| | |
|---|---|
| **Policy Number** | **SUR716.015** |
| **Policy Effective Date** | **02/01/2025** |
| **Policy End Date** | **12/31/2025** |

# Risk-Reducing (Prophylactic) Mastectomy

| Table of Contents |
|---|
|  |
|  |
|  |
|  |
|  |
|  |
|  |

| Related Policies (if applicable) |
|---|
| SUR717.001: Gender Assignment Surgery and Gender Reassignment Surgery with Related Services |
| |
| |
| |
| |

## Disclaimer

**Carefully check state regulations and/or the member contract.**
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

## Coverage

**This medical policy has become inactive as of the end date above. There is no current active version and this policy is not to be used for current claims adjudication or business purposes.**

**This medical policy does NOT address Gender Reassignment Services (Transgender Services). This medical policy IS NOT TO BE USED for Gender Reassignment Services. Refer to SUR717.001, Gender Assignment Surgery and Gender Reassignment Surgery with Related Services.**

Risk-reducing (prophylactic) mastectomy **may be considered medically necessary** in individuals at high-risk of breast cancer, which includes one or more of the following indications:

- Lobular carcinoma in situ;
- A known *BRCA1* or *BRCA2* variant;
- At high-risk of *BRCA1* or *BRCA2* mutation due to a known presence of the mutation in relatives;
- Another gene variant associated with high risk, e.g., *TP53* (Li-Fraumeni syndrome), *PTEN*

(Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome), *CDH1*, and *STK11*, *PALB2*, or a first-degree relative with one of those syndromes;
- High-risk (lifetime risk about 20% or greater) of developing breast cancer as identified by risk prediction models (see section on Calculation of Breast Cancer Risk Assessment Tools below) that are largely defined by family history; or
- Received radiation therapy to the chest between 10 and 30 years of age.

Risk-reducing (prophylactic) mastectomy **may be considered medically necessary** in individuals with such extensive mammographic abnormalities (i.e., calcifications) that adequate biopsy or excision is impossible.

Contralateral risk-reducing (prophylactic) mastectomy **may be considered medically necessary** for individuals who have been diagnosed with breast cancer in the opposite breast.

Risk-reducing (prophylactic) mastectomy **is considered experimental, investigational and/or unproven** for all other indications, including but not limited to:
- Unilateral or bilateral risk-reducing (prophylactic) mastectomy in individuals at moderate-risk of breast cancer;
- Uncontrolled progress of inflammatory breast disease in one or both breasts (e.g., chronic mastitis, macrocystic or fibrocystic disease).

**Documentation for risk-reducing (prophylactic) mastectomy:** All confirmatory lab and pathology reports and/or progress notes shall accompany any request or claim for mastectomy procedures. In the absence of documentation or confirmatory reports, this procedure will be considered cosmetic.

**Calculation of Breast Cancer Risk Assessment Tools:** Websites available to calculate the risk of breast cancer include, but are not limited to the following:
- For the Gail Model from the National Cancer Institute at the National Institutes of Health (breast cancer risk assessment tool) = bcrisktool.cancer.gov.
- For the Claus Model, it is only available to download as an application to an electronic device.
- For the BRCAPRO Model, it is only available to download as an application to an electronic device.
- For the Tyrer-Cuzick Model = ibis-risk-calculator.magview.com.
- Breast Cancer Surveillance Consortium (BCSC) Risk Calculator = tools.bcsc-scc.org.

**NOTE 1:** Breast cancer risk assessment online tools may be frequently updated or changed. There is no standardized method for determining an individual's risk of breast cancer that incorporates all possible risk factors. There are validated risk prediction models, but they are based primarily on family history.

## Policy Guidelines

None.

## Description

Risk-reducing (prophylactic) mastectomy is defined as the removal of the breast in the absence of malignant disease to reduce the risk of breast cancer occurrence.

**Background**

Risk-reducing (prophylactic) mastectomy may be considered in women thought to be at high-risk of developing breast cancer, either due to family history, presence of genetic variants (e.g., *BRCA1, BRCA2, PALB2*), having received radiotherapy to the chest, or the presence of lesions associated with increased cancer risk such as lobular carcinoma in situ. Therefore, bilateral risk-reducing (prophylactic) mastectomy may be performed to eliminate the risk of cancer arising elsewhere; chemoprevention and close surveillance are alternative risk-reduction strategies. Risk-reducing (prophylactic) mastectomies are typically bilateral but can also describe a unilateral mastectomy in a patient who has previously undergone or is currently undergoing a mastectomy in the opposite breast for invasive cancer (i.e., contralateral risk-reducing [prophylactic] mastectomy). Use of contralateral risk-reducing (prophylactic) mastectomy has increased in the United States. An analysis of data from the National Cancer Database found that the rate of contralateral prophylactic mastectomy in individuals diagnosed with unilateral stage I, II, or III breast cancer increased from approximately 4% in 1998 to 9.4% in 2002. (1) Another analysis of data from the National Cancer Database (N=765,487) found that individuals with unilateral stage I breast cancer commonly underwent contralateral risk-reducing mastectomy, with an increase between 2006 (6%) and 2016 (9%). (2)

The appropriateness of a risk-reducing (prophylactic) mastectomy is a complicated risk-benefit analysis that requires estimates of a patient's risk of breast cancer, typically based on the patient's family history of breast cancer and other factors. Several models are available to assess risk of breast cancer. (3) The specific risk factors included in the models vary, but all incorporate characteristics related to age, reproductive history, and family history. Race should also be considered when assessing risk. According to an analysis of the Surveillance, Epidemiology, and End Results program (SEER) from 2000 to 2015 (N=459,916), the risk of invasive contralateral breast cancer was higher in Black (hazard ratio, 1.44; 95% confidence interval, 1.35 to 1.54) and Hispanic individuals (hazard ratio, 1.11; 95% confidence interval, 1.02 to 1.20) compared to White individuals. (4) In addition to the patient's risk assessment, the choice of a risk-reducing (prophylactic) mastectomy is based on patient tolerance for risk, consideration of changes to appearance and need for additional cosmetic surgery, and the risk-reduction offered by mastectomy versus other options.

A number of other factors may increase the risk of breast cancer but do not by themselves indicate high-risk (generally considered to be a lifetime risk of ≥20%). It is possible that combinations of these factors may be indicative of high-risk, but it is not possible to give

quantitative estimates of risk. As a result, it may be necessary to individualize the estimate of risk considering numerous risk factors. A number of risk factors, not individually indicating high-risk, are included in the National Cancer Institute Breast Cancer Risk Assessment Tool, also called the Gail Model.

