Clinical Policy Title: Prophylactic salpingo-oophorectomy

Clinical Policy Number: CCP.1265

Effective Date: January 1, 2017
Initial Review Date: October 19, 2016
Most Recent Review Date: December 3, 2019
Next Review Date: April 2021

Coverage policy

Prophylactic salpingo-oophorectomy is clinically proven, and, therefore, medically necessary when any of the following criteria is met:

- A positive test result for a breast cancer susceptibility gene (BRCA1 or BRCA2) mutation.
- A personal history of breast cancer with at least one first-degree relative (mother, sister, or daughter) with a documented history of ovarian cancer.
- One or more first- or second-degree relatives (maternal or paternal aunt, grandmother, or niece) have a history of ovarian cancer.
- Two or more first-degree relatives (mother, sister, or daughter) have a history of ovarian and/or breast cancer.
- One first-degree relative (mother, sister, or daughter) and one or more second-degree relatives (maternal or paternal aunt, grandmother, or niece) have a history of ovarian cancer.
- The person is beyond childbearing age and has been diagnosed with a known familial cancer, such as Lynch syndrome (hereditary non-polyposis colorectal cancer) or a hereditary ovarian

In addition, Prestige Health Choice considers prophylactic hysterectomy medically necessary when performed in conjunction with prophylactic salpingo-oophorectomy when any of the following criteria are met:

- A documented Lynch syndrome II mutation.
- The person meets the criteria for prophylactic salpingo-oophorectomy and, after a discussion with the physician regarding the risks and benefits, chooses to have prophylactic hysterectomy in conjunction with salpingo-oophorectomy.

**Limitations:**

Before prophylactic salpingo-oophorectomy is performed for a member who is fertile, a sterilization consent form may be required.

Prophylactic salpingo-oophorectomy is investigational and, therefore, not medically necessary for all other conditions.

Coverage determinations are subject to benefit limitations and exclusions as delineated by the state Medicaid authority. The Florida Medicaid website may be accessed at [http://ahca.myflorida.com/Medicaid/](http://ahca.myflorida.com/Medicaid/).

**Alternative covered services:**

Prophylactic mastectomy.

**Background**

Hereditary susceptibility to cancer is now expanding with the growing knowledge of genetic mutation patterns. The National Cancer Institute (2019a) defines criteria for hereditary susceptibility in both the individual patient, and in the patient’s family. The list of criteria in the patient is extensive, and includes existence of multiple tumors, age, histology types, and other genetic traits. The National Cancer Institute defines hereditary susceptibility in the patient’s family to include any of:

- One first-degree relative with the same or a related tumor to that of the patient, and one of the individual features described above.
- Two or more first-degree relatives with tumors at the same site.
• Two or more first-degree relatives with tumor types belonging to a known familial cancer syndrome.
• Two or more first-degree relatives with rare tumors.
• Three or more relatives in two generations with tumors at the same site or etiologically related sites.

Over 20 genes are associated with increased risk for breast and ovarian cancer, among which the BRCA1 and BRCA2 genetic mutations, first identified in 1994, are most common and best understood. They can be inherited from either parent. These mutations account for 5% to 10% of all breast cancers and 10% of ovarian cancers. BRCA mutations mean an increased risk of breast cancer for women by age 70. While the overall lifetime risk of being diagnosed with breast cancer is 12.83% (Howlader, 2019), this risk rises to 72% for BRCA1-positive women and 69% for BRCA2-positive women (Kuchenbaecker, 2017).

Among the estimated 300,000 U.S. women with BRCA mutations, there is considerable variation in the prevalence of mutations among racial and ethnic groups. A survey of 1,727 women younger than age 65 with breast cancer provided the basis for prevalence estimates of the BRCA1 mutation in Northern California. Jewish women of Ashkenazi descent had the highest prevalence at 8.3%, followed by Hispanics (3.5%), non-Hispanic whites (2.2%), African Americans (1.5%), and Asian Americans (0.5%). The authors speculate that the Hispanic rate may be somewhat inflated by the presence of unrecognized Jewish ancestry (John, 2007).

The total prevalence of women with hereditary susceptibility to breast and ovarian cancer cannot be determined by John’s (2007) report, as the survey John describes only estimated the prevalence of BRCA1 mutation, and not BRCA2 or other known mutations. In addition, hereditary mutations are not always detected in high-risk women. For example, in a sample of 236 Ashkenazi Jewish women with breast cancer and a family history of breast or ovarian cancer, the likelihood of detecting a mutation was 32.1% (Robson, 1997).

The probability of a young woman diagnosed with a BRCA mutation surviving to age 70 without treatment is just 53% and 71% for BRCA1 and BRCA2 carriers, respectively, compared to a probability of 84% for the general population (Kurian, 2010).

Dramatic declines in the incidence of breast cancer have been observed in BRCA-positive women after prophylactic salpingo-oophorectomy, which has reduced lifetime breast cancer risk by more than 95%. In addition, breast cancer risk declined 90% among those women who have a strong family history of the disease (Domchek, 2010).

