include appropriate consent processes, access to genetic counselors to discuss testing, and referrals for further testing and treatment in those babies with concerning results.

The BabySeq program will also guide new initiatives, like the pilot program that Genomics England launched in September 2021. As part of that project, the U.K. group intends to look into how practical whole-genome sequencing for newborn screening would be and look at the risks, benefits, and limits of its widespread use.

"For the first time, we're putting real data into these questions that people have basically just speculated and hypothesized and created narratives about," Green says.

But for now, the findings on the psychosocial effects of general newborn genomic screening show that "we should consider genetics to be just one more arrow in our medical quiver."

WebMD Health News

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ARTICLE: GENOMIC SCREENING OF HEALTHY NEWBORNS GETS MORE POPULAR ▼

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David Amor, PhD, pediatric geneticist, Murdoch Children's Research Institute, Australia.

Lilian Downie, clinical genetics PhD candidate, University of Melbourne.

Katie Stoll, genetic counselor; executive director, Genetic Support

Foundation, Olympia, WA.

Cynthia Powell, MD, pediatric geneticist, University of North Carolina, Chapel Hill.

SLIDESHOW: READY FOR BABY

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SLIDESHOW: CONCEPTION: FROM EGG TO EMBRYO
SLIDESHOW ▼

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