Another breast cancer risk assessment tool, used in the Women Informed to Screen Depending on Measures of Risk trial, is the Breast Cancer Surveillance Consortium (BCSC) Risk Calculator (https://tools.bcsc-scc.org). The following information is used in that assessment tool:

- History of breast cancer, ductal carcinoma in situ, breast augmentation, or mastectomy,
- Age/race/ethnicity,
- Number of first-degree relatives (mother, sister, or daughter) diagnosed with breast cancer,
- Prior breast biopsies (positive or negative),
- Breast Imaging Reporting and Data System (BI-RADS) breast density (radiologic assessment of breast tissue density by radiologists who interpret mammograms).

It is strongly recommended that all candidates for risk-reducing (prophylactic) mastectomy undergo counseling regarding cancer risk from a provider skilled in assessing cancer risk other than the surgeon or oncologist, in addition to various treatment options, surveillance, or chemoprevention with tamoxifen or raloxifene.

**Special Comment:** Ductal carcinoma *in situ* (DCIS) is the most common type of breast cancer. Ductal invasive breast cancer begins in the milk duct lining, whereas DCIS is noninvasive, found in the milk duct lining and has not spread outside of the duct to other areas of the breast. DCIS may become an invasive cancer. In contrast, lobular carcinoma *in situ* (LCIS) is a condition in which abnormal cells are found in the lobules of the breast. LCIS is a development of atypical cells that may lead to a tumor which is either benign or malignant.

**Regulatory Status**
Mastectomy is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration (FDA).

## Rationale

Medical policies assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function--including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be

relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

**Risk-Reducing (Prophylactic) Mastectomy**

Clinical Context and Therapy Purpose

The purpose of risk-reducing (prophylactic) mastectomy is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with a high-risk of breast cancer or extensive mammographic abnormalities precluding excision or biopsy.

The following PICO was used to select literature to inform this policy.

*Populations*

The relevant population of interest is women at high risk of breast cancer or extensive mammographic abnormalities precluding excision or biopsy. High-risk is generally considered to be a lifetime risk of 20% or greater. The following list of factors may indicate a high risk of breast cancer:

- Lobular carcinoma in situ (LCIS) which is a precursor to invasive lobular cancer (up to 35% may be bilateral);
- A known *BRCA1* or *BRCA2* variant;
- Another gene variant associated with high risk, e.g., *TP53* (Li-Fraumeni syndrome), *PTEN* (Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome), *CDH1*, *STK11,* and *PALB2*;
- Received radiotherapy to the chest between 10 and 30 years of age.

*Interventions*

The therapy being considered is a risk-reducing (prophylactic) mastectomy.

Risk-reducing (prophylactic) mastectomy is defined as the removal of the breast in the absence of malignant disease to reduce the risk of breast cancer occurrence.

*Comparators*

The following practice is currently being used to treat individuals at high-risk of breast cancer or with extensive mammographic abnormalities precluding excision or biopsy: guideline directed active surveillance or use of chemoprevention.

*Outcomes*

The general outcomes of interest are overall survival (OS), disease-specific survival, functional outcomes, and treatment-related morbidity.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews

Several recent systematic reviews have evaluated the impact of a risk-reducing (prophylactic) mastectomy on health outcomes in women with *BRCA* variants. Li et al. (2016) identified 15 controlled studies evaluating the impact of prophylactic surgeries including bilateral risk-reducing (prophylactic) mastectomy on women with *BRCA1* or *BRCA2* variants. (5) In a meta-analysis of 6 studies with 2555 *BRCA1* or *BRCA2* variant carriers, compared with controls who did not receive a risk-reducing (prophylactic) mastectomy, there was a significantly lower risk of subsequent breast cancer in women who had a bilateral risk-reducing (prophylactic) mastectomy (relative risk [RR], 0.11; 95% confidence interval [CI], 0.04 to 0.32). However, in a meta-analysis of 2 studies in *BRCA1* or *BRCA2* variant carriers with no history of breast cancer, there was no significant effect on breast cancer-specific mortality (hazard ratio [HR], 0.29; 95% CI, 0.03 to 2.61) or on all-cause mortality (HR=0.29; 95% CI, 0.03 to 2.61). Similarly, Ludwig et al. (2016) identified 10 studies on the incidence of breast cancer after bilateral risk-reducing (prophylactic) mastectomy in *BRCA1* or *BRCA2* carriers and found a significant reduction in breast cancer risk ranging from 89.5% to 100%. (6) These reviewers did not conduct pooled analyses of studies on the impact of a risk-reducing (prophylactic) mastectomy on mortality.

Honold and Camus (2018) extracted data from systematic reviews and primary studies to determine if risk-reducing (prophylactic) mastectomy for women with BRCA genes is more effective than active surveillance (periodic clinical examination plus imaging tests) at preventing breast cancer. (7) The authors analyzed data from 13 systematic reviews with a total of 50 studies. The results suggest with high certainty of evidence (based on GRADE system) that active surveillance is less effective at preventing breast cancer than risk-reducing (prophylactic) mastectomy, with 254 per 1000 patients developing breast cancer with only active surveillance and 12 per 1000 with risk-reducing (prophylactic) mastectomy (risk ratio [RR]=0.05; 95% CI: 0.02 to 0.1). Mortality from any cause was also higher for active surveillance than for risk-reducing (prophylactic) mastectomy (RR=0.12; 95% CI: 0.04 to 0.36). The authors also concluded with moderate evidence that up to 64% of women who received the surgery experienced adverse effects (e.g., lower sensitivity, pain, infection, edema, contracture). In addition, they found low certainty of evidence that those who underwent risk-reducing (prophylactic) mastectomy had a decrease in anxiety and depressive symptoms, did not regret having the surgery and were satisfied with the cosmetic results. The results of this meta-analysis do not apply to women with low to moderate risk of breast cancer.

A Cochrane review by Carbine et al. (2018) examined the impact of risk-reducing mastectomy on mortality and other health outcomes. (8) Reviewers did not identify any RCTs. Sixty-one observational studies with some methodologic limitations were identified. The studies presented data on 15,077 individuals with a wide range of risk factors for breast cancer who underwent a risk-reducing mastectomy. Studies on the incidence of breast cancer and/or disease-specific mortality (n=21) reported reductions in both after a bilateral risk-reducing mastectomy, particularly for those with *BRCA1* or *BRCA2* variants.

Section Summary: Risk-Reducing (Prophylactic) Mastectomy

Evidence from systematic reviews has found that risk-reducing (prophylactic) mastectomy reduces the incidence of breast cancer in women at high-risk of breast cancer, especially those with *BRCA1*, *BRCA2*, and other pathogenic variants and those with a formal high-risk familial risk assessment. In addition, 1 study reported that risk-reducing (prophylactic) mastectomy could be associated with high satisfaction levels. Fewer studies have examined the impact of a risk-reducing (prophylactic) mastectomy on overall or breast cancer-specific survival.

