Study reveals flaws in gene testing; results often conflict

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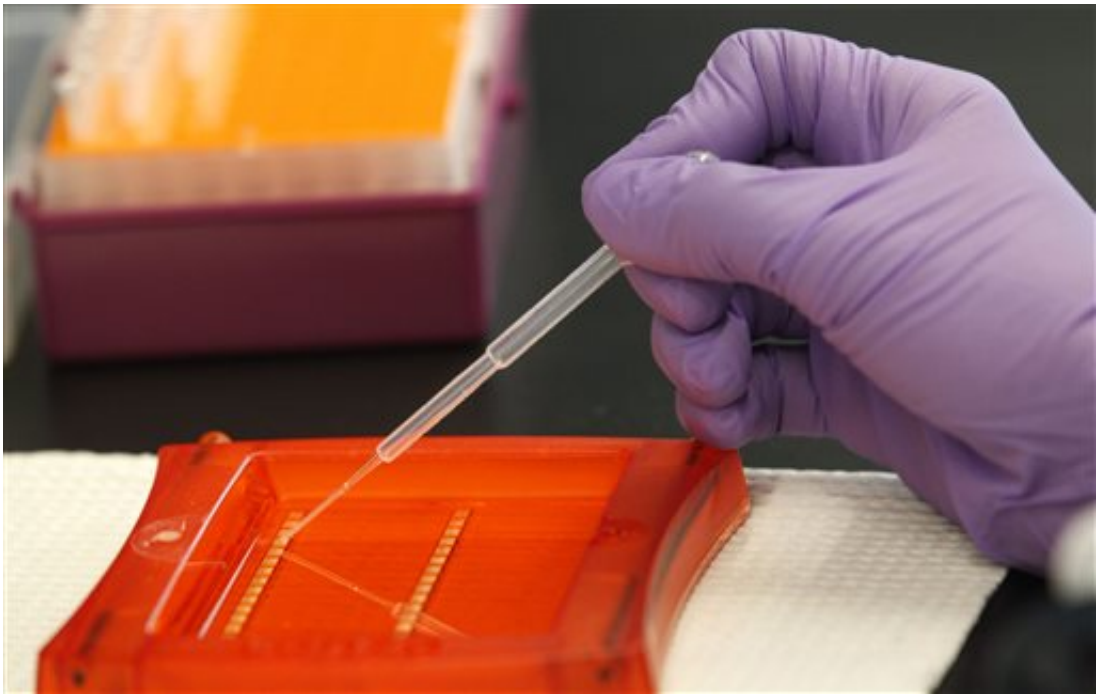

In this Thursday, Sept. 29, 2011 file photo, a scientist works with DNA samples in a New Orleans laboratory. On Wedensday, May 27, 2015, the first report from a big public-private project to improve genetic testing reveals it is not as rock solid as many people believe, with flaws that result in some people wrongly advised to worry about a disease risk and others wrongly told they can relax. (AP Photo/Gerald Herbert)

The first report from a big public-private project to improve genetic testing reveals it is not as rock solid as many people believe, with flaws

that result in some people wrongly advised to worry about a disease risk and others wrongly told they can relax.

Researchers say the study shows the need for consumers to be careful about choosing where to have a gene test done and acting on the results, such as having or forgoing a preventive surgery.

"We have very clear documentation that there are differences in what patients are getting" in terms of how tests on the same gene variations are interpreted, said the study leader, Heidi Rehm, genetics lab chief at Brigham and Women's Hospital in Boston.

When deciding to get tested, either through a doctor's office or by sending in a swab to a private company, "patients need to choose labs that are sharing their data" with the broader research community so scientists can compare and learn from the results and make testing more accurate for everyone, she said.

Dozens of companies now offer gene tests to gauge a person's risk of developing various disorders. One of the newest tests on the market costs $250 and checks about 20 genes that can affect breast cancer risk.

But not all gene mutations, or variants, are equal. Some raise risk a lot, others just a little, and some not at all. Most are of unknown significance—a quandary for doctors and patients alike. And most variants are uncommon, making it even tougher to figure out which ones matter and how much.

To solve these mysteries and give patients better information, the U.S. government several years ago helped form and fund ClinVar, a database for researchers around the world to pool gene findings, coded to keep patients' identities confidential. More than 300 labs contribute to it, including universities such as Harvard and Emory and some private

companies such as Ambry Genetics and GeneDX.

On Wednesday, the group made its first report at a conference in Washington. The study also was published online by the *New England Journal of Medicine*.

So far, the project has tracked more than 172,000 variants in nearly 23,000 genes, a small portion of the millions known to exist but some of the more common ones that have been identified.

More than 118,000 of these variants have an effect on the risk for a disease—and 11 percent have been analyzed by more than one lab so results can be compared. In 17 percent of those cases, labs interpreted the findings differently, as either raising the risk of a disease, having no effect on it or having an unknown effect.

At least 415 gene variants now have different interpretations that could sway a medical decision, such as whether to have healthy breasts or ovaries removed to lower the risk of cancer, or to get a medical device such as an implanted defibrillator to cut the risk of sudden cardiac death.

"The magnitude of this problem is bigger than most people thought," said Michael Watson, executive director of the American College of Medical Genetics and Genomics, one of the study's authors and a partner in the data pooling project.

And it can harm patients. Rehm described a woman who had genetic testing and wrongly was told she did not have elevated risks for breast cancer. She later developed the disease but could have had preventive surgery had the right gene analyses been done.

An independent expert, Dr. Eric Topol, director of the Scripps Translational Science Institute in La Jolla, California, commended the

study leaders and the database project for "cleaning up the mess" from labs that have not shared data in the past.

"We need millions of people sequenced, sharing all the data," to make things better, he said. With more sharing, the mystery gene variant problem " will largely go away, but that's going to take a few years at least."