Surgery to Reduce the Risk of Breast Cancer

What kinds of surgery can reduce the risk of breast cancer?

Two kinds of surgery can be performed to reduce the risk of breast cancer in a woman who has never been diagnosed with breast cancer but is known to be at very high risk of the disease.

A woman can be at very high risk of developing breast cancer if she has a strong family history of breast and/or ovarian cancer, a deleterious (disease-causing) mutation in the *BRCA1* gene or the *BRCA2* gene, or a high-penetrance mutation in one of several other genes associated with breast cancer risk, such as *TP53* or *PTEN*.

The most common risk-reducing surgery is bilateral prophylactic mastectomy (also called bilateral risk-reducing mastectomy). Bilateral prophylactic mastectomy may involve complete removal of both breasts, including the nipples (total mastectomy), or it may involve removal of as much breast tissue as possible while leaving the nipples intact (subcutaneous or nipple-sparing mastectomy). Subcutaneous mastectomies preserve the nipple and allow for more natural-looking breasts if a woman chooses to have breast reconstruction surgery afterward. However, total mastectomy provides the greatest breast cancer risk reduction because more breast tissue is removed in this procedure than in a subcutaneous mastectomy (1).

Even with total mastectomy, not all breast tissue that may be at risk of becoming cancerous in the future can be removed. The chest wall, which is not typically removed during a mastectomy, may contain some breast tissue, and breast tissue can sometimes be found in the armpit, above the collarbone, and as far down as the abdomen—and it is impossible for a surgeon to remove all of this tissue.

The other kind of risk-reducing surgery is bilateral prophylactic salpingo-oophorectomy, which is sometimes called prophylactic oophorectomy. This surgery involves removal of the ovaries and fallopian tubes and may be done alone or along with bilateral prophylactic mastectomy in premenopausal women who are at very high risk of breast cancer. Removing the ovaries in premenopausal women reduces the amount of estrogen that is produced by the body. Because estrogen promotes the growth of some breast cancers, reducing the amount of this hormone in the body by removing the ovaries may slow the growth of those breast cancers.

How effective are risk-reducing surgeries?

Bilateral prophylactic mastectomy has been shown to reduce the risk of breast cancer by at least 95 percent in women who have a deleterious (disease-causing) mutation in the *BRCA1* gene or the *BRCA2* gene and by up to 90 percent in women who have a strong family history of breast cancer (2-5).

Bilateral prophylactic salpingo-oophorectomy has been shown to reduce the risk of ovarian cancer by approximately 90 percent and the risk of breast cancer by approximately 50 percent in women at very high risk of developing these diseases (1).

Which women might consider having surgery to reduce their risk of breast cancer?

Women who inherit a deleterious mutation in the *BRCA1* gene or the *BRCA2* gene or mutations in certain other genes that greatly increase the risk of developing breast cancer may consider having bilateral prophylactic mastectomy and/or bilateral prophylactic salpingo-oophorectomy to reduce this risk.

In two studies, the estimated risks of developing breast cancer by age 70 years were 55 to 65 percent for women who carry a deleterious mutation in the *BRCA1* gene and 45 to 47 percent for women who carry a deleterious mutation in the *BRCA2* gene (6,7). Estimates of the lifetime risk of breast cancer for women with Cowden syndrome, which is caused by certain mutations in the *PTEN* gene, range from 25 to 50 percent (8,9) or higher (10), and for women with Li-Fraumeni syndrome, which is caused by certain mutations in the *TP53* gene, from 49 to 60 percent (11). (By contrast, the lifetime risk of breast cancer for the average American woman is about 12 percent.)

Other women who are at very high risk of breast cancer may also consider bilateral prophylactic mastectomy, including:

- those with a strong family history of breast cancer (such as having a mother, sister, and/or daughter who was diagnosed with bilateral breast cancer or with breast cancer before age 50 years or having multiple family members with breast or ovarian cancer)
- those with lobular carcinoma in situ (LCIS) plus a family history of breast cancer (LCIS is a condition in which abnormal cells are found in the lobules of the breast. It is not cancer, but women with LCIS have an increased risk of developing invasive breast cancer in either breast. Many breast surgeons consider prophylactic mastectomy to be an overly aggressive approach for women with LCIS who do not have a strong family history or other risk factors.)
- those who have had radiation therapy to the chest (including the breasts) before the age of 30 years—for example, if they were treated with radiation therapy for Hodgkin lymphoma [Such women are at high risk of developing breast cancer throughout their lives (12).]

Can a woman have risk-reducing surgery if she has already been diagnosed with breast cancer?

