

## Breast cancer

### Description

Breast cancer is a disease in which certain cells in the breast become abnormal and multiply uncontrollably to form a tumor. Although breast cancer is much more common in women, this form of cancer can also develop in men. In both women and men, the most common form of breast cancer begins in cells lining the milk ducts (ductal cancer). In women, cancer can also develop in the glands that produce milk (lobular cancer). Most men have little or no lobular tissue, so lobular cancer in men is very rare.

In its early stages, breast cancer usually does not cause pain and may exhibit no noticeable symptoms. As the cancer progresses, signs and symptoms can include a lump or thickening in or near the breast; a change in the size or shape of the breast; nipple discharge, tenderness, or retraction (turning inward); and skin irritation, dimpling, redness, or scaliness. However, these changes can occur as part of many different conditions. Having one or more of these symptoms does not mean that a person definitely has breast cancer.

In some cases, cancerous cells can invade surrounding breast tissue. In these cases, the condition is known as invasive breast cancer. Sometimes, tumors spread to other parts of the body. If breast cancer spreads, cancerous cells most often appear in the bones, liver, lungs, or brain. Tumors that begin at one site and then spread to other areas of the body are called metastatic cancers.

A small percentage of all breast cancers cluster in families. These cancers are described as hereditary and are associated with inherited gene mutations. Hereditary breast cancers tend to develop earlier in life than noninherited (sporadic) cases, and new (primary) tumors are more likely to develop in both breasts.

### Frequency

Breast cancer is the second most commonly diagnosed cancer in women. (Only skin cancer is more common.) About one in eight women in the United States will develop invasive breast cancer in her lifetime. Researchers estimate that more than 276,000 new cases of invasive breast cancer will be diagnosed in U.S. women in 2020.

Male breast cancer represents less than 1 percent of all breast cancer diagnoses. Scientists estimate that about 2,600 new cases of breast cancer will be diagnosed in men in 2020.

Particular gene mutations associated with breast cancer are more common among certain geographic or ethnic groups, such as people of Ashkenazi (central or eastern European) Jewish heritage and people of Norwegian, Icelandic, or Dutch ancestry.

## Causes

Cancers occur when a buildup of mutations in critical genes—those that control cell growth and division or repair damaged DNA—allow cells to grow and divide uncontrollably to form a tumor. In most cases of breast cancer, these genetic changes are acquired during a person's lifetime and are present only in certain cells in the breast. These changes, which are called somatic mutations, are not inherited. Somatic mutations in many different genes have been found in breast cancer cells. Less commonly, gene mutations present in essentially all of the body's cells increase the risk of developing breast cancer. These genetic changes, which are classified as germline mutations, are usually inherited from a parent. In people with germline mutations, changes in other genes, together with environmental and lifestyle factors, also influence whether a person will develop breast cancer.

Some breast cancers that cluster in families are associated with inherited mutations in particular genes, such as *BRCA1* or *BRCA2*. These genes are described as "high penetrance" because they are associated with a high risk of developing breast cancer and ovarian cancer and a moderate risk of developing pancreatic cancer and a type of skin cancer called melanoma in women who have mutations. Men with mutations in these genes also have an increased risk of developing several forms of cancer, including breast cancer, pancreatic cancer, prostate cancer, and melanoma. The proteins produced from the *BRCA1* and *BRCA2* genes are involved in fixing damaged DNA, which helps to maintain the stability of a cell's genetic information. They are described as tumor suppressors because they help keep cells from growing and dividing too fast or in an uncontrolled way. Mutations in these genes impair DNA repair, allowing potentially damaging mutations to persist in DNA. As these defects accumulate, they can trigger cells to grow and divide without control or order to form a tumor.

A significantly increased risk of breast cancer is also a feature of several rare genetic syndromes. These include Cowden syndrome, which is most often caused by mutations in the *PTEN* gene; hereditary diffuse gastric cancer, which results from mutations in the *CDH1* gene; Li-Fraumeni syndrome, which is usually caused by mutations in the *TP53* gene; and Peutz-Jeghers syndrome, which typically results from mutations in the *STK11* gene. The proteins produced from these genes act as tumor suppressors. Mutations in any of these genes can allow cells to grow and divide unchecked, leading to the development of a cancerous tumor. Like *BRCA1* and *BRCA2*, these genes are considered "high penetrance" because mutations greatly increase a person's chance of developing cancer. In addition to breast cancer, mutations in these genes increase the risk of several other types of cancer over a person's lifetime. Some of the conditions also include other signs and symptoms, such as the growth of noncancerous (benign) tumors.

