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Patients Armed With Their Own Genetic Data Raise Tough Questions

With the market for direct-to-consumer genetic testing expanding rapidly, clinicians are playing catch-up.

BY CARINA STORRS

Recently, a middle-aged woman arrived at the Preventive Genomics Clinic at the University of California San Francisco (UCSF) asking for help with some troubling results from her 23andMe genetic test. She had initially bought 23andMe's basic ancestry test but on a whim decided to upgrade her purchase to find out whether she had gene variants that are associated with a handful of diseases. The woman did not realize what exactly would be included in the detailed health report, which the Food and Drug Administration (FDA) allowed 23andMe to start marketing last year.[1] When the results arrived, she learned that she had two copies of the *APOE4* gene, which can increase the chance of developing Alzheimer's about twelvefold.[2]

She was "deeply upset," says Bryce Mendelsohn, lead clinician at the UCSF clinic. Before finding her way to the clinic, the woman had bought books about preventing Alzheimer's and started on a slew of unproven diets and supplements. This extreme response to test results "is not typical, but it happens and it can become disabling," Mendelsohn says. Although the woman wanted to hear that there was nothing to worry about, Mendelsohn thinks that he was able to ease her worry by explaining that having the *APOE4* variant does not guarantee that a person will get Alzheimer's. He then connected her with the Memory and Aging Center at UCSF for more information and clinical trials.

In a sense, this woman was fortunate. In a survey of users of direct-to-consumer (DTC) genetic testing services, such as 23andMe, only 4 percent reported getting genetic counseling after receiving their results, although 38 percent said that they would have seen a genetic counselor if one had been available.[3] The UCSF clinic, which opened in August 2017, provides genetic tests for health screening and offers help to people in the Bay Area who have questions about their DTC genetic test results.[4] It is one of the few such clinics at US academic medical centers that provide this type of support.

Most experts feel that adults have the right to buy DTC genetic tests, as a growing number around the world are doing, instead of learning about their genetic information exclusively through doctor-ordered tests.[5,6] In any case, it would be futile to try to reverse course and reduce patients' access, Mendelsohn says. Technology is advancing to make the genetic lab tests cheaper seemingly by the day. At the same time, regulations about what companies can offer are being relaxed.

The problem comes, experts say, when someone learns that they may have a disease-associated genetic variant and do not know how to decipher the information. Genetic counselors are familiar with stories of anxious consumers who fear the worst based on limited information. Just as disturbing are those consumers who mistakenly assume that they have no disease risk because a test says they do not have a certain variant, without understanding that other genetic changes not included in the test, along with lifestyle factors, could contribute to risk. Research suggests that in rare cases (about 1 percent), consumers even take it upon themselves to change their medication after receiving results from a DTC genetic test.[7]

"I am less interested in saying we need to shut [DTC genetic testing] down," says Laura Hercher, director of research at the Joan H. Marks Graduate Program in Human Genetics at Sarah Lawrence College, the first US program established to educate genetic counselors. Instead of trying to limit patients' access to DTC genetic testing, Hercher says, "we need to provide resources for people to help them assess these different tests and understand what is valuable and is not valuable, because this is really hard and confusing."

As the number of people paying for DTC genetic tests climbs, genetic counselors—arguably the best resource for consumers of these tests—are trying to figure out how to help them. New types of genetics services are cropping up that could help fill the gap, at academic medical centers such as the one at UCSF and through private companies that offer remote counseling. But even if counseling is available, consumers may be more likely to talk with their primary care doctors about DTC genetic testing. Primary care doctors around the country are playing catch-up to understand these tests so they can be ready when a patient wants to know what their results mean.

The Menu Of DTC Genetic Test Options

All the signs indicate that the market is booming for DTC genetic tests that provide health information. It totaled $99 million in 2017 and is predicted to triple over the next five years, according to a February 2018 report by Kalorama Information, a health care market re-

search company.[8] 23andMe is the biggest player and the sole survivor of the first generation of DTC companies that let consumers bypass a doctor for information about their genetics-based health risks.

