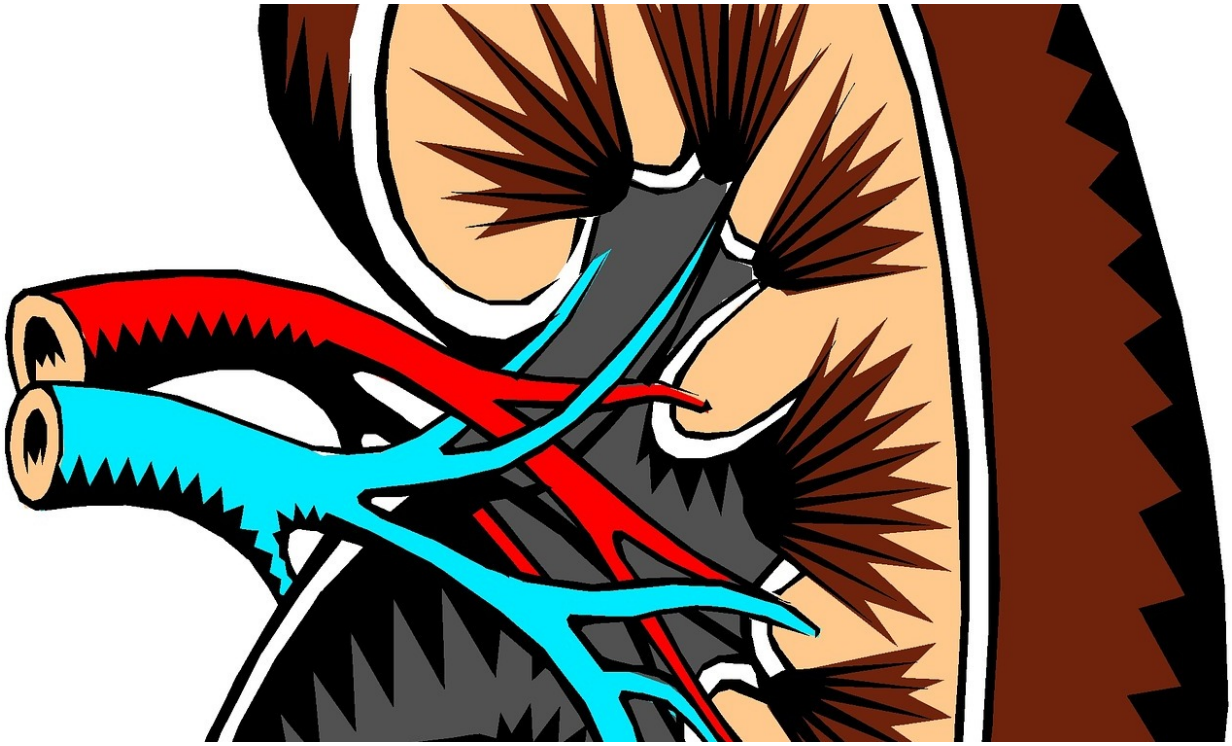
Should people with kidney disease get genetic testing?

July 29 2024



Credit: CC0 Public Domain

About 37 million people in the United States have chronic kidney disease and studies show that genetics may explain between 10% and 20% of cases in adults (and as many as 70% of cases in children).

But genetic testing in kidney disease is not very common compared to

genetic testing in other medical fields, including cancer, pediatrics (for developmental disorders), and obstetrics (prenatal testing).

"There are many benefits of genetic testing for patients with chronic kidney disease, but there's always a lag in adoption whenever a new technology is introduced into practice," says Ali Gharavi, chair of medicine at Columbia University Vagelos College of Physicians and Surgeons.

To help nephrologists make the best use of genetic testing, the National Kidney Foundation convened a working group of experts to develop recommendations for genetic testing and to identify genetic risk factors for complex kidney diseases that have multiple causes.

Gharavi, who has conducted several studies investigating the potential of genetic testing in chronic kidney disease, co-chaired the group with Nora Franceschini, professor of epidemiology at the UNC Gillings School of Global Public Health.

"The recommendations we developed will guide practitioners in selecting the right patients and the right genetic testing modality to advance clinical care and hopefully accelerate the incorporation of genetic testing into practice," Gharavi says.

We spoke with Gharavi to learn more about the new recommendations and which patients may benefit the most from genetic testing.

Why should physicians use genetic testing for some of their patients with kidney disease?

Obtaining a precise diagnosis is very important for clinical care of the patient and for family members. We were among the first groups to

demonstrate the utility of genetic testing for diagnosis: In our study, DNA testing identified a genetic cause of disease in almost 1 out of 10 individuals and reclassified the cause of kidney disease in 1 out of every 5 individuals with a genetic diagnosis. We discovered a genetic cause in nearly 20% of people whose disease could not be identified through the usual clinical workup.

In a growing number of situations, genetic testing leads to a change in treatment. Last year, we and others showed that obtaining a genetic diagnosis can impact clinical management for most patients we tested. Testing led to changes in treatment in about a third of those patients with a positive genetic diagnosis.

Often the treatment changes to avoid immunosuppressive therapies that are not helpful for genetic diseases. However, there are a growing number of targeted therapies available for rare kidney diseases, such as enzyme replacement therapy for Fabry disease or RNAi therapy for primary hyperoxaluria.

Whenever a genetic diagnosis is obtained, we screen family members at risk so we can hopefully intervene in them earlier. Moreover, screening family members helps in the selection of suitable kidney donors for transplantation.

Will genetic testing help all patients with kidney disease?

Studies have shown that many patients could benefit from genetic testing. Testing has a higher diagnostic yield in patients with specific kidney diseases (such as cystic kidney disease, or nephrotic syndrome), those with a young age of onset of disease, those with a family history of kidney disease, and those with multiple organ dysfunction. Genetic

testing can provide a diagnosis in 15% to 20% of patients with kidney failure of unknown cause.

Many kidney diseases are acquired after environmental insults, like toxins, or due to chronic diseases such as long-standing diabetes. There's a lesser need for genetic diagnostics in these situations.

We are still learning about the best indications for genetic testing and our recommendations will change over time as new information comes in.

The news media in the past few years have reported on APOL1 genetic variants that are common in people of African descent and increase the risk of developing chronic kidney disease. Should Black Americans—even those without kidney disease—be tested for APOL1 variants?

This is still an evolving story, so the committee decided not to take this topic on until there are more data available. The APOL1 genetic variants definitely increase the risk of kidney disease, but the variants are present in 13% of African Americans and only a small minority of these individuals go on to develop kidney disease. Therefore, testing is currently not recommended for those without kidney disease.

What should people with chronic kidney disease and their families know about genetic testing right now and what may be possible in the future?

People with chronic kidney disease and their relatives should know that there is a hereditary component to kidney disease. Nowadays, genetic testing is more readily available to clinicians, so patients can discuss

opportunities for testing with their doctors.

In the long term, genetic testing may become part of the initial evaluation for kidney disease and then everyone will have some form of genetic profiling performed routinely.

More information: Nora Franceschini et al, Advancing Genetic Testing in Kidney Diseases: Report From a National Kidney Foundation Working Group, *American Journal of Kidney Diseases* (2024). DOI: 10.1053/j.ajkd.2024.05.010

Provided by Columbia University Irving Medical Center