Largest-ever genetic study of prostate cancer in men of African descent finds new risk factors for the disease

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Prostate cancer takes a greater toll on Black men than on men of other races. In the United States, one in six Black men will get prostate cancer

in their lifetime, compared to one in eight men overall. Black men are also more than twice as likely to die from the disease.

While past studies have identified nearly 270 genetic variants linked to prostate cancer risk, researchers have yet to find a clear explanation for the disproportionate risk among men of African ancestry. Genetic research thus far has also failed to predict which men face a high risk for aggressive prostate cancer, versus those who may get less deadly forms of the disease.

New discoveries from the largest-ever study of prostate cancer in men of African descent are now addressing those long unanswered questions. The meta-analysis, led by researchers at the Keck School of Medicine of USC, includes genome-wide association study data from more than 80,000 men.

The study identified nine new genetic risk factors for prostate cancer, seven of which are found either largely or exclusively in men of African ancestry. For the first time, researchers also found that genetic differences can help determine which men are most likely to develop aggressive prostate cancer. The study was just published in the journal *European Urology*.

"The ability to differentiate between the risk for aggressive and non-aggressive forms of the disease is of critical importance," said Christopher Haiman, ScD, AFLAC Chair in Cancer Research at the USC Norris Comprehensive Cancer Center and senior author of the study. "Until now, risk scores haven't been able to do that."

These findings can be used to refine polygenic risk scores, tools that assess a person's risk for a condition based on the combined influence of multiple genetic factors. More accurate polygenic risk scores for men of African descent could help in identifying high-risk patients early on.

"Prostate cancer survival is significantly lower among men diagnosed with aggressive disease," said Fei Chen, Ph.D., an assistant professor of clinical population and public health sciences at the Keck School of Medicine and the study's first author. "Our findings suggest that these polygenic risk scores could be useful for identifying men who may benefit from earlier and more frequent screenings."

Nine new variants

For the meta-analysis, researchers pooled data from 10 genome-wide association studies—virtually all of the existing data on genetic risk for prostate cancer in men of African ancestry. That includes data collected in the United States, Africa and the Caribbean on 19,378 men with prostate cancer and 61,620 healthy controls.

Haiman, Chen and their colleagues found nine previously undiscovered genetic variants that increased the risk for prostate cancer among men of African descent. Seven of those variants are found primarily—or even exclusively—in this population, which underscores the importance of including diverse populations in large-scale genetic studies, Chen said.

One new variant in the 8q24 region, long known to influence prostate cancer risk, is only found in men of African ancestry. "This particular variant is influencing the risk of aggressive disease in this population," said Haiman, who also co-leads the USC Norris Cancer Epidemiology Program and is the director of the Center for Genetic Epidemiology at the Keck School of Medicine.

The researchers also detected some of the same patterns seen in previous studies, including that genetic influence plays a bigger role in cancer risk for younger men compared with their older counterparts.

Better screening for prostate cancer

The newly identified variants can be incorporated into genetic tests that help patients understand their cancer risk and decide how early and often to get screened, Haiman said.

Through the RESPOND initiative, he and his colleagues are continuing to study the disease among African American men, including how social determinants, access to care and other factors affect prostate cancer recurrence, progression and survival rates. One of their long-term goals is to develop a widely available genetic screening test that can help men of all ages assess their risk levels.

"Through the Robert F. Smith-PCF Special Challenge Award for the Smith Polygenic Risk Test, the Prostate Cancer Foundation is proud to invest in the critical work of the RESPOND investigators to understand and address the reasons why African American men disproportionally experience aggressive prostate cancer, and ultimately advance our shared mission to end death and suffering from this disease," said PCF Executive Vice President and Chief Science Officer Howard R. Soule, Ph.D.

Earlier research by Haiman's team identified many genetic risk factors for prostate cancer and offered early insights on risk among men of African ancestry. Evidence of risk factors specific to this population points to the importance of continuing to collect data from diverse groups, including men of African, Asian and Hispanic descent.

"The vast majority of studies to date have been conducted in populations of European ancestry, which creates a huge bias in our understanding of genetic risk for disease," Haiman said.

More information: Fei Chen et al, Evidence of Novel Susceptibility Variants for Prostate Cancer and a Multiancestry Polygenic Risk Score Associated with Aggressive Disease in Men of African Ancestry,

European Urology (2023). DOI: 10.1016/j.eururo.2023.01.022