Genetic screening algorithm could identify people with kidney disease risk

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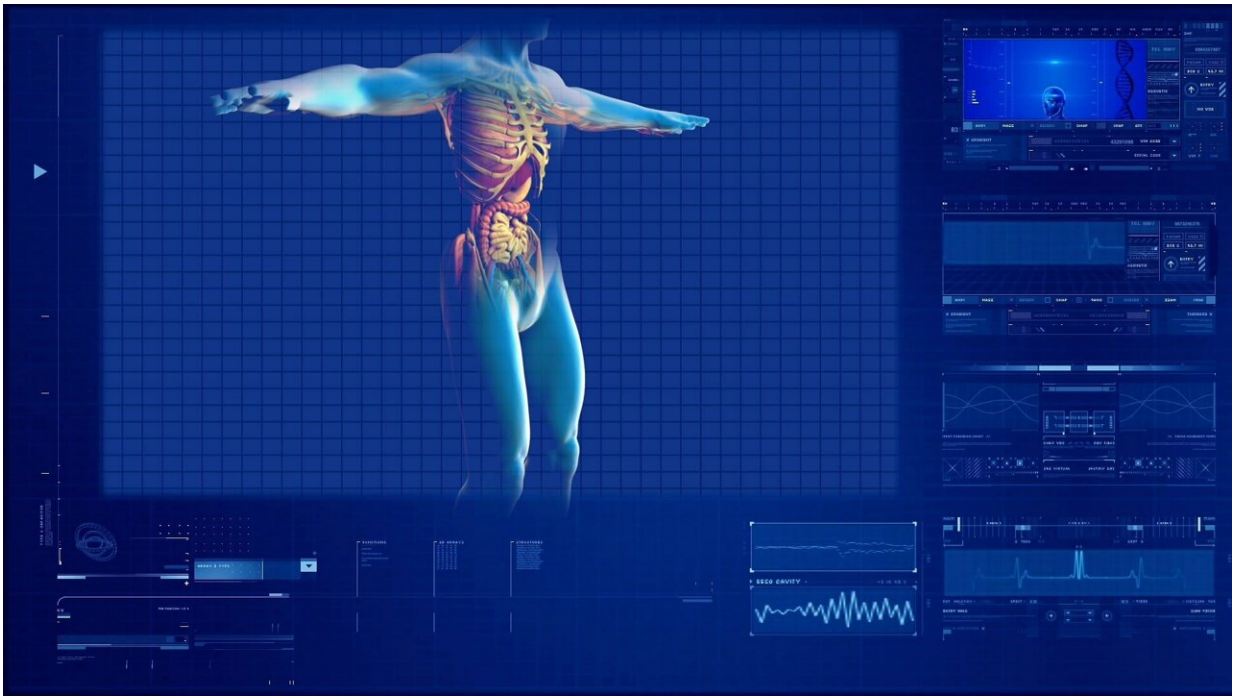

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A new algorithm developed by researchers at Columbia University can analyze thousands of variants across the genome and estimate a person's risk of developing chronic kidney disease—and it works in people of African, Asian, European, and Latinx descent.

"With this polygenic method, we can identify individuals at risk decades

before the onset of kidney disease, and those with high risk might adopt protective lifestyle changes to reduce that risk," says Krzysztof Kiryluk, MD, associate professor of medicine and a physician-scientist in the division of nephrology at Columbia University Vagelos College of Physicians and Surgeons. (Diabetes, high blood pressure, obesity, and certain medications, such as NSAIDs, are known to increase the risk of kidney disease.)

Early detection of kidney disease could prevent many cases of kidney failure and reduce the need for transplant or dialysis, but the disease is often silent until it has caused significant kidney damage.

Genetic testing could offer a way to predict a person's risk of kidney disease well before symptoms appear, but thousands of inherited variants are likely involved and most have only small effects. Adding to the complexity, certain genetic variants are more common in some ethnicities than others.

"In most populations, we can't just look at one or two genetic variants and tell you what your risk is," says Kiryluk. "Thousands of variants are likely contributing."

In a new study published online in *Nature Medicine*, Kiryluk and his team described their method and tested it on 15 different groups of people, including those of European, African, Asian, and LatinX descent. The algorithm analyzes variants of a gene called APOL1—known to be a common cause of kidney disease in people of African descent—and thousands of other kidney disease variants found in people of all ancestries.

Across all ancestries, people with the highest scores (in the top 2%) had triple the risk of kidney disease as the general population, equivalent to having a family history of kidney disease.

The study also confirmed that APOL1 was an important risk factor in people of African descent. But even when APOL1 is present in an individual, other genes can increase or decrease the risk of developing chronic kidney disease. "For people of African ancestry, APOL1 is an important part of the picture, but not the only part," Kiryluk says. This information may be significant when new drugs being developed specifically for people with APOL1 become available.

"Individuals with APOL1 but low polygenic risk may not need specific interventions, since their risk could be comparable to that of the general population," Kiryluk says. "In contrast, individuals with the highest genetic risk—those with APOL1 and a high polygenic risk—may benefit the most from lifestyle changes or drug treatment."

More testing of the new prediction method is needed before it can be used in clinical settings, Kiryluk adds.

The method is being tested in a large national study, called eMERGE-IV, that will screen participants and offer additional follow-up and lab testing for people at high genetic risk. The study will determine if genetic testing for the new risk score affects clinical outcomes, including lifestyle changes and rates of new kidney disease diagnoses.

More information: Atlas Khan et al, Genome-wide polygenic score to predict chronic kidney disease across ancestries, *Nature Medicine* (2022). DOI: 10.1038/s41591-022-01869-1

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algorithm-people-kidney.html