Direct-to-consumer genetic testing: more questions than benefits?

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'...do direct-to-consumer genetic services, which allow consumers to completely bypass the traditional healthcare system, do more harm than good?'

A plethora of genetic tests for susceptibility to common complex disorders have made their way onto the market. Groceries, clothing, hardware equipment, plane tickets and, now, even genetic tests can be ordered directly over the internet, from the comfort of your own home, without ever seeing a physician. Is this simply a natural progression, following in the footsteps of home pregnancy tests and blood-pressure monitors, which many people would admit do fulfill a certain niche and accomplish a lot of good for health-conscious consumers? After all, genetic testing is at the root of personalized medicine within the context of specific drug responses (pharmacogenetics). There are examples of genetic variants that do have a significant and clinically relevant effect on drug response; therefore, testing for them can lead to more efficient and cost-effective treatments [1]. However, there are many more examples with questionable validity and usefulness, so this begs the question: do direct-to-consumer (DTC) genetic services, which allow consumers to completely bypass the traditional healthcare system, do more harm than good?

Direct-to-consumer genetic testing can be understood as including two related aspects: first, the advertising of genetic tests directly to consumers; and second, the direct access or ordering of genetic tests without the intermediate of a healthcare professional [2]. Although both aspects are equally important and do raise important ethical issues, they differ sufficiently to warrant separate analyses. This editorial will focus solely on DTC access to genetic testing. Other publications have tackled the issue of advertising [3,4]. Over 1100 genetic tests are available clinically and several hundreds are available in research settings. Although most genetic tests are still only available through a healthcare provider, a growing number of tests

are being offered directly to consumers within a commercial setting [5]. Moreover, the types of tests available include tests already offered by healthcare establishments, as well as those that have yet to be deemed appropriate to offer to the public by physicians in traditional clinical settings. The term 'genetic test' includes any testing method using DNA, RNA, chromosomes or any other material offering similar information to these three materials. Different categories of genetic tests can be defined based on the different goals of the tests: to gain information regarding paternity, ancestry, health enhancement (nutrigenetics, dermatogenetics), drug response (pharmacogenetics) and genetic diseases. In addition, genetic tests have been developed that claim to predict the sex of a fetus as early as 5 weeks of pregnancy. The different types of tests bring with them different sets of practical and ethical concerns. At the moment, some of the greatest concerns have been raised regarding susceptibility testing for common complex genetic disorders, such as cardiovascular disease, cancer and diabetes. For the time being, most companies test for one to a few specific gene variants in order to provide information regarding one specific disease. However, some companies, such as 23andMe [101], are offering 'genetic profiles', which involves testing over 580,000 SNPs (positions in the genome at which the nucleotide varies within a population), and claim to be able to provide personal information regarding many disorders. It will use information from scientific studies to estimate composite risk factors for diseases based on each customer's SNPs.

Whatever the type of DTC genetic test offered, proponents claim [6,7] that the benefits of offering such a service will include increased access for consumers, added support for consumer autonomy, and greater individual empowerment. As Jenkins (Genetic Health, CA, USA [102]) expressed, 'We're not guaranteeing they will or they will not develop a disease, but I think individuals have a right to know whether they are at increased risk genetically, in the same way that knowing you have high blood pressure puts you at increased risk of heart disease' [8]. It has also been argued that knowledge

of an increased disease risk may allow, and even encourage, individuals to modify their behavior in order to avoid developing the condition [7]. In addition, it has been suggested that, by using saliva samples for analysis, companies offering DTC services are able to increase confidentiality (guarantee their consumer's anonymity), since bypassing a medical physician means that genetic information may not necessarily be kept in the consumer's traditional healthcare file. Despite these potential advantages, based on our review of DTC genetic services, we conclude that most tests marketed for susceptibility testing for common complex disorders have, as yet, not been proven clinically beneficial for consumers, and generate various other concerns regarding psychosocial aspects of genetics.

