Up to 5% of Americans Carry Genetic Mutations Associated with Cancer Risk

Results highlight the importance of routine cancer screenings and suggest genetic testing should go beyond high-risk groups.

November 12, 2025 By Alicia Reale-Cooney and Cleveland Clinic

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New Cleveland Clinic research reveals that up to 5% of Americans – approximately 17 million people – carry genetic mutations or "variants" linked to increased cancer susceptibility, regardless of risk factors like personal or family cancer history.

Published in JAMA, the study suggests that these mutations may be more common than previously thought and highlights the potential for expanded genetic screening to identify more individuals at risk and improve early detection.

The research team, led by Joshua Arbesman, MD, and Ying Ni, PhD, analyzed health records and genetic sequencing data from over 400,000 participants in the National Institute of Health's All of Us Research Program, the country's largest and most comprehensive genetic and healthcare database.

"Genetic testing has traditionally been reserved for individuals with strong family histories or other high-risk indicators," said Dr. Arbesman, a practicing dermatologist and researcher. "Our findings show that many people with pathogenic variants fall outside those criteria, suggesting we may be missing opportunities for early detection and prevention. This research also highlights the importance of regular cancer screenings for all Americans – not just those with a family history or other risk factors."

The team focused on over 70 common cancer-related genes and identified more than 3,400 unique mutations. This builds on prior research by Drs. Arbesman and Ni, which revealed that genetic predisposition to melanoma was 7.5 times higher than national guidelines estimated, underscoring that genetic risk can be underrecognized in routine clinical settings.

As genetic testing becomes more accessible, Drs. Arbesman and Ni say they hope that their findings will support broader adoption of testing and routine cancer screenings such as mammography and colonoscopy.

"Knowing the prevalence of gene variants in the general population will give us a clearer picture

without any pre-assumptions based on lifestyle or family history," said Dr. Ni.

Dr. Arbesman added that "early detection remains the best defense against cancer. Our findings show how widespread cancer risk variants are, underscoring the importance of regular screenings. Long term, we hope to build a truly comprehensive list of genes that guide cancer screening and prevention, so we can find people who would benefit from proactive care."

This news release was published by the Cleveland Clinic on October 27, 2025.