BRCA mutation is also an indicator for greater risk of ovarian cancer by age 70. This risk is 44% for BRCA1-positive women and 17% for BRCA2-positive women (Kuchenbaecker, 2017). The lifetime risk of ovarian cancer in the general female population is just 1.25% (Howlader, 2019). Prophylactic salpingo-oophorectomy has reduced the risk of ovarian cancer by 90% and breast cancer by 50% (Guillem, 2006).
Genetic testing services are underutilized among women who are likely to have a genetic mutation for elevated breast and ovarian cancer risk. An estimated 10% to 15% of at-risk and asymptomatic women have discussed genetic testing with a health professional, only four to eight percent received advice from a professional to undergo a genetic test, and fewer than three percent have had such a test (Levy, 2009).

Despite large demonstrated reductions in breast cancer risks among women at high-risk who elect to undergo prophylactic procedures, only a minority of women with BRCA mutations have elected to undergo prophylactic procedures. A study done at 41 centers within nine countries tracked 2,677 BRCA-positive, asymptomatic women ages 25 to 79 for an average of 3.9 years. The United States was documented as the nation with the highest proportion of these women who elected to undergo prophylactic mastectomy and salpingo-oophorectomy (36.3% and 71.1%, respectively). Poland, whose corresponding numbers were 2.7% and 34.9%, had the lowest such proportion (Metcalfe, 2008). Social beliefs and practices, along with effectiveness of provider counseling, may have accounted for much of this variation.

Prophylactic mastectomy and prophylactic salpingo-oophorectomy were first performed soon after the discovery of BRCA gene mutations and the accompanying genetic tests. Originally, the procedures were performed separately, but now are typically concurrent if the woman elects to undergo prophylactic surgery.

A salpingo-oophorectomy involves removal of the fallopian tubes (salpingectomy) and ovaries (oophorectomy). Removal of both ovaries and fallopian tubes is the standard of care (American College of Obstetricians and Gynecologists, 2017, although either procedure alone may be elected.

Alternatives to prophylactic salpingo-oophorectomy to reduce ovarian cancer risk may include increased surveillance or more frequent screening examinations. Another option is use of oral contraceptives, which has been shown to reduce ovarian cancer risk by 50% over five years, a benefit that lasted for at least 10 years after cessation (Hankinson, 1992). Questions remain about how effective these alternatives are at reducing risk, especially for early-stage ovarian cancer.

Women diagnosed with Lynch syndrome have a 40% to 60% lifetime risk of endometrial cancer, and a 10% to 12% chance of ovarian cancer, along with elevated risks of uterine, stomach, and colorectal cancers. Mutations associated with Lynch syndrome include MLH1, MSH2, and MSH6. Prophylactic salpingo-oophorectomy and hysterectomy for women with these mutations have been considered as a means of reducing the risk of these cancers (Burke, 1997).

**Searches**

Prestige Health Choice searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
• Agency for Healthcare Research and Quality and other evidence-based practice centers.
• The Centers for Medicare & Medicaid Services.
• Cochrane Library.

We conducted searches on September 19, 2019. Search terms were: “prophylactic salpingo-oophorectomy” and “risk-reducing salpingo-oophorectomy.”

We included:
• **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
• **Guidelines based on systematic reviews.**
• **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

The most recent version of several guidelines by the National Comprehensive Cancer Network on BRCA-positive women recommends prophylactic salpingo-oophorectomy, typically at ages 35 to 40 and on completion of childbearing (2019a; 2019b). The American College of Obstetricians and Gynecologists (2017) also endorses prophylactic salpingo-oophorectomy for women at high-risk, based on difficulties in detecting ovarian cancer and poor prognosis for treating advanced cases, and that prophylactic salpingo-oophorectomy include inspection of the peritoneal cavity, pelvic washings, removal of fallopian tubes, and ligation of ovarian vessels at the pelvic brim.

The U.S. Preventive Services Task Force concludes that “fair evidence” exists that prophylactic salpingo-oophorectomy effectively prevents breast and ovarian cancer (2005). The Society of Gynecologic Oncology recommends that physicians counsel high-risk women to have fallopian tubes removed, followed by ovary removal (Society of Gynecologic Oncology, 2013). The Society of Gynecologic Oncology also classifies women with family history of breast and/or ovarian cancer, but with no confirmation of BRCA mutations as “higher-than-average risk” for both diseases (Berek, 2010).

The National Cancer Institute (2019b) recommends that risk-reducing hysterectomy, along with prophylactic salpingo-oophorectomy, be considered as an option for women with Lynch syndrome.

All guidelines emphasize the importance of the provider and patient discussing risks and benefits of prophylactic salpingo-oophorectomy before any procedure is performed. Women who undergo prophylactic salpingo-oophorectomy frequently experience menopausal symptoms, including
osteoporosis, increased heart disease risk, hot flashes, sleep disturbance, and cognitive changes (Domchek, 2007).

