Risk Factors for Breast Cancer

There are a number of risk factors that increase a woman's risk for developing breast cancer. Increasing age is the most significant risk factor for breast cancer, which is rare in women under the age of 25. Incidence increases with increasing age, with a plateau in women aged 50 to 55 years. Additional risk factors for breast cancer are discussed below.

**Family history:** Family history of breast cancer in a first-degree relative; breast cancer occurring in a relative less than 50 years; male relatives with breast cancer; BRCA1 and BRCA2 mutations; ataxia-telangiectasia heterozygotes; Ashkenazi Jewish descent.

**Neoplastic risk factors:** Previous breast cancer; ovarian cancer; endometrial cancer; ductal carcinoma in situ (DCIS); lobular carcinoma in situ (LCIS).

**Benign risk factors:** Hyperplasia (unless mild); complex fibroadenoma; radial scar; papillomatosis; sclerosing adenosis; microglandular adenosis.

**Exogenous hormones:** Oral contraceptives; hormone replacement therapy (HRT).

**Menstrual and obstetric history:** Nulliparity; first term pregnancy greater than 30 years; menarche less than 12 years; menopause greater than 50 years; not breastfeeding.

Other risk factors include: diethylstilbestrol (synthetic estrogen) use; irradiation, particularly in the first decade of life; exposure to dichlorodiphenyldichloroethylene (DDE), a metabolite of the insecticide dichlorodiphenyltrichloroethane (DDT); long-term use of calcium channel blockers; and lifestyle factors such as alcohol consumption, sedentary lifestyle, and adult weight gain.

The Gail Model is a breast cancer risk assessment tool that calculates a woman's risk of developing breast cancer within the next five years and within her lifetime. It takes a number of key risk factors into account, including race, current age, age when menstruation began, age of first live birth, number of close relatives with breast cancer, number of breast biopsies, and presence or absence of atypical hyperplasia on breast biopsies. Women with a calculated five-year risk of 1.67% and higher are classified as “high risk.”

Breast Cancer Screening

Although the U.S. Preventive Services Task Force (USPSTF) does not recommend teaching breast self-examination (BSE), many groups continue to recommend it. Guidelines developed by the American Cancer Society (ACS) state that it is acceptable for women to choose not to do BSE, or to do BSE regularly (monthly) or irregularly. Beginning in their early 20s, women should be told about the benefits and limitations of BSE. In addition, it is important to emphasize the importance of prompt reporting of any new breast symptoms to a health professional. Women who choose to do BSE should receive instruction and have their technique reviewed at a periodic health examination.

A well-trained healthcare provider should perform clinical breast examination (CBE). The ACS does not recommend CBE for breast cancer screening in average-risk women at any age. The National Comprehensive Cancer Network (NCCN) recommends women start CBE at age 25 and continue after they begin having mammograms.
The American Congress of Obstetricians and Gynecologists (ACOG) recommends annual mammograms for women between the ages of 40 and 49. The ACS recommends that average-risk women start annual mammograms at age 45 and consider transitioning to biennial screening at age 55.

Magnetic resonance imaging (MRI) may be used for women at high risk of developing breast cancer, including those with a positive test for BRCA1 or BRCA2 or who have two or more close family members with breast cancer before age 50. Although it is not used for routine screening in the general population, MRI may be useful for women with breast implants or very dense breast tissue.

**Prophylactic Measures to Decrease Risk of Breast Cancer**

Based on careful risk assessment, pharmacotherapy may be recommended for select patients at increased risk for developing breast cancer. Tamoxifen and raloxifene are selective estrogen receptor modulators (SERMs) that block the effects of estrogen in the breast tissue. Despite evidence that it reduces the risk of developing breast cancer in high-risk women, tamoxifen has not been widely accepted for breast cancer prevention. There is no evidence that tamoxifen improves survival when given as a preventive treatment, and it has been associated with serious adverse events, such as uterine cancer and blood clots in the legs or lungs.