**Contralateral Risk-Reducing (Prophylactic) Mastectomy**

Clinical Context and Therapy Purpose

The purpose of contralateral risk-reducing (prophylactic) mastectomy is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with unilateral breast cancer who are not otherwise at high-risk.

The following PICO was used to select literature to inform this policy.

*Populations*

The relevant population of interest is individuals with unilateral breast cancer who are not otherwise at high-risk.

*Interventions*

The therapy being considered is a contralateral risk-reducing (prophylactic) mastectomy.

*Comparators*

The following practice is currently being used to treat individuals with unilateral breast cancer who are not otherwise at high risk: active surveillance with clinical examination, imaging studies and guideline-based treatment of primary breast cancer.

*Outcomes*

The general outcomes of interest are OS, disease-specific survival, functional outcomes, and treatment-related morbidity.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Incidence of Second Primary Breast Cancer

The potential for a contralateral risk-reducing (prophylactic) mastectomy to impact survival is related to its association with a reduced risk of subsequent primary breast cancer in the other breast (i.e., contralateral breast cancer [CBC]). In general, according to data from the U.S. Surveillance, Epidemiology and End Results (SEER) database, annual rates of CBC were stable between 1975 and 1985, after which rates declined about 3% per year (95% CI, 2.7% to 3.5%). (9) Beginning in 1990, the annual decline in CBC rates was only in women with estrogen receptor–positive cancer, with no decrease in women with estrogen receptor–negative cancer. The investigators suggested that the decrease in CBC rates after estrogen receptor–positive cancer might be attributed at least in part to the increased availability of adjuvant hormone therapies.

Studies were sought assessing the risk of CBC in women who met high-risk and average-risk criteria. Molina-Montes et al. (2014) published a systematic review of studies on the risk of a second primary breast cancer in women with and without *BRCA1* or *BRCA2* variants. (10) Twenty studies were included (12 retrospective cohort studies, 2 prospective cohort studies, 6 case-control studies). Most studies included only women who had undergone genetic testing; it is likely that even those who tested negative had other risk factors that motivated testing. A meta-analysis found that the cumulative risk of a second primary breast cancer at 5 years after initial diagnosis was 14% (95% CI, 9% to 19%) in *BRCA1* or *BRCA2* variant carriers and 3% (95% CI, 2% to 5%) in noncarriers. The cumulative risk of a second primary cancer at 10 years after initial diagnosis was 22% (95% CI, 18% to 27%) in *BRCA1* or *BRCA2* variants and 5% (95% CI, 3% to 7%) in noncarriers.

Survival After Contralateral Risk-Reducing (Prophylactic) Mastectomy (CPM)

As is the case for bilateral risk-reducing (prophylactic) mastectomy, no RCTs evaluating the effect of contralateral risk-reducing (prophylactic) mastectomy on health outcomes have been published. There are a number of observational studies, including some with large sample sizes, and a systematic review of those observational studies. Observational studies have attempted to control for potential confounders, but not all relevant factors were measured, and the possibility of selection bias remains.

*Systematic Reviews*

The previously summarized Cochrane review by Carbine et al. (2018) also assessed various outcomes, including mortality and disease-free survival, among individuals who received a contralateral risk-reducing mastectomy. (8) Twenty-six observational studies assessed

outcomes in individuals who received contralateral risk-reducing mastectomy. While results showed a reduced incidence of CBC among those who received a contralateral risk-reducing mastectomy, results on disease-specific mortality were inconsistent. Seven of the included studies showed no survival advantage. One additional study showed an improvement in all-cause mortality associated with contralateral risk-reducing mastectomy; however, significance was lost after adjustment for bilateral risk-reducing salpingo-oophorectomy. The authors attributed the variability in mortality findings, in part, to selection bias, since younger, healthier individuals may be more likely to opt for contralateral risk-reducing mastectomy.

A systematic review and meta-analysis of studies on contralateral risk-reducing (prophylactic) mastectomy was published by Fayanju et al. (2014). (11) The authors conducted a literature search through March 2012 and identified 17 observational studies that compared the incidence of CBC in women with unilateral disease who did and did not undergo a contralateral risk-reducing (prophylactic) mastectomy. Fourteen of the 17 studies were included in various meta-analyses. In a meta-analysis of 4 studies, mortality from breast cancer was lower in the group that had a contralateral risk-reducing (prophylactic) mastectomy (RR=0.69; 95% CI, 0.56 to 0.85). Moreover, in a meta-analysis of data from 6 studies, overall survival was significantly higher in patients who underwent a CPM (n=10,666) than those did not (n=145,490; RR=1.09; 95% CI, 1.06 to 1.11). Reviewers also conducted a subgroup analysis by risk level. A meta-analysis of patients considered high-risk, which included *BRCA* variant carriers and/or with a family history of breast cancer (4 studies, 616 undergoing contralateral risk-reducing (prophylactic) mastectomy, 1318 not undergoing contralateral risk-reducing (prophylactic) mastectomy) found that neither overall survival nor mortality from breast cancer differed significantly among women who had or did not have a contralateral risk-reducing (prophylactic) mastectomy. The RR of breast cancer mortality with and without a CPM was 0.66 (95% CI, 0.27 to 1.64). For overall survival with and without a contralateral risk-reducing (prophylactic) mastectomy, the RR was 1.09 (95% CI, 0.97 to 1.24). The absolute risk-reduction for metachronous breast cancer did not differ between women with and without a contralateral risk-reducing (prophylactic) mastectomy when data from all 8 studies were analyzed (risk difference, -18.0%; 95% CI, -42.0% to 5.9%, but was significantly lower in women with a contralateral risk-reducing (prophylactic) mastectomy in the 4 studies exclusively enrolling women at increased familial/genetic risk (risk difference [RD], -24.0%; 95% CI, -35.6% to -12.4%). Commenting on the totality of findings, reviewers stated that the improvement in survival after a contralateral risk-reducing (prophylactic) mastectomy in the general breast cancer population was likely not due to a decreased incidence of CBC, but rather was secondary to selection bias (e.g., contralateral risk-reducing [prophylactic] mastectomy recipients may be otherwise healthier and have better access to health care).

*Observational Studies*

Studies in the Fayanju et al. (2014) systematic review were published between 1997 and 2005. More recent large observational studies, described below, reported mixed results for OS and disease-specific survival.