Yes. Some women who have been diagnosed with cancer in one breast, particularly those who are known to be at very high risk, may consider having the other breast (called the contralateral breast) removed as well, even if there is no sign of cancer in that breast. Prophylactic surgery to remove a contralateral breast during breast cancer surgery (known as contralateral prophylactic mastectomy) reduces the risk of breast cancer in that breast (2,4,5,13), although it is not yet known whether this risk reduction translates into longer survival for the patient (13).

However, doctors often discourage contralateral prophylactic mastectomy for women with cancer in one breast who do not meet the criteria of being at very high risk of developing a contralateral breast cancer. For such women, the risk of developing another breast cancer, either in the same or the contralateral breast, is very small (14), especially if they receive adjuvant chemotherapy or hormone therapy as part of their cancer treatment (15,16).

Given that most women with breast cancer have a low risk of developing the disease in their contralateral breast, women who are not known to be at very high risk but who remain concerned about cancer development in their other breast may want to consider options other than surgery to further reduce their risk of a contralateral breast cancer.

What are the potential harms of risk-reducing surgeries?

As with any other major surgery, bilateral prophylactic mastectomy and bilateral prophylactic salpingo-oophorectomy have potential complications or harms, such as bleeding or infection (17). Also, both surgeries are irreversible.

Bilateral prophylactic mastectomy can also affect a woman's psychological well-being due to a change in body image and the loss of normal breast functions. Although most women who choose to have this surgery are satisfied with their decision, they can still experience anxiety and concerns about body image (18,19). The most common psychological side effects include difficulties with body appearance, with feelings of femininity, and with sexual relationships (19). Women who undergo total mastectomies lose nipple sensation, which may hinder sexual arousal.

Bilateral prophylactic salpingo-oophorectomy causes a sudden drop in estrogen production, which will induce early menopause in a premenopausal woman (this is also called surgical menopause). Surgical menopause can cause an abrupt onset of menopausal symptoms, including hot flashes, insomnia,

anxiety, and depression, and some of these symptoms can be severe. The long-term effects of surgical menopause include decreased sex drive, vaginal dryness, and decreased bone density.

Women who have severe menopausal symptoms after undergoing bilateral prophylactic salpingo-oophorectomy may consider using short-term menopausal hormone therapy after surgery to alleviate these symptoms. [The increase in breast cancer risk associated with certain types of menopausal hormone therapy is much less than the decrease in breast cancer risk associated with bilateral prophylactic salpingo-oophorectomy (20).]

What are the cancer risk reduction options for women who are at increased risk of breast cancer but not at the highest risk?

Risk-reducing surgery is not considered an appropriate cancer prevention option for women who are not at the highest risk of breast cancer (that is, for those who do not carry a high-penetrance gene mutation that is associated with breast cancer or who do not have a clinical or medical history that puts them at very high risk). However, some women who are not at very high risk of breast cancer but are, nonetheless, considered as being at increased risk of the disease may choose to use drugs to reduce their risk.

Health care providers use several types of tools, called risk assessment models, to estimate the risk of breast cancer for women who do not have a deleterious mutation in *BRCA1*, *BRCA2*, or another gene associated with breast cancer risk. One widely used tool is the Breast Cancer Risk Assessment Tool (BCRAT), a computer model that takes a number of factors into account in estimating the risks of breast cancer over the next 5 years and up to age 90 years (lifetime risk). Women who have an estimated 5-year risk of 1.67 percent or higher are classified as "high-risk," which means that they have a higher than average risk of developing breast cancer. This high-risk cutoff (that is, an estimated 5-year risk of 1.67 percent or higher) is widely used in research studies and in clinical counseling.

Two drugs, tamoxifen and raloxifene hydrochloride, are approved by the U.S. Food and Drug Administration (FDA) to reduce the risk of breast cancer in women who have a 5-year risk of developing breast cancer of 1.67 percent or more (21-23). Tamoxifen is approved for risk reduction in both premenopausal and postmenopausal women, and raloxifene is approved for risk reduction in postmenopausal women only. In large randomized clinical trials, tamoxifen, taken for 5 years, reduced the risk of invasive breast cancer by about 50 percent in high-risk postmenopausal women (23); raloxifene, taken for 5 years, reduced breast cancer risk by about 38 percent in high-risk postmenopausal women (24). Both drugs block the activity of estrogen, thereby inhibiting the growth of some breast cancers. The US Preventive Services Task Force (USPSTF) recommends that women at increased risk of breast cancer talk with their health care professional about the potential benefits and harms of taking tamoxifen or raloxifene to reduce their risk (25).

