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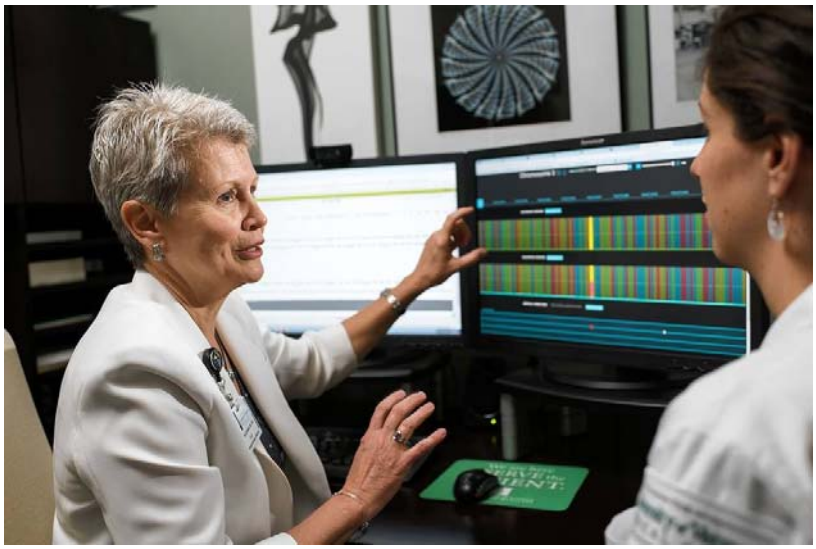
Why Knowing Your Genetic Data Can Be a Tricky Proposition

As genome testing expands, people are dealing with the new information in positive and negative ways.



Debra Leonard of the University of Vermont Medical Center and UVM College of Medicine describes a gene variant for a rare disease discovered in her own genome to a colleague.

By Laura Landro
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Personal genome sequencing may be the next great technology frontier in public health—but how do patients feel about knowing, sharing and acting on their genetic information?

That's a question researchers are exploring as more health-care providers, companies and research groups begin providing results of personal genome sequencing to patients and their doctors.

Unlike gene tests intended to identify the cause of a suspected or diagnosed genetic disease, a growing number of projects known as predispositional personal genome sequencing, or PPGS, aim to identify risks such as heart disease and cancer and provide other potentially useful personal information to ostensibly healthy people, according to a review published in May in the Journal of Personalized Medicine.

The rapidly dropping cost of sequencing in the past five years now makes it possible to execute large-scale PPGS projects to examine the benefits and harms, according to the authors, and there is evidence that patients may use risk predictions to make positive behavioral and lifestyle changes. But there is also the danger that the results could be distressing without any benefit, and false positives or uncertain results could prompt unnecessary and expensive follow-up care.

“If you have a patient with undiagnosed disease that looks genetic and you can’t figure it out, genomic sequencing is a very appropriate diagnostic tool,” says Robert C. Green, a co-author of the review and a medical geneticist at Brigham and Women’s Hospital in Boston and Harvard Medical School.

“What is still controversial is to what extent sequencing or other genomic technology can help you with predicting disease, because there aren’t many clear-cut examples where there is any evidence that genomic information makes any difference in your life,” he says.

Aiming for prevention

Dr. Green is also director of the Genomes2People research program, which is conducting a number of federally funded studies, including the MedSeq Project studying the use of whole genome sequencing in the practice of medicine, and the BabySeq Project, which is investigating the risks and benefits of conducting newborn genome sequencing and giving those results to parents and pediatricians.

Wanting to Know

Apparently healthy adults gave these reasons for taking part in programs offering genomic sequencing

Personal interest in genetics in general	99%
Curiosity about my genetic make-up	98%
Desire to participate in research to help others	92%
Interest in finding out things to do to improve my health	81%
To learn about my personal response to medications	81%
It seemed fun and entertaining	77%
Desire to plan for the future	69%
Interest in my ancestry	66%
Interest in finding out about personal disease risk	41%
Concern about possible/confirmed family genetic condition	21%

Note: Percentages are the total saying very or somewhat important.

Source: PeopleSeq study of 258 adults from the Harvard Personal Genome Project, Illumina Understand Your Genome program and Mount Sinai HealthSeq study

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He also leads the PeopleSeq Consortium, which is surveying healthy adults who plan to obtain or already have their own genomic sequencing information, to ask them about the impact on their health-care choices and behavior.

Debra Leonard, chair of pathology and laboratory medicine at the University of Vermont College of Medicine and UVM Medical Center in Burlington, Vt., recently joined the PeopleSeq project as part of a plan to begin clinical genome sequencing for the university’s patient population within the next two to five years. Dr. Leonard is first planning to sequence patients with cardiovascular and neurological

diseases and undiagnosed genetic diseases; by about 2023, she predicts, “we will be sequencing every patient.”