An analysis of 17 years of SEER data from 245,418 women in California with unilateral breast cancer assessed secondary contralateral cancer incidence and mortality in women who had bilateral mastectomy or breast conserving therapy. (12) The study adjusted for numerous potential confounders, including demographic and socioeconomic characteristics, clinical characteristics and disease state, and year of diagnosis. Patient race/ethnicity was mostly White (65.1%), followed by Hispanic (15.9%) and Black (5.4%). After a median 7 years follow-up, the study found that when compared with breast conserving therapy that included radiotherapy, bilateral mastectomy was associated with a reduced risk of secondary breast cancer (HR=0.11; 95% CI 0.07 to 0.14) while unilateral mastectomy was associated with increased risk (HR=1.07; 95% CI 1.02 to 1.13). However, the study also found bilateral mastectomy was not associated with a significant reduction in breast cancer-related mortality relative to breast-conserving therapy (HR=1.03; 95% CI 0.96 to 1.11). Compared to White patients, Black (HR, 1.23; 95% CI, 1.13 to 1.35) and Filipina (HR, 1.30; 95% CI, 1.17 to 1.44) individuals had a higher risk of second contralateral breast cancer. Compared to White patients, Black patients had an increased risk of breast cancer death (HR, 1.21; 95% CI, 1.14 to 1.28) while individuals of all other races had a reduced risk of death.

Wong et al. (2017) evaluated 496,488 women diagnosed with unilateral invasive breast disease. (13) Within this cohort, 58.6% (n=295,860) underwent breast-conserving surgery (BCS), 33.4% (n=165,888) had a unilateral mastectomy, and 7% (n=34,740) had a contralateral risk-reducing (prophylactic) mastectomy. The median age was 50 years in the contralateral risk-reducing (prophylactic) mastectomy group and 60 years in the breast conservation group ($p<0.001$). Patient race/ethnicity was mostly White (73.3%), followed by Black (9.5%), Hispanic (8.7%), and Asian/Pacific Islander (7.5%). Patients were followed for a median of 8.25 years. In an analysis adjusting for age and other factors including stage of disease, overall survival was significantly higher after breast conservation than after a contralateral risk-reducing (prophylactic) mastectomy (HR=1.08; 95% CI, 1.03 to 1.14). Similarly, breast cancer-specific survival was significantly higher in the breast conservation group than in the contralateral risk-reducing (prophylactic) mastectomy group (HR=1.08; 95% CI, 1.01 to 1.16).

An analysis of SEER data by Kruper et al. (2014) suggested that the association between contralateral risk-reducing (prophylactic) mastectomy and reduced mortality identified in some data analyses could be attributed at least in part to the selection of a healthier cohort of women for contralateral risk-reducing (prophylactic) mastectomy. (14) In the case-control analysis including 28,015 contralateral risk-reducing (prophylactic) mastectomy patients and 28,015 unilateral mastectomy patients in the SEER database, patients were matched by age group, race/ethnicity, extent of surgery, tumor grade, tumor classification, node classification, estrogen receptor status, and propensity score. The investigators were unable to match for *BRCA* or another genetic variant status. Patient race/ethnicity was mostly White (83%), followed by Hispanic (7%), Black (6%), and Asian/Pacific Islander (5%). When all matched patients were included, disease-specific survival and overall survival were significantly lower in women who underwent unilateral mastectomy compared with contralateral risk-reducing (prophylactic) mastectomy. For disease-specific survival, the HR was 0.83 (95% CI, 0.77 to 0.90); for overall survival, it was 0.77 (95% CI, 0.73 to 0.82). Presumably, contralateral risk-reducing

(prophylactic) mastectomy would increase survival by lowering the risk of CBC. The authors conducted another analysis excluding women diagnosed with CBC; the remaining sample was still large (25,924 women with unilateral mastectomy, 26,299 women with contralateral risk-reducing (prophylactic) mastectomy). In the analysis excluding women with CBC, disease-specific survival, and overall survival remained significantly lower in women who had unilateral mastectomy versus contralateral risk-reducing (prophylactic) mastectomy. For disease-specific survival, the HR was 0.87 (95% CI, 0.80 to 0.94); for overall survival, it was 0.76 (95% CI, 0.71 to 0.81). The investigators suggested that the survival benefits found in CBC patients were not due to prevention of CBC but to selection bias (e.g., healthier women choosing CBC). A multivariate analysis showed that Black and Hispanic patients had increased risk of OS compared to White patients (HR, 1.63; 95% CI, 1.45 to 1.82 and HR, 1.21, 95% CI, 1.07 to 1.38, respectively). A limitation of the analysis was the inability to control for risk factors including gene variant status, family history, and a history of radiotherapy to the chest between ages 10 and 30 years.

Yao et al. (2013) evaluated overall survival after CPM using data from the National Cancer Data Base. (1) The database collects information from 1450 Commission of Cancer-accredited cancer programs. The analysis included 219,983 women who had a mastectomy for unilateral breast cancer; 14,994 (7%) of these women underwent a CPM at the time of their mastectomy surgery. The investigators did not report risk factors such as known genetic variants. Patient race/ethnicity was mostly White (83.9%), followed by Black (8.9%), Hispanic (3.6%), and Asian/Pacific Islander (2.2%). The 5-year overall survival rate was 80%. In an analysis adjusting for confounding factors, the risk of death was significantly lower in women who had a CPM than in women who did not. The adjusted HR for overall survival was 0.88 (95% CI, 0.83 to 0.93). The absolute risk of death over 5 years with CPM was 2.0% lower than without. In subgroup analyses, there was a survival benefit after CPM for individuals 18 to 49 years and 50 to 69 years, but not for those 70 years or older. There was also a survival benefit for women with stage I and II tumors, but not stage III tumors. Compared to White patients, Black patients had decreased survival (HR, 1.32; 95% CI, 1.27 to 1.37) while individuals of all other races had improved survival.

In a subsequent study, Pesce et al. (2014) focused on a subgroup of patients who were young (<45 years old) with stage I or II breast cancer. (15) A total of 4338 (29.7%) of 14,627 women in this subgroup had a contralateral risk-reducing (prophylactic) mastectomy. Patient race/ethnicity was mostly White (76.5%), followed by Black (10.9%), Hispanic (7.6%), and Asian/Pacific Islander (4.4%). Median follow-up was 6.1 years. In a multivariate analysis controlling for potentially confounding factors, overall survival did not differ significantly between patients who underwent a unilateral mastectomy and those who also had a contralateral risk-reducing (prophylactic) mastectomy (HR=0.93; 95% CI, 0.79 to 1.09). Moreover, among women younger than 45 years with estrogen receptor--negative cancer, there was no significant improvement in overall survival in those who had a contralateral risk-reducing (prophylactic) mastectomy or a unilateral mastectomy (HR, 1.13; 95% CI, 0.90 to 1.42). Compared to White patients, Black patients had decreased OS (HR, 1.48; 95% CI, 1.24 to 1.78). Among other races, OS was similar to White patients.