'If a company's profits are dependent on selling tests, how could employees hired by that same company be completely impartial and not routinely suggest testing to potential clients?'

First, concerns revolve around technical issues such as the analytic and clinical validity, and the clinical utility, of the tests. Analytic validity refers to 'the accuracy with which a particular genetic characteristic (e.g., a DNA sequence variant) can be identified in a given laboratory test [9]'. Although there is, as yet, no report regarding the performance of the genotyping methods within a commercial setting, most researchers consider the analytic validity of the methods used to be rather high [10]. Clinical validity refers to the strength of the association between the genotype and disease. Basically, if the risk genotype is identified in an individual, what are the chances that he or she will develop the disease [6]? Within the context of common multifactorial diseases, apart from a small number of exceptions, most genotype-disease associations are not very strong. Moreover, in a recent article in which they assess the scientific basis of commercial genomic profiles used to measure health risks, Janssens *et al.* state that 'there is insufficient evidence to conclude that genomic profiles are useful in measuring genetic risk for common diseases or in developing personalized diet and lifestyle recommendations for disease prevention' [11]. Likewise, in the USA, the Government Accountability Office (GAO) investigated the legitimacy of claims made by nutrigenetics companies who advertised being able to provide personalized

nutrition and lifestyle recommendations based on genetic information [12]. The GAO concluded that 'the tests we purchased (from these nutrigenetics companies) mislead the consumer by making health-related predictions that are medically unproven and so ambiguous that they do not provide meaningful information to consumers'. Multifactorial disorders are hypothesized to occur due to a complex interaction of multiple genes and environmental factors; both individual and compounded factors are poorly understood. Each genetic and environmental factor often contributes only a modest fraction of the risk of developing the disorder, therefore making it extremely difficult to assign an accurate and meaningful degree of risk to each different factor. Ultimately, the reason that we would want to undergo genetic testing at all is based on a test's clinical utility. That is to say, once a genetic variant known to increase one's risk of developing a disease has been identified, how can this be useful in clinical practice? How can this be of any use to the patient who is trying to reduce his/her risk of developing a disease? Will this genetic information add to our knowledge of what should be done to prevent disease? At present, physicians routinely recommend one or more of the following preventive measures for cardiovascular disease, diabetes and obesity: do not smoke, exercise regularly, eat a nutritious and balanced diet, reduce stress and control blood pressure. Genetic information is not likely to change these recommendations. Moreover, one should also question the clinical utility of testing for conditions that have no known treatment, such as Alzheimer's disease.

Second, concerns should be raised regarding the pre- and post-test counseling offered within the DTC services. This is a far-reaching concern, since without the obligation to meet with a physician, pre- and post-test genetic counseling is the only way to increase consumer knowledge and understanding of the testing process, the meaning of the test results, and the possible consequences for the consumer and his/her relatives. Although some companies, such as DNAdirect (CA, USA) [103] and MediChecks (London, UK) [104], do require pre-test counseling for conditions such as breast cancer, most tests offered do not require any counseling at all. As for post-test counseling, some companies provide some form of this automatically with the test results (e.g., DNAdirect), while others make little, if any, mention of this particular service on their

websites (e.g., Graceful Earth). Further worries stem from questions regarding the qualifications and impartiality of genetic counselors hired by these companies. If a company's profits are dependent on selling tests, how could employees hired by that same company be completely impartial and not routinely suggest testing to potential clients? Interestingly, when we filled out the multiple choice pre-test questionnaire for breast and ovarian cancer from DNAdirect, choosing all the options with the lowest risk (including choosing male as the gender), the message provided by the company still suggested that testing could be appropriate under some circumstances: "Your answers do not indicate that you are at increased risk for hereditary breast and ovarian cancer. According to the information you provided, medical guidelines do not recommend testing for you. However, there are certain circumstances in which testing may be appropriate". It is also worth noting that even if genetic counselors are properly qualified and are nondirective, the genetic counseling sessions in this context occur over the telephone, the effectiveness of which still remains to be determined [13].