Prophylactic salpingo-oophorectomy has been shown to reduce breast cancer risk by 47% to 68%, and reduce risk of cancers of the ovary, fallopian tube, and peritoneum by 71% to 96% if completed before menopause, based on six trials (Rebbeck, 2009). Several meta-analyses and systematic reviews found that prophylactic salpingo-oophorectomy:

- Was associated with a reduction (versus non-surgical BRCA cases) of 68%, and a reduction of ovarian cancer risk of 80% in studies followed 3.4, 5.6, and 6.2 years (Marchetti, 2014).
- Reduced breast cancer risk in BRCA-positive women. The procedure also significantly reduced all-cause mortality in these women, while bilateral prophylactic mastectomy did not (Li, 2016).
- Was associated with large decreases in breast and ovarian cancer incidence, plus mortality from all causes (Nelson, 2014).
- Was estimated to be associated with increased survival to age 70 among women who had salpingo-oophorectomy at either age 40 or 50, with or without prophylactic mastectomy (Kurian, 2010). Among BRCA1 carriers, the highest increases in survival were estimated among women who had salpingo-oophorectomy at age 40. Among BRCA2 carriers, estimated survival was increased for both women who had surgery at age 40 and age 50, with fewer differences between the two groups.

A cost-effectiveness study (Norum, 2008) of BRCA-positive Norwegian women estimated that each mutation-carrying woman who undergoes prophylactic bilateral mastectomy at age 30 and prophylactic salpingo-oophorectomy at age 35 would gain 6.4 discounted life years (19.0 undiscounted life years). If all women found to carry the mutation accepted prophylactic salpingo-oophorectomy but not bilateral mastectomy, this would result in 3.1 discounted life-years (9.5 undiscounted years) gained. (Note: the epidemiological statistical method of discounting life years weights mortality among older individuals more heavily, the opposite of how years of potential life lost weights younger deaths more heavily.) The cost per life-year gained was 1,973 euros (prophylactic salpingo-oophorectomy alone) and 1,749 euros (both procedures); researchers concluded that these interventions were cost-effective.

In a comparison of the outcomes of prophylactic salpingo-oophorectomy with prophylactic salpingectomy, with and without delayed oophorectomy, prophylactic salpingo-oophorectomy was associated with the lowest cost, greatest life expectancy, and greatest declines in breast and ovarian cancer risk (Kwon, 2013). However, after adjusting for quality-of-life measures, prophylactic salpingectomy with delayed oophorectomy was associated with the highest life expectancy. Younger age at prophylactic salpingo-oophorectomy was associated with lower social functioning and greater anxiety, while playing a sport and avoiding weight gain were highly related to better quality of life after surgery (Touboul, 2011).

Research has addressed whether salpingectomy alone reduces ovarian cancer risk. One large population-based study showed that women with prior unilateral salpingectomy had a 35% lower risk of ovarian cancer, and that this risk was further decreased to 71% lower with bilateral salpingectomy,
compared with women who had no salpingectomy procedure. This finding supports the belief that most ovarian cancers originate in the fallopian tubes (Falconer, 2015).

In 1997, the Cancer Genetic Studies Consortium found insufficient evidence to conclude that prophylactic hysterectomy and salpingo-oophorectomy would reduce cancer risk in women with Lynch syndrome (Burke, 1997). Subsequently, a study of Lynch syndrome compared those 61 who underwent hysterectomy (47 of whom also had prophylactic bilateral salpingo-oophorectomy) to 210 who had no surgery. Cases and controls were followed for an average of 13 and seven years, respectively. Cases had no subsequent endometrial or ovarian cancer, while controls were diagnosed with 12 cases of ovarian cancer and 69 cases of endometrial cancer (Schmeler, 2006).

A review of 21,067 Australian women diagnosed with primary breast cancer from 1997 to 2008 compared those undergoing hysterectomy, prophylactic bilateral salpingo-oophorectomy, both procedures, and no surgery. Each participant was tracked for five to seven years. Those with both procedures had an improvement in 10-year survival from 78.5% to 85%, while those with only one of these procedures showed no change (Obermair, 2014).

Policy updates:

In 2017, three guidelines were added to the reference list.

In 2018, we updated five guidelines and added two guidelines and two peer-reviewed publications to the reference list. The policy ID changed from 13.03.03 to CCP.1265.

In 2019, we added two publications to the reference list and updated seven others. We revised language in the coverage policy to include transsexual and nonbinary gender populations.

References

Professional society guidelines/other:


Peer-reviewed references:


**Centers for Medicare & Medicaid Services National Coverage Determinations:**

No National Coverage Determinations identified as of the writing of this policy.

**Local Coverage Determinations:**

No Local Coverage Determinations identified as of the writing of this policy.

**InterQual:**
