Genetics inMedicine | CORRESPONDENCE

First, do no harm: direct-to-consumer genetic testing

To the Editor:

We are writing to share one patient's experience with direct-to-consumer (DTC) *BRCA* genetic testing. We believe this case illustrates the current questions and concerns surrounding DTC testing.

A healthy 47-year-old woman came to the Adult Genetic Medicine Clinic for a family history of two first-degree relatives with breast cancer. Clinical molecular genetic testing identified a heterozygous pathogenic variant in the *BRCA2* gene. Pre- and post-test genetic counseling allowed her to correctly understand her results, and to implement appropriate medical care. Several siblings who subsequently underwent genetic counseling, also received positive test results, and underwent risk-reducing surgery. One year later, she was given DTC genetic testing as a gift. To her surprise, this reported a "low risk of breast cancer," causing her to recontact our clinic. She communicated: "I recently did the 23andme genetic test. My results came back that I have a lower than average chance of breast cancer, and that I did not test positive for either of the *BRCA* mutation markers. 23andme mentions that their test isn't exhaustive of all the *BRCA* mutation forms, but I feel like this information/disclosure could be easily overlooked/dismissed by the general population. Honestly, if I had done this test (and not spoken with you, etc.), I may have received the results of my 23andme, and thought I was off the hook. Especially, given that the other test is approx $5,000. When you have a moment, can you explain (in more scientifically specific terms), why my Myriad test came back positive and 23andme negative?"

This case illustrates a real-life example of potential harm from DTC genetic testing. Had this patient undergone DTC testing first, she could have been falsely reassured by receiving a "low risk" based on a genetic test, and might not have been referred to a genetics professional. Fortunately, based on her family history, which included a sister diagnosed with breast cancer prior to age 40 years, this patient was referred to a genetics clinic, and correctly counseled that her lifetime risk of breast and ovarian cancer was higher than average. Because similar cases may not come to the attention of a genetics clinic, the frequency of these occurrences cannot be estimated.

DTC genetic testing is marketed directly to consumers, and makes genetic testing appear easy and inexpensive. According to an article published in *MIT Technology Review*, based on company reports, an estimated 3 million people have undergone 23andMe DTC genetic testing (https://www.technologyreview.com/s/610233/2017-was-the-year-consumer-dna-testing-blew-up/?utm_campaign=add_this&utm_source=email&utm_medium=post). Some DTC companies have a disclaimer that results are not intended for medical care and should be discussed with a medical professional. However, in a survey of 369 DTC customers, 78% underwent DTC genetic testing to learn about potential future diseases and 77% hoped to improve their health.[1] Proponents of DTC claim they are empowering consumers by providing their genomic information. To date, most studies of DTC genetic testing have focused on the consumer's perspective, and concluded that there is little harm from DTC testing.[2] Of further concern, recently the accuracy of DTC tests has come into question. Tandy-Connor et al. performed follow-up sequencing in a clinical molecular genetics laboratory of variants reported to 49 DTC patients. The authors found discrepant sequencing results in 40% of variants tested.[3] In addition, some variants listed as "risk factors" that were received by DTC participants were actually common in population databases and classified as benign by one or more clinical laboratories.[3] Because of these trends, DTC genetic testing should be of concern to health care professionals in all specialties.

In the field of genetics, the potential for harm is very real, but typically does not result in an acute event such as an adverse medication reaction or a surgical complication. Examples of harm in genetics practice include (1) failure to diagnose a genetic condition; (2) inappropriate diagnosis of a genetic condition, resulting in unnecessary treatment, or failure to find the true etiology; and (3) emotional distress from a misdiagnosis or misunderstanding of risk. The potential for harm in genetic medicine can impact not only the patient, but also their relatives.

Elsewhere in medicine allowing patients to order or interpret testing has been approached only with great caution and in some domains, such as diagnostic imaging or pathology, remains inconceivable. Evaluation by a board-certified genetics professional remains the gold standard for the care of individuals with concerns about a genetic condition. Genomic medicine has great potential for disease prevention and individualized treatment based on genetic information. Proponents of DTC genetic testing argue that patients have the "right" to the information within their own genome. We are of the opinion that genetic and genomic testing for medically significant diseases and for treatment and prognostic information should be ordered and interpreted only by qualified medical professionals. We believe DTC testing jeopardizes precision medicine, and should be regulated to prevent patient harm.

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DISCLOSURE

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