When 23andMe first came on the scene in 2007, it marketed health reports on 254 medical conditions, but in 2013 the FDA sent the company a "warning letter" to cease and desist marketing these health reports.[9] In April 2017 the FDA eased its stance to once again allow 23andMe to market DTC tests that include health reports that give the genetic risk of several medical conditions, along with its ancestry test offering.[10] The 2017 decision represents a significant change in the agency's attitude about the utility of DTC genetic testing, according to Hercher. And it revived the market: The number of consumers of 23andMe and other DTC tests (for both medical and ancestry information) shot up to more than twelve million in 2017, most of them in the US, after steadily increasing over the previous five years.[11]

Any consumer can purchase a kit from 23andMe online or at a local pharmacy. The package includes a plastic tube into which the consumer spits until they've provided about 2 ml of saliva. Then it is as simple as sealing the tube, packing it up, and mailing it off. For $199 the company will search DNA recovered from the consumer's saliva for specific genetic variants—called single nucleotide polymorphisms (SNPs)—associated with ancestry information as well as seven health conditions, including Alzheimer's and Parkinson's disease, celiac disease, and several blood disorders. The consumer gets a report outlining their risk of developing the conditions. In March 2018 the FDA authorized 23andMe to tell consumers whether they possess three mutations in the *BRCA1* and *BRCA2* genes that increase the risk of breast and ovarian cancer.[12]

Although 23andMe and similar smaller companies explicitly offer genetics-based health information, some consumers are taking another route: ancestry-only genetic tests. These tests from providers such as AncestryDNA and MyHeritage offer only ancestry testing and not health reports. But these customers can download their own raw data files (as can the customers of23andMe and other services). The data files contain all of the gene variants identified by the test, and consumers can analyze the files on a third-party site such as Promethease to find out which of a long list of disease-linked variants they have. These companies do not promote this approach, but consumers who have learned about it elsewhere pursue the analysis nonetheless. In a recent survey of genetic counselors, many respondents noted how time-consuming it was to help patients sift through these analyses.[13]

All Tested And Nowhere To Go

In this fertile environment for DTC genetic testing, genetic counselors across the US have been getting more requests in recent years from people who want help interpreting their own test results. "It is still rare, but there is definitely an uptick, so the majority of genetic counselors now say that they do occasionally see it," says Hercher, referring to a recent unpublished survey conducted by graduate students at Sarah Lawrence.[14]

It remains to be seen whether the proportion of consumers who get genetic counseling will inch above the 10 percent or so that studies have reported, although Amy Sturm, president-elect of the National Society of Genetic Counselors (NSGC), hopes it does. But even if it doesn't, a small percentage could really add up, considering the growing number of consumers of DTC genetic tests overall, Sturm says.

But there are several roadblocks to consumers in search of a genetic counselor. First, as of May 2017 there were only 4,242 certified genetic counselors in North America.[15] Becoming a certified genetic counselor typically involves completing a master's program, getting clinical experience, and passing an exam through the American Board of Genetic Counseling. According to a 2018 report by a genetic counselors working group, that number is not projected to grow enough even to meet traditional needs such as genetic screening for a person who has a family history of cancer or who wants to become pregnant.[15] However, Sturm points out that the situation may be less dire than it seems, as the number of genetic counselor master's programs increased in the past year, and programs are accepting more students. Still, someone with a burning question about their DTC genetic test may have to wait months to see a genetic counselor at a medical center who is handling referrals from physicians within their hospital.

A second challenge is the fact that genetic counselors tend to specialize in specific areas, such as cancer or prenatal care, and might not feel prepared to field wide-ranging questions about every variant outlined by certain DTC tests, Sturm says. The NSGC is trying to help by offering plenary sessions at its annual conference and webinars for members on the quality of DTC tests, for example—including whether they look at enough specific potential gene variants to provide clinically useful information.