Mutations in dozens of other genes have been studied as possible risk factors for breast cancer. These genes are described as "low penetrance" or "moderate penetrance"

because changes in each of these genes appear to make only a small or moderate contribution to overall breast cancer risk. Some of these genes provide instructions for making proteins that interact with the proteins produced from the *BRCA1* or *BRCA2* genes. Others act through different pathways. Researchers suspect that the combined influence of variations in these genes may significantly impact a person's risk of developing breast cancer.

In many families, the genetic changes associated with hereditary breast cancer are unknown. Identifying additional genetic risk factors for breast cancer is an active area of medical research.

Researchers have identified many personal and environmental factors that contribute to a person's risk of developing breast cancer. These factors include sex, age, ethnic background, a history of previous breast cancer, certain changes in breast tissue, and hormonal and reproductive factors. A history of breast cancer in closely related family members is also an important risk factor, particularly if the cancer occurred in early adulthood. In addition, exposure to cancer-causing compounds (carcinogens) can increase the rate at which somatic mutations occur, contributing to a person's risk of developing breast cancer.

#### Learn more about the genes associated with Breast cancer

- ATM
- BRCA1
- BRCA2
- CDH1
- CYP19A1
- FGFR2
- H19
- MAP3K1
- NBN
- PTEN
- RAD51
- STK11
- TERT
- TP53

#### **Additional Information from NCBI Gene:**

- BARD1
- BRIP1
- CASP8
- CHEK2

- CTLA4
- LSP1
- MRE11
- PALB2
- RAD51C
- TOX3
- XRCC2
- XRCC3

## **Inheritance**

Most cases of breast cancer are not caused by inherited genetic factors. These cancers are associated with somatic mutations in breast cells that are acquired during a person's lifetime, and they do not cluster in families.

In hereditary breast cancer, the way that cancer risk is inherited depends on the gene involved. For example, mutations in the *BRCA1* and *BRCA2* genes are inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to increase a person's chance of developing cancer. Although breast cancer is more common in women than in men, the mutated gene can be inherited from either the mother or the father.

In the other syndromes discussed above, the gene mutations that increase cancer risk also have an autosomal dominant pattern of inheritance. It is important to note that people inherit an increased likelihood of developing cancer, not the disease itself. Not all people who inherit mutations in these genes will ultimately develop cancer.

In many cases of breast cancer that clusters in families, the genetic basis for the disease and the mechanism of inheritance are unclear.

## **Other Names for This Condition**

- Breast cancer, familial
- Breast carcinoma
- Cancer of breast
- Malignant neoplasm of breast
- Malignant tumor of breast
- Mammary cancer

## **Additional Information & Resources**

### Genetic Testing Information

- Genetic Testing Registry: Breast cancer, familial male (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1861906/>)
- Genetic Testing Registry: Breast cancer, susceptibility to (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3469522/>)
- Genetic Testing Registry: Malignant tumor of breast (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0006142/>)

#### Genetic and Rare Diseases Information Center

- Breast cancer, male (<https://rarediseases.info.nih.gov/diseases/9312/index>)
- Breast-ovarian cancer, familial, susceptibility to, 1 (<https://rarediseases.info.nih.gov/diseases/12351/index>)
- Breast-ovarian cancer, familial, susceptibility to, 2 (<https://rarediseases.info.nih.gov/diseases/12352/index>)
- Familial breast cancer (<https://rarediseases.info.nih.gov/diseases/10415/index>)
- Inflammatory breast cancer (<https://rarediseases.info.nih.gov/diseases/6784/index>)
- Metaplastic carcinoma of the breast (<https://rarediseases.info.nih.gov/diseases/10804/index>)
- Phyllodes tumor of the breast (<https://rarediseases.info.nih.gov/diseases/9514/index>)

#### Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

#### Clinical Trials

- ClinicalTrials.gov ([https://clinicaltrials.gov/search?cond=%22Breast cancer%22](https://clinicaltrials.gov/search?cond=%22Breast+cancer%22))

#### Catalog of Genes and Diseases from OMIM

- BREAST CANCER (<https://omim.org/entry/114480>)
- BREAST-OVARIAN CANCER, FAMILIAL, SUSCEPTIBILITY TO, 1; BROVCA1 (<https://omim.org/entry/604370>)
- BREAST-OVARIAN CANCER, FAMILIAL, SUSCEPTIBILITY TO, 2; BROVCA2 (<https://omim.org/entry/612555>)

#### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28Breast+Neoplasms%5BMAJ>)

R%5D%29+AND+%28%28breast+cancer%5BTI%5D%29+AND+%28hereditary%5BT  
IAB%5D%29%29+AND+review%5Bpt%5D+AND+english%5Bla%5D+AND+human  
%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

## References

- American Cancer Society: Cancer Facts and Statistics (<https://www.cancer.org/research/cancer-facts-statistics.html>)
- Apostolou P, Fostira F. Hereditary breast cancer: the era of newsusceptibility genes. *Biomed Res Int*. 2013;2013:747318. doi: 10.1155/2013/747318. Epub 2013 Mar 21. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23586058>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3618918/>)
- Economopoulou P, Dimitriadis G, Psyrris A. Beyond BRCA: new hereditary breastcancer susceptibility genes. *Cancer Treat Rev*. 2015 Jan;41(1):1-8. doi:10.1016/j.ctrv.2014.10.008. Epub 2014 Nov 6. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/25467110>)
- Filippini SE, Vega A. Breast cancer genes: beyond BRCA1 and BRCA2. *FrontBiosci (Landmark Ed)*. 2013 Jun 1;18(4):1358-72. doi: 10.2741/4185. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23747889>)
- Foulkes WD. BRCA1 and BRCA2 - update and implications on the genetics ofbreast cancer: a clinical perspective. *Clin Genet*. 2014 Jan;85(1):1-4. doi:10.1111/cge.12291. Epub 2013 Oct 25. No abstract available. Erratum In: *ClinGenet*. 2014 Mar;85(3):302. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24116874>)
- National Cancer Institute: Genetics of Breast and Gynecologic Cancers (PDQ®)– Health Professional Version (<https://www.cancer.gov/types/breast/hp/breast-ovarian-genetics-pdq>)
- Njiaju UO, Olopade OI. Genetic determinants of breast cancer risk: a review ofcurrent literature and issues pertaining to clinical application. *Breast J*. 2012Sep;18(5):436-42. doi: 10.1111/j.1524-4741.2012.01274.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22957996>)
- Petrucelli N, Daly MB, Pal T. BRCA1- and BRCA2-AssociatedHereditary Breast and Ovarian Cancer. 1998 Sep 4 [updated 2023 Sep 21]. In: AdamMP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. *GeneReviews(R)* [Internet]. Seattle (WA): University ofWashington, Seattle; 1993-2024. Available from<http://www.ncbi.nlm.nih.gov/books/NBK1247/> Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20301425>)
- Shiovitz S, Korde LA. Genetics of breast cancer: a topic in evolution. *AnnOncol*. 2015 Jul;26(7):1291-9. doi: 10.1093/annonc/mdv022. Epub 2015 Jan 20. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/25605744>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4478970/>)
- Tung N, Battelli C, Allen B, Kaldete R, Bhatnagar S, Bowles K, Timms K, GarberJE, Herold C, Ellisen L, Krejdovsky J, DeLeonardis K, Sedgwick K, Soltis K, RoaB, Wenstrup RJ, Hartman AR. Frequency of mutations in individuals with breastcancer referred for BRCA1 and BRCA2 testing using next-generation sequencing witha 25-

gene panel. Cancer. 2015 Jan 1;121(1):25-33. doi: 10.1002/cncr.29010. Epub2014 Sep 3. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/25186627>)

**Last updated May 28, 2021**