Raloxifene is used for the prevention and treatment of osteoporosis in postmenopausal women. Some studies suggest that raloxifene can reduce the risk of developing estrogen receptor-positive breast cancer in postmenopausal women at high risk of developing breast cancer.

Prophylactic mastectomy is the surgical removal of one or both breasts before cancer develops. Either the whole breast (i.e., total or simple mastectomy) or the underlying breast tissue excluding the nipple (i.e., subcutaneous mastectomy) is removed, and lymph nodes are left intact. Reconstruction may occur immediately after the procedure or may be delayed. Cases in which prophylactic mastectomy should be considered include: mutated BRCA genes found by genetic testing; previous cancer in one breast, especially when there is a strong family history; strong family history (breast cancer in several close relatives); and biopsy specimens showing LCIS.

**Professional Society Guidelines**

Guidelines developed by the NCCN state that risk-reducing mastectomy should generally be considered only in women with a genetic mutation that is associated with a high risk of breast cancer, a compelling family history, LCIS, and/or previous thoracic radiation therapy before age 30.

USPSTF guidelines include a number of interventions that may reduce risk for cancer or cancer-related death in women who are BRCA mutation carriers. These include: earlier, more frequent, or intensive cancer screening; risk-reducing medications (e.g., tamoxifen, raloxifene); and risk-reducing surgery (e.g., mastectomy, salpingo-oophorectomy).

**Determining Medical Necessity for Prophylactic Mastectomy**

Most health plans cover prophylactic mastectomy in patients at high risk of developing breast cancer when specific criteria are met, for example:

- Women diagnosed with breast cancer at 45 years of age or younger; or
- Women who are at increased risk for specific mutation(s) due to ethnic background (for instance: Ashkenazi Jewish descent) and who have one or more relatives with breast cancer or epithelial ovarian cancer at any age; or
- Women who carry a genetic mutation in the TP53 or PTEN genes (Li-Fraumeni syndrome and Cowden and Bannayan-Riley-Ruvalcaba syndromes); or
- Women who possess BRCA1 or BRCA2 mutations confirmed by molecular susceptibility testing for breast and/or epithelial ovarian cancer; or
- Women who received radiation treatment to the chest between ages of 10 and 30 years, such as for Hodgkin disease; or
- Women with a first- or second-degree male relative with breast cancer; or
- Women with multiple primary or bilateral breast cancers in a first- or second-degree blood relative; or
- Women with multiple primary or bilateral breast cancers; or
- Women with one or more cases of epithelial ovarian cancer and one or more first- or second-degree blood relatives on the same side of the family with breast cancer; or
- Women with three or more affected first- or second-degree blood relatives on the same side of the family, regardless of age at diagnosis.

Independent medical review determines medical necessity based on medical policy and published clinical criteria. These high-quality, defensible determinations not only control over-utilization of procedures and therapies but also facilitate safe and effective treatment of patients. Medical necessity must be supported by thorough clinical documentation of breast cancer risk factors and any previous medical treatment. Effective care for patients requires an in-depth understanding of the continually evolving therapies and guidelines for breast cancer.

Independent reviews are designed to meet a variety of needs, including pre-authorizations, internal and external appeals, state and federal appeals, concurrent review of inpatient stay and provider quality of care, and fraud reviews.

As an independent review organization (IRO), AllMed provides access to more than 400 peer review specialists covering more than 80 American Board of Medical Specialties (ABMS) specialties and subspecialties. These specialists are on the cutting edge of the latest medical research and standards of care. Working with an IRO like AllMed allows faster turnaround time for determinations and removes bias from the review process by eliminating conflicts of interest, which can relate to economics, lack of specialists to review cases, or having the same doctor who denied a case review an appeal.

Conclusions

Improvements in risk reduction measures and early detection of cancer through screening have resulted in decreased cancer incidence and mortality in the United States. Prophylactic mastectomy has been a mainstay of preventive care for women at very high risk of breast cancer. However, the potential benefits of the procedure may be limited in women who are not at high risk.
Bibliography

American Congress of Obstetricians and Gynecologists. ACOG Practice Advisory on Breast Cancer Screening. 2015.


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