Genetic testing can be a powerful tool for uncovering one's predisposition to disease. But when Kathy Giusti decided to undergo gene sequencing, it triggered a complex family discussion. Photo: Steven Ladner for The Wall Street Journal

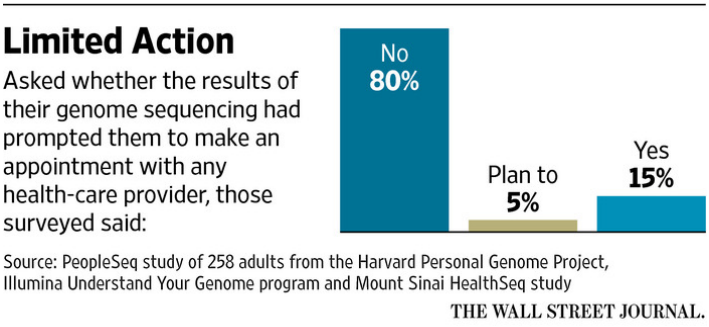
The broad aim is to understand people’s genetically based risks and develop strategies to keep them healthy, rather than just treating their diseases, Dr. Leonard says, as well as to identify genetic variants that might affect the way an individual responds to medications, a science known as pharmacogenomics.

Earlier this year, to create awareness of the plan, 73 people who work at UVM Medical Center or at the university’s college of medicine had their genome sequenced as part of an Understand Your Genome program offered by gene-sequencing company Illumina Inc. The cost per participant was $2,900, or $211,700 total, paid for by Dr. Leonard’s department and other UVM funds.

Participants provided blood specimens and had their first meeting with a genetics counselor in January, and got results in April, meeting again with a genetics counselor to discuss any significant findings in their report. They later attended a one-day symposium where they were provided with an iPad to review their entire genome sequence, and they were given guidance on how to navigate through it and explore their results beyond the clinical report.

Motivations and concerns

Dr. Leonard is also using PeopleSeq-designed surveys to understand the experience, concerns, risks and benefits of the participants. One question being asked is what motivated people to get their genome sequenced, such as providing disease-risk information for children, having a medical condition that may be genetic or has been confirmed to be genetic, or simply getting reassurance about their health.



The participants’ doctors are also being surveyed to understand their concerns and how they feel about future clinical genome sequencing at the medical center. And some staffers who declined to participate after initially agreeing are being surveyed for their reasons and concerns, such as privacy, the possibility they might receive unwanted information, and what impact the results might have on their ability to get health insurance.

How different people handle uncertainty is also a concern. The surveys include questions such as whether unforeseen events are highly upsetting and whether participants can function well in a climate of uncertainty.

The survey results aren't final yet. But Dr. Leonard says one concern people have is "learning about something they just don't want to know about."

Comparing Attitudes

About a quarter of the people in the study were health-care providers. How they and other participants compared in the following:

	Providers	Others
Very comfortable with the idea of sharing genome data	71%	64%
Discussed results with a health-care provider	62%	46%
Health insurance should cover personal genome sequencing	50%	71%
Genetic information should be part of a standard medical record	71%	89%
Tests like these should only be available through a doctor	39%	22%
People have a right to access their own genetic info without going through a medical professional	62%	86%

Source: PeopleSeq study of 258 adults from the Harvard Personal Genome Project, Illumina Understand Your Genome program and Mount Sinai HealthSeq study

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Among the ethical issues she is exploring is "whether someone should be given the choice not to know about a disease risk for which there are preventive or monitoring strategies that would reduce the severity of the disease and therefore the cost of care."

Not for everyone?

Preliminary results from PeopleSeq surveys at other consortium members have already provided insights into the relationship between why people are motivated to get their genome sequenced and their perceptions of the usefulness of the information.

For example, about 20% of participants cited specific concerns about their family history, and those were more likely to report learning something that they believe will improve their health than those who didn't report family-history concerns.

Robert Hayward, an obstetrician and gynecologist at the University of Vermont Medical Center, says he agreed to participate in the genome-sequencing project because he has always been interested in genetics and is himself a specialist in a field where patients often have genetic tests for breast cancer or birth defects.

He learned some things from his own genetic sequencing that he plans to discuss with family members. But generally, he doesn't believe all patients should have their genomes sequenced "because you could be chasing after red herrings and doing a lot of harm."

Instead, Dr. Hayward says, "start with a patient that has a condition and then do testing, rather than looking for things in perfectly healthy people."

Patients may also vary widely in their interest and sophistication. "There are people who want to drill down and are interested in the genetic code and what it means," Dr. Hayward says. "But some just want to know if they have something they might pass on to their children or whether an illness is inherited or acquired."

Dr. Leonard, who had her own genome sequenced, learned she is a carrier for a few rare disorders—information that she will share with her two biological sons so they can chose to learn if they have them as well and may be at risk for having an affected child if they were to have children with someone who is also a carrier.

At this point, she says "we are moving forward under the assumption that an individual's genome sequence is fundamental medical information, which will not explain everything about a person's illnesses and risks, but can explain a lot now, and more in the future."

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