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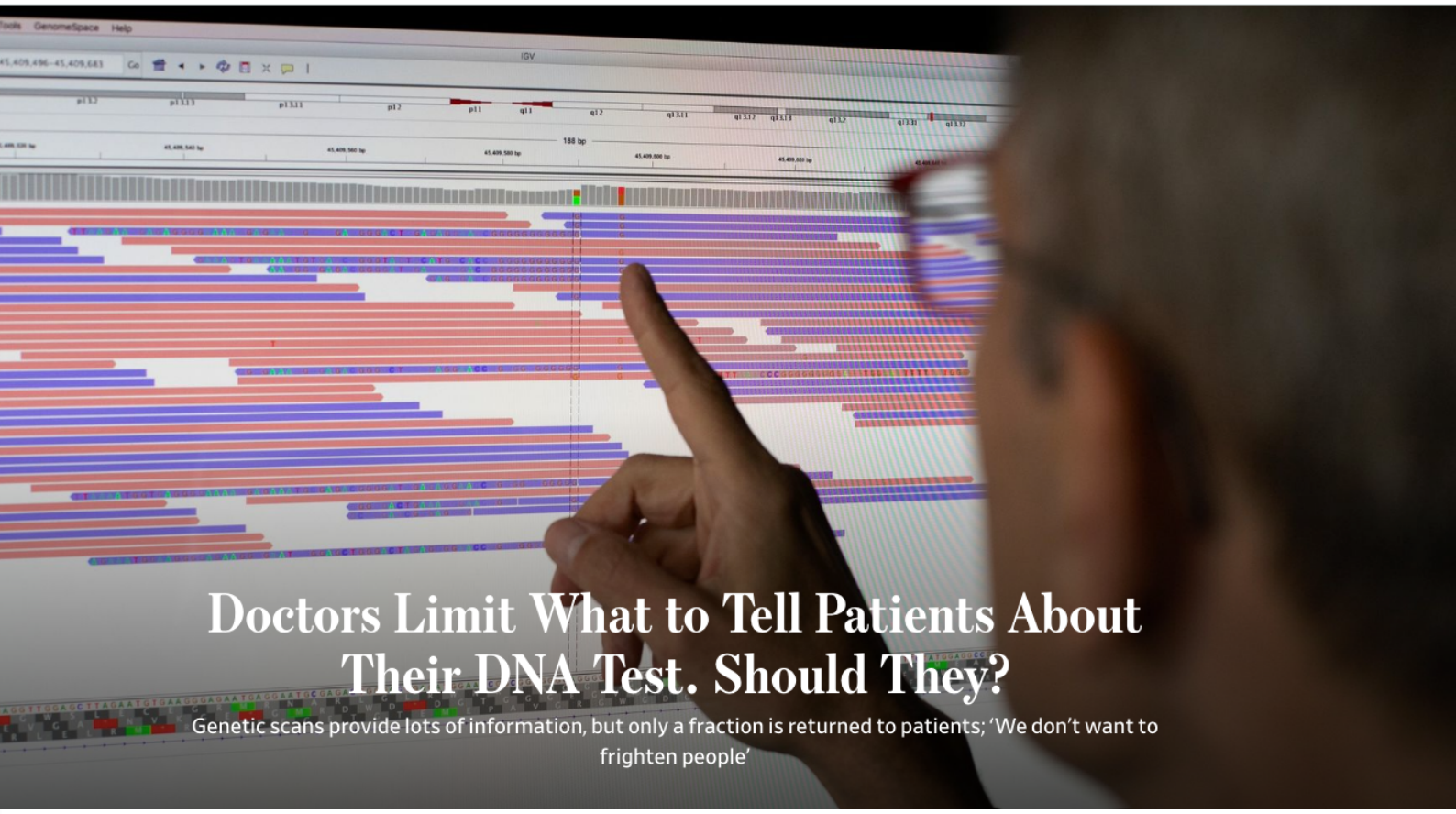


Doctors Limit What to Tell Patients About Their DNA Test. Should They?

Genetic scans provide lots of information, but only a fraction is returned to patients; 'We don't want to frighten people'

The Mayo Clinic is scanning 20,000 genes for thousands of patients to study genes' role in disease. It will hand over results for just 59.

Mayo will look for certain disease-causing gene variants for heart disease or breast cancer, and offer results to patients who have them. But it doesn't look at variants for early-onset Alzheimer's or Lou Gehrig's disease, meaning patients will remain in the dark.

"There is a risk of causing undue anxiety," said Dr. Keith Stewart, director of the Mayo Clinic's Center for Individualized Medicine.

