Genetic risk tests aren't always useful—and could even be harmful

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Polygenic risk scores currently account for only a small proportion of your total genetic risk. Credit: Shutterstock

Genetic testing used to be something that happened in a specialist clinic for those few families that had serious inherited conditions, like Huntington's Disease or rare cancers.

Now, new genetic tests called "polygenic risk scores" have increased access to genetic risk information for a wide range of conditions. With a

few clicks of a mouse and a few hundred dollars, anyone can access their or their genetic risk scores for diabetes, obesity, breast cancer, autism, and schizophrenia.

These scores aren't always useful, and, in some cases, they could be harmful.

Results can be misleading

Previous approaches to genetic testing looked at just one gene for which particular mutations are known to cause a disease. The newer technology of polygenic risk scores are calculated from hundreds, if not thousands, of genetic markers measured from your DNA at many points on the genome. These measurements are fed into a formula, based on studying people who do or do not have a condition, to produce a "personalised" genetic risk score.

While researchers are looking at how these tests might be used by doctors to predict type 1 diabetes in newborns, or prescribe the right medications for people with heart disease, companies like 23andme are forging ahead with products that offer polygenic risk scores for diabetes and other conditions to their customer base of over 10 million. As these are classified as "general wellness" products by US regulators, they can be provided without medical support.

Before we jump wholeheartedly into the new world of genetic health and medicine, it's important to consider the implications for patients and clinicians, and especially for consumers outside the clinic. Even if risk scores incorporate information from many different genes, there are two things they currently miss.

First, polygenic risk scores currently account for only a small proportion of a person's total genetic risk. Second, environmental risk factors are

also important, and likely multiply the risks associated with genetic factors. A genetic risk score alone can give a misleading picture of your actual disease risk.

They can be inaccurate

There are questions about the accuracy of the genetic scores. Scores are calculated using past research into genetic associations with a particular condition. That is, the gene variants that are more commonly seen in people with the disease.

But knowing what gene variants are more common in people with a disease is different to knowing what gene variants will predict that someone without the disease will get it later in life. While more research is needed to develop genetic tests that are useful for predicting complex chronic diseases, some companies are forging ahead with genetic risk products of doubtful accuracy.

Companies marketing genetic risk scores might use their own specific formula drawing on different published data to generate the risk predictions they return to their consumers. This means that one person could submit their samples to multiple companies and have different—and sometimes conflicting—results returned to them.

Some consumers of genetic ancestry tests know this well, as results from the same company drastically change when they update their formulas.

In rare cases, the results of genetic testing can be plain wrong, with distressing consequences. One woman had her breasts surgically removed to reduce her risk of breast cancer after receiving a genetic test result that turned out to be incorrect.

In addition, the jury is still out on whether knowing you are at an

increased genetic risk for something will lead to a decrease in your risk of developing the condition. There is evidence from research on depression, for example, that suggests knowing you are genetically at risk may hinder rather than help recovery.

Testing could increase health disparities

Even if the predictive power of a particular genetic risk score is beyond doubt, it may only be accurate for a minority of the population who have only European ancestors.

About 80% of the data used to derive the scores have come from studies of people of European descent (who account for only 16% of the world's population).

So these scores might be less accurate for people from other backgrounds. If these new tools are applied to improve health for people of European ancestry, they could actually increase health disparities.

The ethics of 'designer babies'

All these issues are compounded if the person buying the test is a prospective parent seeking to select an embryo for implantation.

Within the clinical setting, pre-implantation genetic testing—used in tandem with IVF—can help parents who want to ensure their future child does not develop a serious genetic disease that runs in their family. But some companies are now offering to calculate polygenic risk scores that allow prospective parents to select embryos that have a lower risk score for diabetes, heart disease, cancer, short stature or low intelligence irrespective of the family history.

These products raise serious and wide-ranging scientific and ethical

concerns. Researchers have questioned whether selecting embryos on the basis of these tests will actually produce the outcomes parents might expect. Others have raised broader concerns about the long term effects of embedding inequities in our genes.

National agencies that regulate the use of these emerging technologies will need to tread carefully when considering how polygenic risk scores could be used in embryo selection.

For now, more research is required to improve the accuracy of polygenic risk scores, to assess their appropriate use outside of the clinical setting, and to work out how to best support consumers who may find themselves in an uncertain position.

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