Yang et al. (2021) conducted an analysis of SEER data from 1998 to 2016 of 5118 men with unilateral breast cancer who underwent contralateral risk-reducing mastectomy (n=209 [4.1%]). (16) Patient race/ethnicity was mostly White (82.3%), followed by Black (12.4%), and other races (4.8%). In 1998, contralateral risk-reducing mastectomy was undertaken in 1.7% of men compared to 6.3% in 2016 (p<.0001). Compared to unilateral mastectomy, contralateral risk-reducing mastectomy improved OS (HR, 0.58; 95% CI, 0.37 to 0.89) but a survival benefit was not seen after propensity score-matching (HR, 0.83; 95% CI, 0.46 to 1.52). Contralateral risk-reducing mastectomy did not improve disease-specific survival compared to unilateral mastectomy.

Adverse Events

There are risks and benefits associated with contralateral risk-reducing (prophylactic) mastectomy. In particular, several analyses have found higher rates of surgical complications in women undergoing contralateral risk-reducing (prophylactic) mastectomy (bilateral mastectomy) compared with women undergoing unilateral mastectomy. Besides morbidity associated with these complications, surgical complications may delay receiving adjuvant therapy.

Murphy et al. (2021) published a systematic review and meta-analysis evaluating the complications associated with contralateral risk-reducing mastectomy. (17) Fifteen cohort studies (14 retrospective; 1 prospective) were included (N=6,583). Definitions of what constituted as a complication varied amongst the included studies. In patients who underwent unilateral plus contralateral prophylactic mastectomy, the diseased breast was significantly more susceptible to complications compared to the contralateral breast (RR, 1.24; p=.03). Studies that were stratified by reconstructive method reported that complication risk was significantly higher for unilateral plus contralateral prophylactic mastectomy compared to unilateral mastectomy alone in patients with no reconstruction (RR, 2.03; p=.0003), autologous reconstruction (RR, 1.32; p=.005), and prosthetic-based reconstruction (RR, 1.42; p=.003)

Schroeder et al. (2020) conducted a population-based study of 12959 women who underwent unilateral mastectomy or contralateral risk-reducing mastectomy using data from the New York Statewide Planning and Research Cooperative System. (18) Of these, 1384 underwent a contralateral risk-reducing mastectomy and 11,575 underwent a unilateral mastectomy. After controlling for confounding factors (i.e., race, ethnicity, year of operation, and type of insurance) and stratifying by breast reconstruction, no difference was found in the likelihood of complications or additional breast-related procedures needed between women who received contralateral risk-reducing mastectomy and those who received unilateral mastectomy (both without breast reconstruction). Addition of breast reconstruction was associated with significant increases in complications and breast-related procedures, both in women with unilateral mastectomy (odds ratio [OR], 3.6; p<.001 and OR, 13.7; p<.001, respectively) and in those with contralateral risk-reducing mastectomy (OR, 3.3; p<.001 and OR, 30.1; p<.001, respectively). Patients who underwent contralateral risk-reducing mastectomy were also significantly more likely to undergo breast reconstruction compared to those who underwent unilateral mastectomy (93.1% vs. 46.3%; p<.001).

Silva et al. (2015) published a large multicenter study including 20,501 women with unilateral breast cancer from the American College of Surgeons National Surgery Quality Improvement Program database. (19) A total of 13,268 (64.7%) women underwent a unilateral mastectomy, and 7233 (35.3%) had a bilateral mastectomy. The analysis did not report on high-risk factors such as *BRCA* variant status or family history. All women had breast reconstruction; a higher proportion of women who had a unilateral mastectomy (19.5%) than bilateral mastectomy (8.9%) had autologous reconstruction; the remainder had implant-based reconstruction. The authors conducted analyses controlling for confounding variables (i.e., age, race, smoking, diabetes, chronic pulmonary disease, hypertension) and stratifying by type of implant. The rate of overall complications was significantly higher for women who had a bilateral mastectomy, regardless of reconstruction type. Among women with implant reconstructions, overall complication rates were 10.1% after a bilateral mastectomy and 8.8% after a unilateral mastectomy (adjusted odds ratio [OR], 1.20; 95% CI, 1.08 to 1.33). In women with autologous reconstructions, overall complication rates were 21.2% after a bilateral mastectomy and 14.7% after a unilateral mastectomy (adjusted OR=1.60; 95% CI, 1.28 to 1.99). The most common complication was reoperation within 30 days, followed by surgical site complications. Transfusion rates were also significantly higher ($p<0.001$) in women with bilateral mastectomies who had either type of reconstruction. The rates of medical complications were relatively low-approximately 1% of women who had implant reconstructions and 3% of women who had autologous reconstructions experienced a medical complication (i.e., pneumonia, renal insufficiency or failure, sepsis, urinary tract infection, venous thromboembolism) - and did not differ significantly between unilateral and bilateral mastectomies.

Several single-center studies have also reported significantly higher surgical complication rates after bilateral compared with unilateral mastectomy. For example, in a study by Miller et al. (2013), which included 600 women with unilateral breast cancer, contralateral risk-reducing (prophylactic) mastectomy remained associated with a significantly higher risk of any complication (OR=1.53; 95% CI, 1.04 to 2.25) and a significantly higher risk of major complications (OR=2.66; 95% CI, 1.37 to 5.19) compared with unilateral mastectomy. (20) Moreover, in a study by Eck et al. (2014), which assessed 352 women with unilateral breast cancer, 94 (27%) women had complications, 48 (14%) in the unilateral mastectomy group, and 46 (13%) in the bilateral mastectomy group. (21) The difference between groups was not statistically significant ($p=0.11$), but this study might have been underpowered. Eck found a significant delay in adjuvant therapy after surgical complications: women with complications waited longer before receiving adjuvant therapy than those without complications (49 days versus 40 days, $p<0.001$).

Section Summary: Contralateral Risk-Reducing (Prophylactic) Mastectomy

Large observational studies have reported inconsistent findings on the survival benefit of contralateral risk-reducing (prophylactic) mastectomy in women with unilateral breast cancer who do not otherwise meet high-risk criteria. Researchers have suggested that improvements in survival after contralateral risk-reducing (prophylactic) mastectomy in the general breast cancer population found in some studies are due at least in part to selection bias. Moreover,

there are risks of complications associated with both the surgical and the reconstruction procedures.

