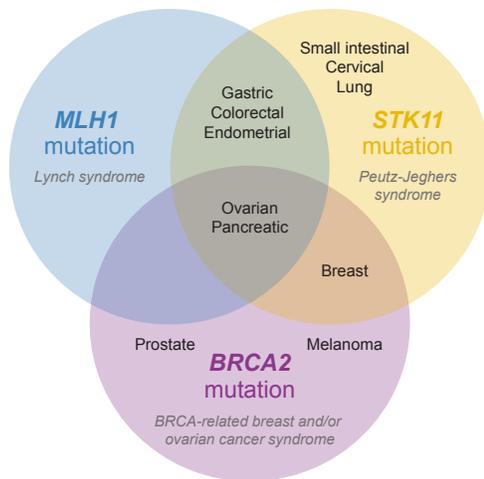


Spotlight on Health

Hereditary Cancer

Hereditary cancer accounts for 5% to 10% of all cancers.¹ People who have inherited a mutation (pathogenic variant) in a cancer-susceptibility gene are at significantly greater risk of developing certain types of cancer compared with those without the mutation. For example, a woman with a *BRCA1* mutation has a 65% lifetime risk of developing breast cancer, whereas a woman without a mutation has a lifetime risk of only 12%.²

Numerous cancer-susceptibility genes have been identified. Many of these genes are associated with multiple cancer types. Conversely, a single cancer type can be linked to mutations in several genes (see **Figure**).



Identifying At-Risk Patients

Patients at risk for hereditary cancer are identified by taking a detailed personal and family history of cancer. This may include the type and number of primary cancer(s), age at onset for each cancer, the individual's relationship to affected family members, and their maternal versus paternal lineage. A person has an increased risk of hereditary cancer if he or she has any of the following:

- A blood relative with a pathogenic or likely pathogenic variant in a cancer-susceptibility gene
- A personal history of ≥ 1 of the following:
 - Cancer diagnosed at age ≤ 50 years
 - Bilateral or multiple primary cancers
 - Cancer diagnosed at any age and significant family history



Degree of Cancer Risk Associated With a Pathogenic Variant

The degree of cancer risk depends on penetrance, gene-gene and gene-environment interactions, as well as patient age and lifestyle. Mutations in high-penetrance genes, such as *BRCA1* and *BRCA2*, are associated with an approximate 70% to 100% lifetime risk of cancer for at least one cancer type.³ The risk is 30% to 60% for mutations in moderate-penetrance genes.³

- Rare cancer (eg, male breast cancer or ovarian cancer)
- Cancer and Ashkenazi Jewish ancestry
- A family history of cancer with ≥ 1 of the following:
 - ≥ 3 Blood relatives on same side of the family with the same or related cancer type
 - ≥ 2 Blood relatives on same side of the family with the same or related cancer type, at least 1 of whom was diagnosed at age ≤ 50 years
 - ≥ 1 Blood relative on same side of the family with the same or related cancer type and Ashkenazi Jewish ancestry

Genetic Testing

Genetic testing is recommended for at-risk patients.⁵ Testing can be performed using a single-site test, a single-gene test, or a multigene panel. Multigene panels may target genes linked to a specific type of cancer or multiple cancer types. Panels may also be designed to analyze genes of a specific penetrance (eg, high and/or moderate penetrance).

Test selection depends on a patient's personal and family history. If a patient has a relative with a known mutation, then a single-site or a single-gene targeted test may be most appropriate. However, if the history is consistent with more than one hereditary cancer syndrome or if the patient's family history is unknown, then a multigene panel test may be considered.

In some patients, use of a multigene panel may be more efficient and cost-effective than sequentially testing single genes. Their use, however, is associated with a higher probability (17% to 38%) of detecting a variant of unknown clinical significance (VUS).⁵ Presence of a VUS should not be viewed as increasing a patient's risk for cancer. Patients with a VUS should be managed based on his or her personal and family history.

Managing Patients With a Positive Genetic Test Result

If a patient tests positive for a known or likely pathogenic variant, then he/she has a greater risk of developing cancer that is linked to the mutation. Steps can be taken to lower that cancer risk or to facilitate early detection of cancer. These steps may include:

- Patient education
- Lifestyle modifications
- Increased and targeted cancer screenings
- Chemopreventive medicines
- Prophylactic surgery

Guidelines recommend referring these patients to specialty oncology centers.

Advancing Awareness of Hereditary Cancer

Of the estimated 941,000 individuals in the United States with a *BRCA* mutation, less than 10% have chosen to be tested and have had mutations identified.⁴

The ability to identify at-risk patients, offer the appropriate tests, and direct them to genetic counselors could narrow this gap in awareness of hereditary cancer. It is, however, important to recognize that the choice to undergo genetic testing is always a personal one.

Hereditary Cancer Testing From Quest Diagnostics

QuestVantage™ includes a comprehensive menu of tests for assessing hereditary cancer risk. These tests, which are performed using next-generation sequencing, detect point mutations, deletions, and duplications.

Our [Hereditary Cancer Test Selection Guide](#) is designed to help doctors select the right test for the right patient. Doctors can select from among single-gene tests, cancer-specific multigene panels, and more comprehensive multigene panels. The more comprehensive multigene panels include:

- **Qvantage™**: a women's health hereditary cancer panel that includes analysis of 14 genes linked to cancer in the breast, colon, endometrium, ovary, rectum, and other tissues.
- **Glvanage™**: a hereditary colorectal cancer panel that includes analysis of 13 genes linked to cancer in the colon, rectum, and other tissues.
- **MYvanage™**: a hereditary cancer panel that includes analysis of 34 genes linked to cancer in the breast, colon, endometrium, ovary, pancreas, prostate, rectum, neuroendocrine system, and other tissues.

Please visit QuestVantage.com for more information about the hereditary cancer tests and services provided by Quest.

References

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