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Study uncovers genetic cancer risks in 550 patients

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Current screening protocols fail to catch a notable number of people carrying genetic mutations associated with hereditary breast and ovarian cancer syndrome and Lynch syndrome, which increase the risk of developing certain cancers. This issue is particularly pronounced among underrepresented minorities.

These research findings, published in *JCO Precision Oncology*, are based on genetic screenings of more than 44,000 study participants from diverse backgrounds.

For this Mayo Clinic Center for Individualized Medicine Tapestry project, researchers sequenced the exomes—the protein-coding regions of genes—because this is where most disease-causing mutations are found. They identified 550 people, or 1.24%, as carriers of the hereditary mutations.

Importantly, half of these people were previously unaware of their hereditary genetic risk and 40% did not meet existing clinical guidelines for genetic testing.

"This study is a wake-up call, showing us that current national guidelines for genetic screenings are missing too many people at high risk of cancer," says lead author Niloy Jewel Samadder, M.D., a Mayo Clinic gastroenterologist and cancer geneticist at the Center for Individualized Medicine and the Mayo Clinic Comprehensive Cancer Center.

"Early detection of genetic markers for these conditions can lead to proactive screenings and targeted therapies, potentially saving lives of people and their family members."

Hereditary breast and ovarian cancer syndrome is linked to mutations in the BRCA1 and BRCA2 genes. Mutations in BRCA1 can lead to a 60% lifetime risk of developing breast cancer and a 40% risk of having ovarian cancer, among other cancers. BRCA2 mutations increase the risk of developing breast cancer to 50% and ovarian cancer to 20%, with additional risks for prostate and pancreatic cancers in males.

Lynch syndrome is associated with an 80% lifetime risk of developing colorectal cancer and 50% risk of uterine/endometrial cancer.

The study also showed disparities in how underrepresented minority participants met genetic screening guidelines compared to other groups.

"These results suggest the existing guidelines for genetic testing inadvertently introduce biases that affect who qualifies for testing and who receives coverage through health insurance. This leads to disparities in cancer prevention," Dr. Samadder says.

"Our results emphasize the importance of expanding genetic screening to identify people at risk for these cancer predisposition syndromes."

Advancing precision medicine with Tapestry

Altogether, the Tapestry project has now sequenced the exomes of more than 100,000 patients and is integrating these results into the patients' electronic health records. This not only personalizes patient care but also provides a rich dataset for further genetic research.

The overarching mission of Tapestry is to advance personalized medicine and tailor prevention and treatment strategies for individuals, thereby paving the way for targeted health care interventions for all.

More information: N. Jewel Samadder et al, Exome Sequencing Identifies Carriers of the Autosomal Dominant Cancer Predisposition Disorders Beyond Current Practice Guideline Recommendations, *JCO Precision Oncology* (2024). DOI: 10.1200/PO.24.00106

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