Experts predict that consumers with DTC genetic test results in hand will increasingly go to genetic counselors at private companies that offer remote fee-for-service counseling over the phone or via video chat. A number of these companies have cropped up in recent years, such as Genome Medical, Grey Genetics, and Watershed DNA, and they may offer the only real option for people in rural areas and those with DTC genetic test results. "We really want to make sure that people have access to services when they need it and can usually offer appointments in twenty-four to forty-eight hours," says Erynn Gordon, vice president of clinical operations at Genome Medical. The companies typically charge $150–$250 for a session and vary in whether they accept insurance or provide receipts that patients can submit themselves. Although Genome Medical requires patients to pay up front for appointments, the company will submit claims to insurance providers and refund patients the amount reimbursed through insurance.

Decoding Genetic Information

For all of the people who seek genetic counseling for their DTC test results, there are many more who do not realize that a genetic counselor could help them. "A lot of people say, 'I don't need therapy.' They hear 'counseling' and think it is more psychological counseling," Gordon says. But in some cases,

genetic counseling can help people even if they do not have a specific concern about their test results. For example, someone who finds out that they do not have one of the *BRCA1/BRCA2* variants in the new 23andMe breast cancer risk test may still benefit from genetic counseling if they have a family history of breast cancer to see if they could be at elevated risk, such as if they possess other *BRCA* variants or mutations in other genes associated with breast cancer. Gordon, who worked for 23andMe until last year, hopes that the company's health report for the breast cancer risk test will make that point clear.

Geneticists and bioethicists in one camp argue that it is the responsibility of DTC testing companies to provide genetic counseling for their customers.[16] "On the other hand, they are trying to sell a product, and they are going to want their product to sound good or be important," says Sara Katsanis, an instructor in science and society at Duke University. That desire to underscore their product's value may, in subtle ways, affect how a testing company counsels patients, Katsansis says. "I personally would prefer to see the medical advice coming external to the company."

In July 2017, Helix, a DTC genetic testing company that sequences a customer's entire set of genes for $80, started marketing products for interpreting gene sequence data. Included in the cost of products that provide health information is the option of speaking with a genetic counselor through a third-party group such as Genome Medical. Smaller companies, such as Gene by Gene, offer complimentary counseling in cases where a customer finds out that they carry a gene linked to increased risk of a specific disease. 23andMe takes a more hands-off approach, advising its clients to talk with a genetic counselor and referring them to the NSGC's "Find a Genetic Counselor" resource.[17]

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Surveys of consumers of DTC genetic tests have found that if they talk with a physician about their test results, it is most likely to be a primary care doctor, and about 30 percent of them bring up their results in these settings.[18] However, small surveys of primary care doctors suggest that the majority of them do not feel prepared to help their patients make sense of these test results.[19] A survey of nearly 500 primary care doctors in New York City published in this issue of *Health Affairs* found that only 24 percent trusted the companies that sell genetic tests.[20] Similarly, many patients report being dissatisfied with interactions with their providers about these tests, and among the reasons cited is that their doctor does not seem interested in the results.[18]

To date, large professional organizations such as the American Academy of Family Physicians (AAFP) and the American College of Physicians do not have policy statements or offer member resources around DTC genetic testing. However, hospital systems and clinics are working locally to prepare their clinicians to have conversations about DTC testing with patients and decide when to order follow-up tests based on the results. For example, genetic counselors within the Johns Hopkins Institute of Genetic Medicine led a grand rounds gathering where they taught internal medicine doctors about which disease risks the tests report, while members of the Cleveland Clinic Genomic Medicine Institute offered an educational session for Cleveland Clinic staff.

"As some of this DTC testing is becoming more prevalent, you are going to have physicians…craving more information and more help with the overall assessment," says Michael Munger, president of the AAFP and a family physician in the Kansas City metropolitan area. Munger has had a few patients mention in passing that they had gotten a DTC genetic test, and one of them recently told him that they have the Alzheimer's disease risk gene *APOE4*. "It gave us a good opportunity to talk about how the disease is multifactorial and talk about things you can do based on the current evidence to reduce your risk," he says. ■

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NOTES

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