Another drug, exemestane, was recently shown to reduce the incidence of breast cancer in postmenopausal women who are at increased risk of the disease by 65 percent (26). Exemestane belongs to a class of drugs called aromatase inhibitors, which block the production of estrogen by the body. It is not known, however, whether any of these drugs reduces the very high risk of breast cancer for women who carry a known mutation that is strongly associated with an increased risk of breast cancer, such as deleterious mutations in *BRCA1* and *BRCA2*.

Some women who have undergone breast cancer surgery, regardless of their risk of recurrence, may be given drugs to reduce the likelihood that their breast cancer will recur. (This additional treatment is called adjuvant therapy.) Such treatment also reduces the already low risks of contralateral and second primary breast cancers. Drugs that are used as adjuvant therapy to reduce the risk of breast cancer after breast cancer surgery include tamoxifen, aromatase inhibitors, traditional chemotherapy agents, and trastuzumab.

What can women at very high risk do if they do not want to undergo risk-reducing surgery?

Some women who are at very high risk of breast cancer (or of contralateral breast cancer) may undergo more frequent breast cancer screening (also called enhanced screening). For example, they may have yearly mammograms and yearly magnetic resonance imaging (MRI) screening—with these tests staggered so that the breasts are imaged every 6 months—as well as clinical breast examinations performed regularly by a health care professional (27). Enhanced screening may increase the chance of detecting breast cancer at an early stage, when it may have a better chance of being treated successfully.

Women who carry mutations in some genes that increase their risk of breast cancer may be more likely to develop radiation-associated breast cancer than the general population because those genes are involved in the repair of DNA breaks, which can be caused by exposure to radiation. Women who are at high risk of breast cancer should ask their health care provider about the risks of diagnostic tests that involve radiation (mammograms or x-rays). Ongoing clinical trials are examining various aspects of enhanced screening for women who are at high risk of breast cancer.

Chemoprevention (the use of drugs or other agents to reduce cancer risk or delay its development) may be an option for some women who wish to avoid surgery. Tamoxifen and raloxifene have both been approved by the FDA to reduce the risk of breast cancer in women at increased risk. Whether these drugs can be used to prevent breast cancer in women at much higher risk, such as women with harmful mutations in *BRCA1* or *BRCA2* or other breast cancer susceptibility genes, is not yet clear, although tamoxifen may be able to help lower the risk of contralateral breast cancer among *BRCA1* and *BRCA2* mutation carriers previously diagnosed with breast cancer (28).

Does health insurance cover the cost of risk-reducing surgeries?

Many health insurance companies have official policies about whether and under what conditions they will pay for prophylactic mastectomy (bilateral or contralateral) and bilateral prophylactic salpingo-oophorectomy for breast and ovarian cancer risk reduction. However, the criteria used for considering these procedures as medically necessary may vary among insurance companies. Some insurance companies may require a second opinion or a letter of medical necessity from the health care provider before they will approve coverage of any surgical procedure. A woman who is considering prophylactic surgery to reduce her risk of breast and/or ovarian cancer should discuss insurance coverage issues with her doctor and insurance company before choosing to have the surgery.

The Women's Health and Cancer Rights Act (WHCRA), enacted in 1999, requires most health plans that offer mastectomy coverage to also pay for breast reconstruction surgery after mastectomy. More information about WHCRA can be found through the Department of Labor.

Who should a woman talk to when considering surgery to reduce her risk of breast cancer?

The decision to have any surgery to reduce the risk of breast cancer is a major one. A woman who is at high risk of breast cancer may wish to get a second opinion on risk-reducing surgery as well as on alternatives to surgery. For more information on getting a second opinion, see NCI's Finding Health Care Services page.

A woman who is considering prophylactic mastectomy may also want to talk with a surgeon who specializes in breast reconstruction. Other health care professionals, including a breast health specialist, medical social worker, or cancer clinical psychologist or psychiatrist, can also help a woman consider her options for reducing her risk of breast cancer.

Many factors beyond the risk of disease itself may influence a woman's decision about whether to undergo risk-reducing surgery. For example, for women who have been diagnosed with cancer in one breast, these factors can include distress about the possibility of having to go through cancer treatment a second time and the worry and inconvenience associated with long-term breast surveillance (29). For this reason, women who are considering risk-reducing surgery may want to talk with other women who have considered or had the procedure. Support groups can help connect women with others who have had similar cancer experiences. The searchable NCI database National Organizations That Offer Cancer-Related Services has listings for many support groups.

Finally, if a woman has a strong family history of breast cancer, ovarian cancer, or both, she and other members of her family may want to obtain genetic counseling services. A genetic counselor or other healthcare provider trained in genetics can review the family's risks of disease and help family members obtain genetic testing for mutations in cancer-predisposing genes, if appropriate.

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