**Summary of Evidence**
For individuals who have a high-risk of breast cancer or extensive mammographic abnormalities precluding excision or biopsy who receive a risk-reducing (prophylactic) mastectomy, the evidence includes systematic reviews. Relevant outcomes are overall survival, disease-specific survival, functional outcomes, and treatment-related morbidity. The studies have found that a risk-reducing (prophylactic) mastectomy lowers subsequent breast cancer incidence and increases survival in select high-risk patients. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have unilateral breast cancer but are not otherwise at high risk who receive a contralateral risk-reducing (prophylactic) mastectomy, the evidence includes systematic reviews and observational studies. Relevant outcomes are overall survival, disease-specific survival, functional outcomes, and treatment-related morbidity. Available studies do not demonstrate a consistent survival benefit in women without high-risk criteria. Moreover, there are risks associated with a risk-reducing (prophylactic) mastectomy for both the primary surgical and reconstruction procedures. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

**Practice Guidelines and Position Statements**
American College of Medical Genetics and Genomics
In 2021, the American College of Medical Genetics and Genomics (ACMG) published a guideline on management of individuals with *PALB2* variants, which recommends that risk-reducing mastectomy be considered as an option based on personal risk. (22) In 2023, the ACMG published a guideline on the management of individuals with CHEK2 variants, which also recommends that risk-reducing mastectomy be considered as an option based on personal risk. (23)

American Society for Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology
In 2020, the American Society for Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology published joint guidelines on management of hereditary breast cancer. (24) The guideline discusses management of patients with breast cancer with germline mutations in breast cancer susceptibility genes (e.g., *BRCA1/2*, *ATM*, *TP53*) and makes the following recommendations regarding risk-reducing mastectomy:

"Surgical management of the index malignancy (...contralateral risk-reducing mastectomy [CRRM]) in *BRCA1/2* mutation carriers should be discussed, considering the increased risk of CBC [contralateral breast cancer] and possible increased risk of an ipsilateral new primary breast cancer compared with noncarriers (Type: formal consensus; Evidence quality: intermediate; Strength of recommendation: strong)."

"For women with breast cancer who have a *BRCA1/2* mutation and who have been treated or are being treated with unilateral mastectomy, CRRM should be offered. CRRM is associated with a decreased risk of CBC; there is insufficient evidence for improved survival."

"Decisions regarding risk-reducing mastectomy (bilateral or contralateral) are highly personal and must be individualized for every patient. Studies show that women who opt for prophylactic mastectomy report positive outcomes, including decreased concern about developing breast cancer. This benefit must be weighed against possible problems with implants or reconstructive therapy and potential adverse feelings related to body image, femininity, and sexuality. Most patients who opt for prophylactic mastectomy demonstrate satisfaction with their decision."

"For women with breast cancer who have a mutation in a moderate-penetrance breast cancer predisposition gene and who have been treated or are being treated with unilateral mastectomy, the decision regarding [contralateral risk-reducing mastectomy] CRRM should not be based predominantly on mutation status. Additional factors that predict CBC such as age at diagnosis and family history should be considered, as they are in all cases. The impact of CRRM on decreasing risk of CBC is dependent on the risk of CBC for each individual gene. Data regarding the risk of CBC resulting from moderate-penetrance genes are limited (Type: formal consensus; Evidence quality: low; Strength of recommendation: moderate)."

The guideline also provides recommendations for assessing the risk of CBC and role of risk-reducing mastectomy in *BRCA1/2* mutation carriers (Evidence quality: low; Strength of recommendation: moderate) and in women with breast cancer who have a *BRCA1/2* mutation who have been treated or are being treated with unilateral mastectomy when considering contralateral risk-reducing mastectomy (Evidence quality: intermediate; Strength of recommendation: moderate). The guideline recommends consideration of the following:

- Age at diagnosis (the strongest predictor of future CBC);
- Family history of breast cancer;
- Overall prognosis from this or other cancers (e.g., ovarian);
- Ability of patient to undergo appropriate breast surveillance (magnetic resonance imaging [MRI]);
- Comorbidities;
- Life expectancy.

<u>Society of Surgical Oncology</u>

In 2017, the Society of Surgical Oncology updated its position statement on risk-reducing (prophylactic) mastectomy. (25) The position statement concluded the following about risk-reducing (prophylactic) mastectomy:

- “There is no single-risk threshold above which risk-reducing mastectomy is clearly indicated, and it is important for treating physicians and surgeons to explain to individuals not only the risk assessment but also all available treatment strategies to facilitate a shared decision-making process.”

- "The available data suggest that BPM [bilateral prophylactic mastectomy] confers a survival advantage in women with the highest risk who undergo the procedure at a relatively early age … the impact of CPM [contralateral prophylactic mastectomy] in women with invasive breast cancer is more difficult to assess … however, CPM does not appear to confer a survival advantage."

National Cancer Institute

In 2024, the National Cancer Institute updated its fact sheet on risk-reducing surgery for breast cancer. (26) The fact sheet stated individuals may consider bilateral risk-reducing mastectomy if they are known to have inherited a harmful mutation that increases their risk of developing breast cancer. The Institute states that individuals who are at high risk of breast cancer but have not inherited a harmful mutation, should talk to their doctors about the potential advantages and disadvantages of a risk-reducing mastectomy. These individuals include those who have radiation therapy to the chest (including the breasts) prior to the age of thirty, as well as those who have pleomorphic lobular carcinoma in situ (PLCIS) together with a strong family history of breast cancer.

Considering contralateral risk-reducing (prophylactic) mastectomy, the Institute stated that some individuals who have been diagnosed with cancer in one breast, especially those who are known to be at very high risk, may think about having the contralateral breast, removed; however, it is noted that physicians frequently advise against contralateral preventive mastectomy because these patients have a very low chance of getting breast cancer again, especially if they had adjuvant chemotherapy or hormone therapy during their treatment. Additionally, a contralateral mastectomy may raise the risk of complications and cause delays in treatment for the diagnosed cancer. Furthermore, there is currently insufficient evidence to suggest that contralateral prophylactic mastectomy lowers mortality.

American Society of Breast Surgeons

In 2016, a consensus statement from the American Society of Breast Surgeons made the following recommendations on contralateral risk-reducing (prophylactic) mastectomy (27):

- "CPM [contralateral prophylactic mastectomy] should be considered for those at significant risk of CBC [contralateral breast cancer]:
  - Documented *BRCA1/2* carrier,
  - Strong family history, but patient has not undergone genetic testing,
  - History of mantle chest radiation before age 30 years."
- "CPM can be considered for those at lower risk of CBC:
  - Gene carrier of … *CHEK-2*, *PALB2*, *p53*, *CDH1*,
  - Strong family history, patient *BRCA* negative, no known *BRCA* family member."
- "CPM may be considered for other reasons:
  - To limit contralateral breast surveillance (dense breasts, failed surveillance, recall fatigue).
  - To improve breast symmetry in reconstruction.
  - To manage risk aversion … [or] extreme anxiety." (Note: anxiety may better be measured through psychological support.)

- "CPM should be discouraged:
  - Average-risk women with unilateral breast cancer.
  - Women with advanced stage index cancer….
  - Women at high risk of surgical complications (e.g., … comorbidities, obesity, smoking, diabetes).
  - … *BRCA* negative with a family of *BRCA*-positive carriers.
  - Males with breast cancer, including *BRCA* carriers."

