# Direct-to-Consumer Nutrigenomic Testing:
## Is It Valuable in Spite of Its Limitations?

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Genetic testing is available for nearly 300 specific targeted mutations associated with various disorders [1]. Advances in genomic technology such as genome-wide association studies (GWAS) made possible the discovery of many such associations, and these advances have also ushered in an era of direct-to-consumer (DTC) genomic testing. Such testing is marketed directly to consumers, who can purchase it without any involvement on the part of their health care provider. There has been much discussion about regulation of such testing (and regulation of the marketing claims made regarding such testing), but DTC genomic testing is currently not regulated in the United States [2]. A 2008 survey [3] found that 23 companies were providing DTC genomic testing, and a 2012 review [2] found that 12 of those companies continued to offer such services.

Over the past decade, great advances have been made in discovering the genetic basis of monogenic diseases such as Tay-Sachs disease and cystic fibrosis, but finding meaningful associations between genetic variants and polygenic diseases such as diabetes, cancer, and cardiovascular disease is more difficult and will require more time. The clinical validity of currently available DTC nutrigenomic tests is limited, because the associations that have been discovered between gene variants and health conditions such as obesity and cancer are only small pieces of the puzzle; an individual's risk of disease ultimately results from the interaction of many genetic and environmental factors, only some of which are understood [2].

The idea of receiving nutrition recommendations based on one's unique genetic makeup is certainly attractive and can be perceived as empowering, especially in an age that calls for consumers to take charge of their own health. A recurrent marketing theme employed by companies that offer DTC genetic testing is to evoke a sense of empowerment in consumers by giving them genetic information; however, such marketing often fails to clearly disclose the lack of evidence for the tests' claims and the limitations in their ability to predict risk [4].

One of the presumed benefits of genetic testing is its potential to motivate lifestyle changes, although the ability of such testing to encourage healthy behavior is disputable [2]. Current research suggests that consumers believe that they will change their health behavior once they know their genetic test results. However, studies of actual changes in behavior after people receive the results of genetic testing have come to mixed conclusions. In a randomized trial of the use of personalized genetic risk counseling to motivate diabetes prevention [5], subjects were randomly assigned to receive genetic testing or no genetic testing. Those who had been tested were then ranked from highest to lowest risk, and those in the top and bottom quartiles were enrolled in a diabetes prevention program along with untested control subjects. Few significant differences were found in motivation, program attendance, and weight loss when the lowest-risk and highest-risk groups were separately compared with the control group [5].

One of the concerns surrounding DTC genetic testing is that it could cause consumers undue psychological stress and anxiety. However, studies that have investigated whether or not this is the case have not found data

genetic tests are being marketed to healthcare providers and the general public" [8].

In 2011, a survey showed that DTC genomic testing companies were offering testing for a host of mental health–related conditions—including alcohol dependence/abuse, autism, depression, nicotine dependence, schizophrenia, and smoking [9]—despite evidence that the markers being measured contribute only a small proportion of the genetic contribution to these conditions [10]. Although there seems to be strong public interest in testing for susceptibility to psychiatric disorders, little is known about the impact on individuals of receiving the results of such genetic tests [11]. Moreover, the low predictive power and uncertain clinical validity of DTC genomic testing for psychiatric disorders leads to significant difficulty interpreting such test results.

Further contributing to the potential for confusion among consumers are claims made by companies on their Web sites and in their marketing materials. The 23andMe Web site (https://www.23andme.com/) currently displays a link to a "life-changing story" about a woman who suffered from gastrointestinal symptoms for years before her doctor suggested DTC genomic testing, which revealed an elevated risk of celiac disease. This prompted her physician to obtain standard clinical testing, leading to a diagnosis of celiac disease in both the patient and her daughter. Such claims conflate marginally elevated risk assessment with diagnostic testing, the former being no substitute for appropriate clinical assessment and diagnostic evaluation.

Critics have worried that the confusion created by complicated risk profiles in the absence of proper genetic counseling may provoke unnecessary fear and worry in consumers. Current data, however, have not shown this to be a significant cause for concern. In a 2011 study, patients expressed no significant worries [12]. A more recent study showed that most consumers of DTC genomic testing services showed no difference in anxiety after long-term follow-up, compared with baseline, and 98.6% of respondents reported no test-related distress [13].

Nevertheless, geneticists are becoming aware of anecdotal incidents suggesting that some consumers may be

to substantiate that concern [6, 7]. This may be because consumers who purchase such tests tend to have high educational levels and knowledge of genetics [2].

Some companies claim to offer a genetically tailored diet plan and nutritional supplement recommendations that will protect against the diseases to which an individual is genetically predisposed and/or that will compensate for loss of function caused by a genetic variant. A study by the Government Accountability Office [8] failed to find support for these claims; instead, this study found that the advice offered usually consists of only standard sensible dietary suggestions and lifestyle recommendations.

The research community insists that current work in nutrigenomics is merely the tip of the iceberg and that it is still premature to determine the validity and utility of such testing. In the meantime, existing nutritional recommendations should be followed. For example, to decrease blood pressure and the risk of cardiovascular disease, diabetes, and certain cancers, patients should be encouraged to follow current evidence-based guidelines with regard to everyday eating and to consume a balanced diet—one containing a colorful and plentiful variety of vegetables and fruits; moderate amounts of lean animal and/or plant proteins, healthy fats, and whole grains; and appropriate calcium sources. Patients should also be encouraged to avoid consuming too many calories and to cultivate an emotionally healthy approach to eating. At the present time, personalized advice on how to accomplish these goals will be more helpful to patients than personalized genomic test results. NCMJ

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suffering as a result of DTC genomic testing, and there is certainly a potential for serious untoward incidents. 23andMe is now testing for the *APOE4* variant associated with increased risk for Alzheimer disease, as well as for several *BRCA1* and *BRCA2* mutations, which are associated with risk of breast and ovarian cancer. Reports of these test results are "locked," and there is genetic counseling information provided on the Web site, but all it takes to unlock these results is the click of a button. The Web site forums reveal that a number of individuals are concerned after learning that they are homozygous for the *APOE4* allele.

Positive outcomes from DTC genomic testing have also been reported. A small study carried out by 23andMe included 11 women and 14 men who had received an unexpected test result—the finding of a *BRCA1* or *BRCA2* mutation—and none of them reported more than transient moderate anxiety [14]. Furthermore, most of these individuals sought medical advice that resulted in confirmatory testing, risk-reducing procedures, screening of at least 30 relatives, and identification of 13 additional mutation carriers.

A major claim made by proponents of DTC testing is that simply knowing whether one is at increased risk for a particular condition may be enough to motivate significant lifestyle change. Some studies of DTC genomic testing customers have shown a trend toward both intended and actual behavior changes in individuals who learn that they may have a greater risk for conditions such as colon cancer [12, 15]. However, it is important to keep in mind that early adopters of DTC genomic testing services are likely to be among those most motivated to make health-related changes.

Those who work in primary care know that changes in patient behavior require more than just information, such as knowledge of cardiovascular disease risk factors or statistics regarding the impact of cigarette smoking on common health conditions. Although the notion of using genomic data to encourage preventive health strategies is appealing, early studies suggested that only a minority of consumers act on this information [16-20]. Furthermore, a primary care visit often includes collection of a family health history that identifies relatives with early heart disease or type 2 diabetes,