

Genomic Testing (Secondary Findings) ACT Sheet *BRCA1 and BRCA2* Pathogenic Variants (Hereditary Breast and Ovarian Cancer)

Pathogenic or likely pathogenic heterozygous variants (mutations) in the *BRCA1* or *BRCA2* gene are associated with a significantly increased risk for female breast and ovarian cancer, and less often, for other cancers (e.g., male breast, prostate, and pancreatic cancer, and melanoma).

YOU SHOULD TAKE THE FOLLOWING ACTIONS:

- Inform the individual (or parent/guardian) of the result of the genomic screening result and that there is a high lifetime risk of developing cancer.
 - Obtain and review family and medical history.
 - Refer for genetic consultation and counseling.
-

Clinical Considerations:

Females with a heterozygous pathogenic *BRCA1* or *BRCA2* gene variant have a lifetime risk of 38% - 87% for breast cancer and 16% - 63% for ovarian cancer (includes fallopian tube and primary peritoneal cancers). Males with a pathogenic variant in *BRCA1* or *BRCA2* have a lifetime risk of 1% - 9% for breast cancer. Such males also have a higher risk for prostate cancer (9-15% by age 65). Those with pathogenic/likely pathogenic *BRCA2* variants from both sexes have a higher risk for other cancers such as pancreatic and melanoma. Earlier, frequent, and more comprehensive cancer screening is necessary in these patients. Certain medications have been shown to prevent breast cancer in the high-risk population. For individuals with pathogenic variants, risk-reducing mastectomy and salpingo-oophorectomy can substantially lower the risk of cancer.

Prevalence: About 1 in 300 in the general U.S. population, 1 in 40 in the Ashkenazi Jewish population.

Mode of Inheritance: Hereditary cancer predisposition due to a pathogenic variant in the *BRCA1* or *BRCA2* gene is inherited as an autosomal dominant disorder with incomplete penetrance and variability in disease expression. Immediate and extended family members should be offered genetic testing for at least the familial pathogenic variant in the *BRCA1* or *BRCA2* gene. More extensive genetic testing for family members might be appropriate, depending on personal and family history. Note, carriers of a pathogenic *BRCA2* gene variant are at risk of having a child with Fanconi anemia if their partner is also a carrier.

Additional Information:

[NCI Fact Sheet \(BRCA I and II\)](#)

[GeneReviews](#)

[Medline Plus](#)

[ClinGen Actionability Report](#)

Referral (local, state, regional and national):

[Testing](#)

[Find Genetic Services](#)

Disclaimer: This guideline is designed primarily as an educational resource for clinicians to help them provide quality medical care. It should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. Adherence to this guideline does not necessarily ensure a successful medical outcome. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this guideline. Clinicians also are advised to take notice of the date this guideline was adopted, and to consider other medical and scientific information that become available after that date.

LOCAL RESOURCES: Insert local website links

State Resource site *(insert website information)*

Name

URL

Comments

Local Resource Site *(insert local and regional website information)*

Name

URL

Comments

APPENDIX: Resources with Full URL Addresses

Additional Information:

NCI Fact Sheet (BRCA I and II)

<https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet?redirect=true>

Gene Reviews

<https://www.ncbi.nlm.nih.gov/books/NBK1247/>

Medline Plus

<https://medlineplus.gov/genetics/gene/brca1/>

ClinGen Actionability Report

<https://actionability.clinicalgenome.org/ac/Adult/ui/stg2SummaryRpt?doc=AC133>

Referral (local, state, regional and national):

Testing

<https://www.ncbi.nlm.nih.gov/qtr/all/tests/?term=BRCA1>

Find Genetic Services

<https://clinics.acmg.net>

Disclaimer: This guideline is designed primarily as an educational resource for clinicians to help them provide quality medical care. It should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. Adherence to this guideline does not necessarily ensure a successful medical outcome. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this guideline. Clinicians also are advised to take notice of the date this guideline was adopted, and to consider other medical and scientific information that become available after that date.