National Comprehensive Cancer Network (NCCN)

The NCCN has made recommendations on several cancers relevant to this medical policy. On breast cancer risk-reduction (v.1.2025), the NCCN recommends:

"Risk-reducing mastectomy should generally be considered in individuals with a pathogenic/likely pathogenic genetic variant in high penetrance breast cancer susceptibility genes, compelling family history, or those receiving chest wall radiation before 30 years of age. Risk estimation is a complex and individualized process; the NCCN Panel does not recommend a specific risk cutoff for decision making regarding risk reducing mastectomy. Individualizing management is important." (28)

For invasive breast cancer (v.6.2024), the NCCN has discouraged contralateral risk-reducing (prophylactic) mastectomy, except for certain high-risk situations (noted in the risk-reduction guideline previously discussed). (29) The guidelines state:

"...risk reduction mastectomy of a breast contralateral to a known unilateral breast cancer treated with mastectomy or breast-conserving therapy is discouraged by the panel."

As part of genetic/familial high-risk assessment for breast and ovarian cancer (v.2.2025), the NCCN recommends that the option of risk-reducing (prophylactic) mastectomy be discussed in women with *BRCA*-related breast and/or ovarian syndrome, Li-Fraumeni syndrome, and Cowden syndrome or *PTEN* hamartoma tumor syndrome. (30) In addition, the NCCN guidelines recommend that risk-reducing (prophylactic) mastectomy be considered based on family history in women with certain genetic variants including *ATM, NF1*, *STK11*, *PALB2, CHEK2* and *CDH1*.

**Ongoing and Unpublished Clinical Trials**

A search of ClinicalTrials.gov in August 2024 did not identify any ongoing or unpublished trials that would likely influence this policy.

## Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

| | |
|---|---|
| **CPT Codes** | 19303 |
| **HCPCS Codes** | None |

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

## References


1. Yao K, Winchester DJ, Czechura T, et al. Contralateral prophylactic mastectomy and survival: report from the National Cancer Data Base, 1998-2002. Breast Cancer Res Treat. Dec 2013; 142(3):465-476. PMID 24218052
2. Baskin AS, Wang T, Bredbeck BC, et al. Trends in contralateral prophylactic mastectomy utilization for small unilateral breast cancer. J Surg Res. Jun 2021; 262:71-84. PMID 33548676
3. McCarthy AM, Guan Z, Welch M, et al. Performance of breast cancer risk-assessment models in a large mammography cohort. J Natl Cancer Inst. May 01 2020; 112(5):489-497. PMID 31556450
4. Watt GP, John EM, Bandera EV, et al. Race, ethnicity and risk of second primary contralateral breast cancer in the United States. Int J Cancer. Jun 01 2021; 148(11):2748-2758. PMID 33544892
5. Li X, You R, Wang X, et al. Effectiveness of prophylactic surgeries in BRCA1 or BRCA2 mutation carriers: a meta-analysis and systematic review. Clin Cancer Res. Aug 01 2016; 22(15):3971-3981. PMID 26979395
6. Ludwig KK, Neuner J, Butler A, et al. Risk reduction and survival benefit of prophylactic surgery in BRCA mutation carriers, a systematic review. Am J Surg. Oct 2016; 212(4):660-669. PMID 27649974
7. Honold F, Camus M. Prophylactic mastectomy versus surveillance for the prevention of breast cancer in women's BRCA carriers. Medwave. Jul 09 2018; 18(4):e7161. PMID 30052622
8. Carbine NE, Lostumbo L, Wallace J, et al. Risk-reducing mastectomy for the prevention of primary breast cancer. Cochrane Database Syst Rev. Apr 05 2018; 4(4):CD002748. PMID 29620792
9. Nichols HB, Berrington de Gonzalez A, Lacey JV, et al. Declining incidence of contralateral breast cancer in the United States from 1975 to 2006. J Clin Oncol. Apr 20 2011; 29(12):1564-1569. PMID 21402610
10. Molina-Montes E, Perez-Nevot B, Pollan M, et al. Cumulative risk of second primary contralateral breast cancer in BRCA1/BRCA2 mutation carriers with a first breast cancer: A systematic review and meta-analysis. Breast. Dec 2014; 23(6):721-742. PMID 25467311
11. Fayanju OM, Stoll CR, Fowler S, et al. Contralateral prophylactic mastectomy after unilateral breast cancer: a systematic review and meta-analysis. Ann Surg. Dec 2014; 260(6):1000-1010. PMID 24950272

12. Kurian AW, Canchola AJ, Ma CS, et al. Magnitude of reduction in risk of second contralateral breast cancer with bilateral mastectomy in patients with breast cancer: Data from California, 1998 through 2015. Cancer. Mar 01 2020; 126(5):958-970. PMID 31750934
13. Wong SM, Freedman RA, Sagara Y, et al. Growing use of contralateral prophylactic mastectomy despite no improvement in long-term survival for invasive breast cancer. Ann Surg. Mar 2017; 265(3):581-589. PMID 28169929
14. Kruper L, Kauffmann RM, Smith DD, et al. Survival analysis of contralateral prophylactic mastectomy: a question of selection bias. Ann Surg Oncol. Oct 2014; 21(11):3448-3456. PMID 25047478
15. Pesce C, Liederbach E, Wang C, et al. Contralateral prophylactic mastectomy provides no survival benefit in young women with estrogen receptor-negative breast cancer. Ann Surg Oncol. Oct 2014; 21(10):3231-3239. PMID 25081341
16. Yang Y, Pan L, Shao Z. Trend and survival benefit of contralateral prophylactic mastectomy among men with stage I-III unilateral breast cancer in the USA, 1998-2016. Breast Cancer Res Treat. Dec 2021; 190(3):503-515. PMID 34554371
17. Murphy Al, Asadourian PA, Mellia JA, et al. Complications Associated with Contralateral ProphylacticMastectomy: A Systematic Review and Meta-Analysis. Plast Reconstr Surg. Oct 01 2022; 150:61S-72S. PMID 35943952
18. Schroeder MC, Tien YY, Erdahl LM, et al. The relationship between contralateral prophylactic mastectomy and breast reconstruction, complications, breast-related procedures, and costs: A population-based study of health insurance data. Surgery. Nov 2020; 168(5):859-867. PMID 32819721
19. Silva AK, Lapin B, Yao KA, et al. The effect of contralateral prophylactic mastectomy on perioperative complications in women undergoing immediate breast reconstruction: a NSQIP analysis. Ann Surg Oncol. Oct 2015; 22(11):3474-3480. PMID 26001862
20. Miller ME, Czechura T, Martz B, et al. Operative risks associated with contralateral prophylactic mastectomy: A single institution experience. Ann Surg Oncol. Dec 2013; 20(13):4113-4120. PMID 23868655
21. Eck DL, Perdikis G, Rawal B, et al. Incremental risk associated with contralateral prophylactic mastectomy and the effect on adjuvant therapy. Ann Surg Oncol. Oct 2014; 21(10):3297-3303. PMID 25047470
22. Tischkowitz M, Balmaña J, Foulkes WD, et al. Management of individuals with germline variants inPALB2: a clinical practice resource of the American College of Medical Genetics and Genomics (ACMG). Genet Med. Aug 2021; 23(8):1416-1423. PMID 33976419
23. Hanson H, Astiazaran-Symonds E, Amendola LM, et al. Management of individuals with germline pathogenic/likely pathogenic variants in CHEK2: A clinical practice resource of the American College of Medical Genetics and Genomics (ACMG). Genet Med. Oct 2023; 25(10):100870. PMID 37490054
24. Tung NM, Boughey JC, Pierce LJ, et al. Management of Hereditary Breast Cancer: American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Guideline. J Clin Oncol. Jun 20 2020; 38(18):2080-2106. PMID 32243226
25. Hunt KK, Euhus DM, Boughey JC, et al. Society of Surgical Oncology Breast Disease Working Group Statement on prophylactic (risk-reducing) mastectomy. Ann Surg Oncol. Feb 2017; 24(2):375-397. PMID 27933411