DNA sequencing is creating vast amounts of data that promise to unlock the secrets of disease. But the information is being collected faster than the medical world can interpret what it all means. That is raising a question for doctors and scientists who perform the scans: How much should they tell patients?

The answer, often, is not much. Many clinics and studies will return only a few dozen results that researchers have deemed "medically actionable"—meaning they reveal genetic causes for conditions that can be treated.

Doctors often don't analyze and return other results because the risk of a trait isn't well-understood or because there is no treatment. Not everyone with disease-causing variants will end up with a related condition, because of other genetic and environmental factors. The risk may be low for some.

If told, some patients could seek unnecessary or harmful care, or unduly worry about a disease they may not get.

Some doctors, however, say it is paternalistic to withhold information if patients want it. Several studies have suggested that most patients want to learn their own genetic results.

“It’s their body and their DNA. We have a responsibility to scientific truth and clear communication,” including helping patients integrate results into their care, said Dr. Robert Green, a geneticist who is a professor at Harvard Medical School. He said doctors shouldn’t “take the Jack Nicholson line, ‘You can’t handle the truth!’ ”

Dr. Robert Green, who leads the Preventive Genomics Clinic at Brigham and Women’s Hospital in Boston, meets with a patient before DNA sequencing. PHOTO: KAYANA SZYMCZAK FOR THE WALL STREET JOURNAL

The debate is heating up as more large-scale research projects, along with labs offering services at ever-cheaper prices, are performing broad genetic scans. These scans, often intended for medical studies or drug development, differ from the DNA test kits consumers use at home, which look at a narrow set of preselected variants. Mayo this year will begin sequencing genes for 100,000 patients in one effort.

Many patients volunteer to have their DNA sequenced at hospitals for research. Around 1.5 million human genomes had been sequenced—the process of scanning through DNA and deciphering its order—as of January. The number is projected to increase to more than 13.5 million by 2023, according to BCC Research LLC, a market-research firm.

How—or if—the findings are relayed to patients varies widely, depending on who does the testing. The Million Veteran Program, a federal genetic-research project that has enrolled more than 780,000 participants, hasn’t yet returned any individual results. Instead, the results are used anonymously in studies.

On the other end, a newly launched preventive genomics clinic at Harvard-affiliated Brigham and Women’s Hospital, led by Dr. Green, offers feedback on as many as 3,734 genes. Dr. Green is also a co-founder and adviser to a company that does genetic counseling.

SHARE YOUR THOUGHTS

Would you want to know genetic-test results even if they are ambiguous? Join the conversation below.

In between, studies and clinics rely on a variety of measures to decide which results to return to patients. Many, including Mayo, use a list of 59 genes with variants that the American College of Medical Genetics and Genomics recommends returning to patients in some cases.

The list doesn't include genetic traits that the group viewed as having weaker links to disease. It also leaves out disease-causing gene variants for conditions for which doctors have no clear options to prevent or treat, such as amyotrophic lateral sclerosis, known as Lou Gehrig's disease.

"We are using that as our anchor," said Dr. Lincoln Nadauld, who oversees an effort at Intermountain Healthcare, Utah's biggest hospital system, to sequence 500,000 people in five years with biotechnology company Amgen Inc.

Scientists announced they mapped the human genome in 2003, but researchers are still figuring out the meaning of specific genetic traits. Studying the genomes of those diagnosed with a disease and their relatives, researchers can sometimes make a connection between gene variants and disease.

But they can't always answer a critical question: For a healthy person with the variant, how likely is an illness?

Khara Hanlon, a freelance graphic designer in New York, got a call in December from Mount Sinai Health System. She previously volunteered blood samples for research. Mount Sinai was now offering results of gene screening, she was told. "I was sort of excited and also very curious," she said.

Her results revealed a higher risk of breast and ovarian cancer. Her family had a history of breast cancer, she said. The ovarian-cancer risk came as a surprise.

