Studying Personal Genomics: Expanding the Pool

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by Robert C. Green

It may not be long before healthy people routinely have their genomes sequenced to identify potential health risks. Given that we have been talking about this possibility (or eventuality, perhaps) for a while now, it's easy to forget that this is a big deal.

Even though this type of personal genome sequencing could make waves in modern medicine, some basic questions remain. Will it really improve clinical outcomes? Will it lead to unnecessary expenses for patients and the healthcare system? Will healthcare providers be equipped to interpret genomic findings and advise patients on next steps?

While a good deal of research has focused on finding information within the human genome that can diagnose rare conditions, far less work has been done to understand the longer-term consequences of identifying genetic risks in apparently healthy people.

Our project, the PeopleSeq Consortium, plans to explore the implications of genomic risk through a longitudinal study that tracks the actions and outcomes of healthy adults who have chosen to be screened with personal genome sequencing. We have just received a grant from the National Human Genome Research Institute of the National Institutes of Health to support this activity.

For this research, we are partnering with four other academic research centers and six commercial labs to recruit and follow ostensibly healthy adults who have sought or are seeking elective personal genome sequencing. This approach gives us unique access to real-world information from early adopters. We can learn their motivations for obtaining sequencing, knowing that participation in this study was not a factor.

That said, there is a problem with going all-in on this approach. If we want answers that apply to a broader population, we should be striving for a representative sample of our entire society. If our sample is made up entirely of "early adopters," how representative can it be? To help answer this, it helps to examine the demographics of the early adopters.

Thus far, in our pilot work within the PeopleSeq Consortium, early adopters of genome sequencing are more likely to be male, married, and in a higher tax bracket. A large number have advanced degrees, and in a cohort of past PeopleSeq participants, one in four were healthcare providers or researchers. African and Hispanic ancestry tends to be especially underrepresented among early adopters. In that same PeopleSeq cohort, 85% of participants identified as white.

This fits a broader trend in genomic research. A paper published in *Health Affairs* earlier this year examined public genomic databases and genome sequencing studies, finding in both cases that populations of non-European ancestry were significantly underrepresented. This could limit the usefulness of genetic testing for people of African, Latin American, and Asian ancestry, both by potentially causing certain gene-disease relationships to be overlooked among non-European patients, and by broadly shaping the way clinicians translate genetic research into practice.

"We're seeing parallels between the underrepresentation of diverse populations and the underuse of genetic services in diverse populations,

including genetic testing and counseling," says Dr. Latrice Landry, a genetics fellow at Harvard Medical School and first author on the paper.

Indeed, we have very little information about the impact of sequencing apparently healthy individuals from underrepresented minorities. Finding a sample that truly represents the vast diversity of the U.S. population (let alone the rest of the world) is a tall order, but with our new funding, PeopleSeq will make significant progress. In addition to the self-selecting "early adopter" participants, we are creating opportunities for minority participants thanks to relationships with three Historically Black Colleges and Universities (HBCUs), the Minority Coalition for Precision Medicine, and the Buffalo Institute for Genomics.

Our long-term goal is to inform guidelines for the adoption of genome sequencing in clinical practice. This study, with its large and diverse group of participants, should provide an invaluable evidence base to advance that goal—and, we hope, to move us toward a future where the benefits of genomic medicine are more equitably distributed.

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