26. National Cancer Institute. Fact Sheet: Surgery to Reduce the Risk of Breast Cancer (2024). Available at: <https://www.cancer.gov> (accessed December 10, 2024).
27. Boughey JC, Attai DJ, Chen SL, et al. Contralateral prophylactic mastectomy (CPM) consensus statement from the American Society of Breast Surgeons: data on CPM outcomes and risks. Ann Surg Oncol. Oct 2016; 23(10):3100-3105. PMID 27469117
28. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice Guidelines in Oncology: Breast Cancer Risk Reduction. Version 1.2025. Available at: <https://www.nccn.org> (accessed December 10, 2024).
29. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 6.2024. Available at: <https://www.nccn.org> (accessed December 10, 2024).
30. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version 2.2025. Available at: <https://www.nccn.org> (accessed December 10, 2024).

## Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

## Policy History/Revision

| Date | Description of Change |
|---|---|
| 12/31/2025 | Document became inactive. |
| 02/01/2025 | Document updated with literature review. Coverage unchanged. References 17 and 23 added; others updated. |
| 10/15/2023 | Reviewed. No changes. |
| 12/15/2022 | Document updated with literature review. The following change was made to Coverage: Added "*PALB*" to list of gene variants associated with high risk. Added/updated the following references: 2, 4, 8, 16, 17, 21, and 25-28. |
| 04/01/2021 | Document updated with literature review. The following change was made to Coverage: Replaced "High-risk (lifetime risk about 20% or greater) of developing breast cancer as identified by models (Claus or Gail) that are largely defined by family history; or" with "High-risk (lifetime risk about 20% or greater) of developing breast cancer as identified by risk prediction models (see section on Calculation of Breast Cancer Risk Assessment Tools |

| | |
|---|---|
| | below) that are largely defined by family history; or". No new references added. |
| 01/15/2021 | Document updated with literature review. The following change was made to Coverage: "prophylactic" mastectomy changed to "risk-reducing (prophylactic)" mastectomy throughout policy to reflect preferred terminology in the literature and by NCCN; intent of the statements remain unchanged. Added/updated the following references: 2, 7, 11, and 21-23. Title changed from: Prophylactic Mastectomy (PM)/Risk-Reducing Mastectomy (RRM). |
| 10/15/2019 | Reviewed. No changes. |
| 02/15/2019 | Document updated with literature review. Coverage unchanged. "Risk-Reducing Mastectomy" added to Title. References 4, 5, 9, 15, 17 were added; several removed. |
| 11/15/2017 | Reviewed. No changes. |
| 02/01/2017 | Document updated with literature review. The following was changed in the coverage statement for prophylactic mastectomy: 1) The separate medically necessary statement on lobular carcinoma in situ removed and added to the coverage criteria listing for patients at high-risk; 2) The wording "Another gene mutation associated with high-risk, e.g.," was added to the criterion of specific mutations as a clarification of these types of mutations; and, 3) A revision in the same coverage statement from ""20% to 25%" changed to "20%". "Tyrer-Cuzick" scoring model was added to the listing of Calculation of Breast Cancer Risk Assessment Tools. Otherwise, coverage unchanged |
| 08/15/2015 | Document updated with literature review. The following mutations were added to the medically necessary coverage statement for prophylactic mastectomy for patients considered to be high-risk for breast cancer, "PTEN, TP53, CDH1, and STK11." Experimental, Investigational, and/or Unproven statement regarding contralateral PM (CPM) in women with breast cancer who do not meet high-risk criteria has been removed, and replaced with Contralateral PM (CPM) may be considered medically necessary for women who have been diagnosed with breast cancer in the opposite breast. |
| 07/01/2014 | Document updated with literature review. Coverage unchanged. Link information for online addresses provided in coverage section to assist in calculation of breast cancer risk assessment. Rationale and References updated. |
| 03/01/2014 | Document updated with literature review. The following was changed: 1.) Prophylactic mastectomy (PM) may be considered medically necessary in patients at high-risk of breast cancer when specific criteria have been met; 2.) PM may be considered medically necessary in patients with lobular carcinoma in situ (LCIS); 3.) PM may be considered medically necessary in patients with such extensive mammographic abnormalities (i.e., calcifications) that adequate biopsy or excision is impossible; and 4.) PM is considered experimental, investigational or unproven for all other |

| | |
|---|---|
| | indications, including but not limited to contralateral PM in women with breast cancer who do not meet high-risk criteria, unilateral or bilateral PM in women at moderate-risk of breast cancer, and uncontrolled progress of inflammatory breast disease in one or both breasts (i.e., chronic mastitis, macrocystic or fibrocystic disease). Title changed from Breast Surgery for Prophylaxis or Cancer Prevention. Description, Rationale, and References completely revised. |
| 07/01/2008 | Policy reviewed without literature review; new review date only. |
| 06/01/2005 | Revised/updated entire document |
| 08/01/2003 | Revised/updated entire document |
| 08/01/1999 | Rationale revised |
| 02/01/1999 | Medical policy title changed |
| 05/01/1996 | Medical policy number changed. Revised/updated entire document |
| 01/01/1996 | Revised/Updated Entire MP. Medical policy title changed |
| 07/01/1992 | Revised/Updated Entire MP |
| 03/01/1991 | Revised/Updated Entire MP |
| 05/01/1990 | New medical document |