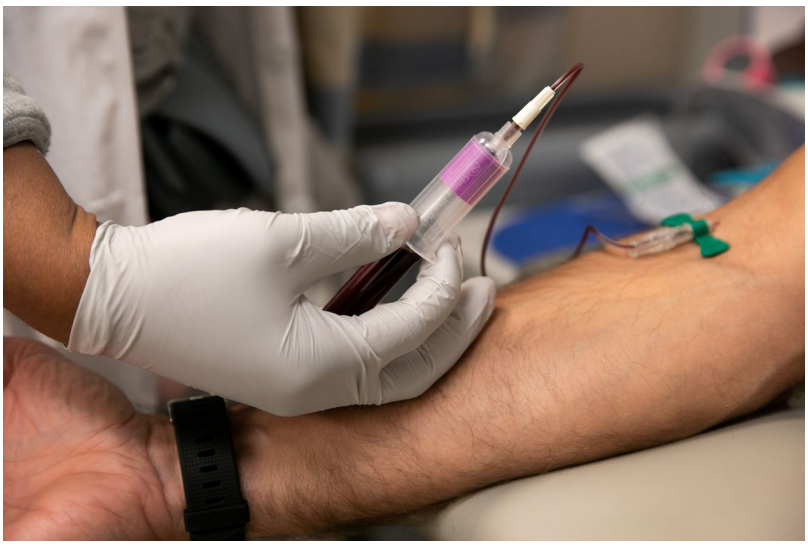
"That was eye-opening to me and a new worry," she said. Her head swam with what she could now do to reduce her cancer risks. "I immediately started thinking, well, then I'm going to get this surgery and I'm going to get that surgery." After getting the results, she saw a breast surgeon in August to consider having a prophylactic mastectomy.

Ms. Hanlon recalls Mount Sinai told her she would receive results from her DNA sequencing for conditions she could do something about. "I remember the word 'actionable'," she said. She said

she would choose to know more of what her DNA revealed if it were offered.

"If a doctor knows something about me, it's not their call to make whether I should be able to be told that or not," she said. "Even if I couldn't do anything medically, perhaps, that doesn't mean I couldn't do something emotionally or financially."

Mount Sinai in 2016 entered into an agreement with New York-based drugmaker Regeneron Pharmaceuticals Inc. to perform genetic sequencing for more than 30,000 patients.



A patient gets blood drawn at the Preventive Genomics Clinic at Brigham and Women's Hospital in Boston, which sequences and interprets genes. The clinic returns results for as many as 3,734 genes. PHOTO: KAYANA SZYMCZAK FOR THE WALL STREET JOURNAL

The hospital system returns results for 10 genes with disease-causing variants out of the roughly 20,000 genes it scans for research.

"We want to do this very carefully," making sure the hospital has genetic counselors and doctors prepared to meet with patients, said Dr. Noura Abul-Husn, clinical director of the Mount Sinai Center for Genomic Health.

Researchers face growing pressure from patient groups to disclose ambiguous information or results for genes tied to diseases that can't be treated. A survey completed by 219 research participants about 11 different types of genetic test results, including some that couldn't be prevented or cured, found that 72.5% wished to receive all of them, according to a 2016 paper in the Journal of Genetic Counseling.

Harvard's Dr. Green led a study, published in the New England Journal of Medicine, that involved 162 patients. It found patients who were told of a genetic risk for Alzheimer's suffered "transient, modest distress," but 98% said they would get the testing again.

A decade ago, when the Million Veteran Program was being planned, "it was not the norm" for genomic-research projects to return information to participants, said Suma Muralidhar,

program director for the Department of Veterans Affairs project, which is running broad genetic scans on a limited share of its total participants. “We didn’t have enough information about everything, about how to do it, whether the system would be ready,” she said.

The VA is planning two pilot studies to test sharing certain genetic findings with specific participants whose care could be affected by the results, Dr. Muralidhar said, with the goal of moving toward broader disclosure. Project leaders are focused on information that is “actionable, where we can clearly explain to them what it means, or doesn’t mean.”

More than 200,000 patients of Geisinger, a Pennsylvania hospital system, have agreed to DNA sequencing for research. Geisinger stores blood samples from volunteers at its laboratory in Danville, Pa. PHOTO: JESSE NEIDER FOR THE WALL STREET JOURNAL

Caroline Barnes, a 51-year-old illustrator who lives in Brookline, Mass., faced the question a few years ago when she joined a study called MedSeq funded by the National Institutes of Health, which returned information for around 5,860 genes. It was among early efforts to return fuller information to patients, working through their primary-care doctors.

When results came back, Ms. Barnes’s doctor walked her through the implications. Her results revealed a slightly elevated diabetes risk, and that she carried genes for a few recessive conditions unlikely to affect her descendants.

“I couldn’t imagine myself not being the recipient of all the information,” she said. “It’s strange to take someone’s blood, and say, ‘We’re not going to share everything with you that we can learn.’ ”

The NIH’s All of Us research program, which began broad enrollment of patients last year, aims to sequence a million genomes of U.S. residents to glean genetic links that could lead to medical advances. Officials said they heard from focus groups that participants wanted genetic information related to their health. Participants will get results for a certain number of genes

that could affect health conditions. They are also expected to get other information on traits such as lactose intolerance and earwax characteristics.

But the program doesn't currently plan to return health-related results not seen as "actionable."

