It is game over for 23andMe, and rightly so

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DNA peddling needs to be banned. Credit: home_of_chaos

The market for personal genome services is facing a reality check. While the most prominent and innovative company 23andMe has flourished so far, in the past few years many of its competitors have gone out of business. Now, with the latest warning from the US Food and Drug Administration (FDA), the rest of the genome testing industry may be counting its days too. This is because 23andMe has failed to provide scientific evidence for their genetic tests and the FDA has urged them in a public letter to halt the marketing of their services until further notice.

The FDA treats genetic testing as a "medical device", and it wants all such devices to meet high quality standards. In this the FDA is right. 23andMe provides information that may lead its users to self-medicate, which, if based on faulty information can lead to serious adverse effects. The FDA does not mind if people would like to know what their DNA sequence is, but it is concerned about the interpretation of that data by 23andMe.

The FDA's letter is unlikely to have surprised the people at 23andMe. They acknowledge their own concern in their Terms of Service. They are also aware of the limited predictive ability of their tests for common diseases. 23andMe follows scientific progress in genetic risk prediction research closely, and by now they must have realised that the promise of personal genome services has faded.

In 2009, when the company first filed for marketing authorisation of their service, the future of genetic prediction looked very bright. The discovery of genetic markers for common diseases had just started to take off. Each issue of *Nature Genetics*, the top journal for scientific discoveries in genetics and genomics, reported new markers for different diseases. It seemed global collaborations would soon rapidly unravel the genetic origins of disease.

But the reality appeared more complex.

Genomics researchers caught the bigger fish first, as new markers had increasingly smaller effects on disease risk. By now, only four years later, many scientific studies have investigated the predictive ability of risk models similar to those on which 23andMe's tests are based. Their results have been mostly discouraging, even though researchers have never used that word. Genetic markers are generally unable to predict risk of common diseases, and adding more markers to risk models does not improve their predictive ability that much.

The results of these studies are no surprise: most of them have investigated risk predictions that are based on relatively few genetic markers. For instance, 23andMe uses only 15 markers to predict the risk of coronary heart disease, 11 for type-2 diabetes, two for melanoma and obesity, and one for esophageal and stomach cancer. These numbers are much lower than the dozens that have already been discovered. Predictive ability can be good only if markers have a lot of impact on disease risk, such as in age-related macular degeneration and several autoimmune diseases.

Champions of the genetic medicine revolution could have been warned by looking at the degree of "heritability" of diseases. The lower this percentage, the less predictive the test can become. 23andMe discloses these estimates:

Heritability of melanoma is estimated at around 20%; type-2 diabetes at 26%; colorectal, esophageal and stomach cancer all around 30%; coronary heart disease between 39% and 56%; and type-1 diabetes between 72% and 88%.

But what does this mean? The high heritability of type-1 diabetes means that genes play a dominant role in causing the disease. If scientists manage to unravel all genetic markers for type-1 diabetes, a genetic test will be able to predict with high accuracy if a person will get diabetes.

Unfortunately, due to all the complex interactions between the markers, this full unravelling is impossible. The number of interactions is probably so high that every patient will have his or her own unique complex cause of disease. And what has never happened cannot be identified or predicted by big data.

Advances in genome science will improve what tests offer, but these improvements will be small. While the hope is based on big data, the

reality is that most diseases are simply not genetic enough. Other risk factors such as diet, body weight, smoking, exercise and stress are too important. And big data cannot change the biology of diseases – it will not make them more genetic.

That is why genetic testing for common diseases will never become as predictive as champions of genetic testing hope.

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