The lack of adequate counseling and consequent misunderstanding of test results could lead to confusion and apprehension regarding results. Genetic results for common complex disorders are complicated by the fact that they are probabilistic in nature, and must be interpreted in the context of family history, present health status and other environmental conditions. Consumers who obtain a test revealing a form of increased risk may overestimate the risk they have of developing disease and this may cause undue stress and anxiety and unnecessary follow-up tests or treatments. Meanwhile, consumers with results that suggest standard or inferior-than-average risk of developing a disorder may understand this as meaning that they no longer have to worry about leading a healthy lifestyle. Moreover, without consumers having to consult an impartial healthcare professional or being required to participate in genetic counseling, it is difficult to envisage how companies can ensure that fully informed consent is obtained. Informed consent entails providing the patient with all the relevant information regarding a test, including the potential risks and benefits, making sure the patient truly understands the material and, finally, ensuring that the patient is, in fact, competent to make a decision.

Third, present DTC services are organized in such a way that there is no control over the origin of the samples being analyzed. Most companies

send mouth-swab kits, as these are easier and more practical than having to send the client to a clinic where blood is drawn. Since the mouth swab is performed in the privacy of the clients' home, there is no way of controlling for the identity of the sample provider. Testing of third parties, such as incompetent minors or incapacitated adults, becomes possible and rather impossible to control.

Fourth, DTC services challenge the organization of public healthcare systems. It may be true that some genetic tests (e.g., *BRCA* test) are not offered to certain individuals because they do not meet specific risk criteria (e.g., no family risk of breast cancer), and these individuals may wish to seek testing outside the public healthcare system. One could argue that this is beneficial because it relieves anxiety and provides these women with reassurance. However, this practice challenges the entire rationale of providing services only when they are considered to be medically necessary or clinically relevant. Would adequate genetic counseling not be a better substitute to relieve stress and offer peace of mind than testing, which provides dubious and ambiguous results? Furthermore, providing genetic services outside the traditional path of medical genetics departments may nonetheless challenge the public healthcare system owing to the outcomes of these services. DTC services may stimulate consumers to visit healthcare professionals after a measurement of their risk of developing a disorder, and therefore there is a potential risk of overconsumption of healthcare services.

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With this long list of well-founded apprehensions regarding DTC genetic testing, it is no surprise that a number of professional [5,14] and governmental organizations [105,106] and advisory bodies [15,16] have issued statements and reports warning consumers to be skeptical of the claims made by companies selling these tests. What is more startling and troubling is the lack of any concrete and clear regulatory framework or basic oversight of such services and company practices [17,107].

Although a specific analysis of each DTC test would be necessary to support our statement, based on our review, most DTC genetic tests being sold at the present time can be seen as an

uninformative waste of consumers' money and time. Moreover, they have the potential to cause concrete and extensive harm to consumers' health and wellbeing. It is imperative that regulatory guidelines be imposed in order to control the sale of genetic testing. This might be implemented by an independent body that analyzes the analytical validity, the clinical validity and the clinical utility of each test proposed and assesses whether bypassing a healthcare professional in this context is acceptable. This should apply to *in vitro* diagnostics, which are tests that can be packaged and sold in drugstores as kits or medical devices, as well as to home-brew tests, which are elaborated in laboratories and sold as services. It will also be essential to place a weighty emphasis on ensuring that impartial and qualitative genetic counseling is available for consumers. Finally, it will be necessary to properly train physicians so that they are capable of engaging in an effective and constructive dialogue when patients ask questions regarding these services.

At a time when there is a pull from consumers, as well as a push from the healthcare system, for consumers to take on more and more responsibility for their own health, it is understandable that there is an increased interest in do-it-yourself testing schemes. However, owing to the potential for harm caused by the direct sale of genetic tests to consumers and the dubious clinical utility of the test results, this is an area where governmental regulations must be established and where public education must be improved before consumer autonomy can be properly supported.

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