"We don't want to frighten people, have them potentially change medical care, unless we're really confident in that result," said Brad Ozenberger, genomics program director for All of Us. Those in the program will be able to obtain the raw data from their whole-genome scans so they can get it interpreted on their own.

Pennsylvania hospital system Geisinger, which runs one of the most extensive gene-testing programs in the country, has begun to return some results that aren't actionable—meaning the conditions can't be treated. It is going slowly, vetting changes with doctors and ethics advisers.

Geisinger sequences about 20,000 genes for each person. Its standard report returns results of 61 genes with disease-causing variants, a "high and conservative bar," said Geisinger geneticist Christa Martin, who is helping oversee its effort to expand reporting.

Last year, Geisinger began a program offering certain patients an option to get information about additional genomic variants known to increase risks for brain disorders—some of which doctors can do little or nothing to treat. The patients all had a history of related conditions in their medical records, including bipolar disorder, depression and intellectual disability.

Nearly 90% wanted results, the hospital system says. The rest didn't respond.

Geisinger surveyed patients after returning the results and six months later. News of the genomic variants relieved guilt and worry that environmental circumstances or trauma had led to their illness, patients told geneticists. "I think it does change a sense of self," said Dr. Martin, associate chief scientific officer for Geisinger.

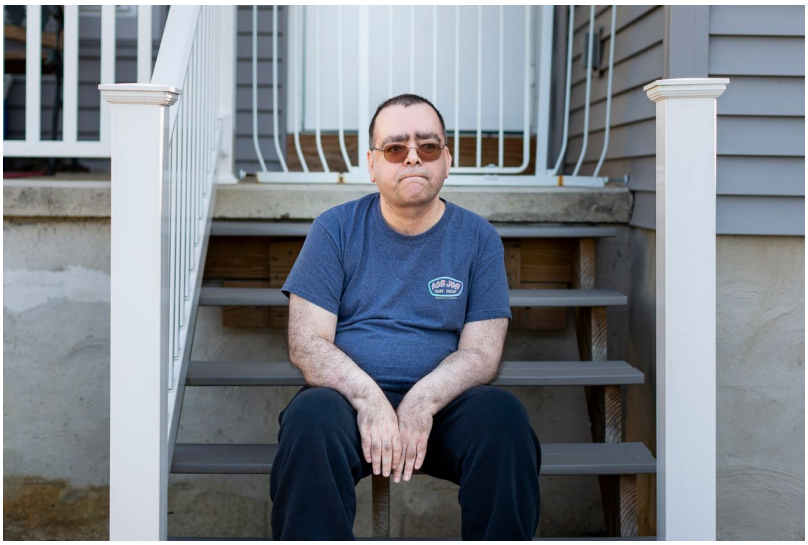
Michael Koza was one of them. He got a call from the hospital in December.

"I felt so relieved," said Mr. Koza, who has a learning disability and has suffered seizures. The genomic variant caused both, the counselor told him.

He said he is glad to have the information, though he can't do much with it. "There is nothing I can do about that missing DNA."

Geisinger's next decision was whether every patient with these genomic variations should be offered the information, even those with no history of illness in their records.

In April, Dr. Martin faced a room crowded with doctors, patients, ethicists and counselors



Michael Koza, a patient at Geisinger, a Pennsylvania hospital system, was relieved to get his results. PHOTO: JESSE NEIDER FOR THE WALL STREET JOURNAL

charged with helping Geisinger make such decisions. “Do we think we’re ready?” Dr. Martin asked the committee.

Some advisers voiced reservations to be considered. What happens when it is someone whose life is “perfectly normal?” asked the Rev. Kevin FitzGerald, a bioethics professor at Creighton University in Omaha, Neb. “Now, somehow they’ve been genetically tainted.”

What about the possibility some could shift too much blame for their conditions to genetics, overlooking other factors, such as trauma, asked Bernard Prusak, a philosophy professor at King’s College in Wilkes-Barre, Pa. “It seems to me that’s probably an over-simple story.”

Dr. Christa Martin, associate chief scientific officer for Geisinger, a Pennsylvania hospital system with one of the most extensive DNA sequencing programs in the U.S. PHOTO: JESSE NEIDER FOR THE WALL STREET JOURNAL

As the group neared a vote, Sara Kirkland, a participant in Geisinger’s sequencing effort, spoke up: “We don’t have a right to withhold information,” she said.

The group ultimately agreed to give results to patients with the genomic variants if they want them. Notification will halt if patients react poorly.

“Am I totally comfortable? No,” Ms. Kirkland said weeks after the decision. “But I’m rarely comfortable with any decision we reach because this stuff is really complex. I am willing to say that it is a responsible approach to take.”

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