



Kansas City

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Prophylactic Oophorectomy

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Last Review: 5/2014

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Next Review: 5/2015

Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for prophylactic oophorectomy when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered

Prophylactic oophorectomy may be considered **medically necessary** for women:

- With a confirmed BRCA mutation, after childbearing has been completed or after the age of 35; or
- Who are confirmed members of a site-specific ovarian cancer family, after childbearing has been completed or after the age of 35; or
- Who are diagnosed with an estrogen receptor positive breast cancer who still have functioning ovaries (pre-menopausal); or
- Who have two first degree relatives (e.g., mother, sister, daughter) with a history of ovarian cancer; or
- With a personal history of breast cancer and at least one first degree relative with a history of ovarian cancer; or
- With one first degree relative and one or more second degree relatives (e.g., maternal or paternal aunt, grandmother, niece) with ovarian cancer; or
- With an androgen-producing ovary unresponsive to medical therapy; or
- With a hereditary nonpolyposis colorectal cancer (HNPCC) or Lynch syndrome
- With severe endometriosis unresponsive to nonoperative therapy
- With recurrent ovarian cyst

When Policy Topic is not covered

Prophylactic oophorectomy is considered **investigational** for all other indications, including but not limited to:

- Women with average risk for breast or ovarian cancer. This is investigational due the lack of evidence that prophylactic oophorectomy reduces cancer risk or improves survival in this population.

Considerations

Site-specific ovarian cancer syndrome applies to women with two or more first-degree, or first- and second-degree relatives who have had **ovarian** cancer.

- First degree relative – Any relative who is one meiosis away from a particular individual in a family (i.e., parent, sibling, offspring).
- Second degree relative – Any relative who is two meioses away from a particular individual in a pedigree; a relative with whom one quarter of an individual's genes is shared (i.e., grandparent, grandchild, uncle, aunt, nephew, niece, half-sibling)

Description of Procedure or Service

Prophylactic oophorectomy is the removal of the ovaries for the potential benefit of preventing long-term morbidity and mortality. The term prophylactic implies that the ovaries are normal at the time of removal. Oophorectomy can be performed either alone as a planned surgical procedure or in

conjunction with other planned surgical procedures such as hysterectomy or colectomy. Incidental oophorectomy is a term commonly used when the ovaries are removed at the time of another indicated surgery, and this term should not be used interchangeably with prophylactic oophorectomy. The term incidental implies that the surgery occurs by chance or without consequence. There are obvious consequences associated with oophorectomy; therefore, when oophorectomy is performed for future benefit, the surgery should be termed prophylactic.

Rationale

Evidence evaluated for this report was obtained primarily from a search in the MEDLINE and EMBASE databases spanning the years 1998 to October 2002, in addition to the evidence from 1993 to 1998 included in the earlier version of this technology assessment. Search terms included *ovarian cancer* combined with *prevention*, *prophylactic oophorectomy*, *genetics*, *colorectal cancer*, *Lynch Syndrome*, *breast cancer*, *BRCA1*, or *BRCA2*. The search was limited to the English language and to human subjects. Additional information was obtained from the National Cancer Society (NCI), the American Cancer Society (ACS), the National Institutes of Health (NIH), and the American College of Obstetricians and Gynecologists (ACOG).

The efficacy of prophylactic oophorectomy for reducing breast and gynecologic cancer risk has been investigated in decision analyses, and cohort and case-control studies. There were no prospective randomized controlled trials in the published, peer-reviewed medical literature that examined the efficacy and safety of prophylactic oophorectomy for the prevention of breast and gynecologic cancer in women at high genetic or familial risk for the disease, or that compared prophylactic oophorectomy with surveillance or chemoprevention. The goals of the existing studies have been to determine if this surgery reduces incidence of ovarian and/or breast cancer and to evaluate the effect on life expectancy and quality of life. The decision analyses relied on theoretical models to guide clinical decision-making. In these studies, simulated cohorts of women at high risk for ovarian cancer were used to construct survival models based on cumulative breast and gynecologic cancer incidence rates and survival data. For these models, assumptions were made regarding the efficacy of prophylactic oophorectomy, i.e., quantitative estimates of its ability to reduce cancer risks for women with varying levels of risk for the disease as well as assumptions regarding follow-up. The efficacy of oophorectomy was compared with alternative strategies, including surveillance, bilateral mastectomy, and chemoprevention, using mathematical models based on certain assumptions regarding surgical efficacy, cancer incidence, and survival. The decision analyses evaluated the outcome after prophylactic oophorectomy in women with *BRCA1* and *BRCA2* mutations using a simple mathematical tool called the Markov model, which is useful when a decision problem involves a risk that is ongoing or continuous over time. Markov models of prognosis assume that a patient is always in one of a finite number of discrete health states called Markov states. For example, in these two studies, the states might be good health, breast cancer, ovarian cancer, and death. All events of interest are represented as transitions from one state to another (Sonnenberg and Beck, 1993). The decision analyses also included sensitivity analyses to assess the stability of the results of the model using different baseline probabilities and assumptions (Schrag et al., 1997; Grann et al., 1998; Grann et al., 1999; Grann et al., 2002; van Roosmalen et al., 2002).

In addition to these decision analyses, there were a number of cohort and case-control studies that focused on effect of prophylactic oophorectomy in women at increased risk for breast and ovarian cancer (Rebbeck et al., 1999; Kauff et al., 2002; Rebbeck et al., 2002). One study did not specify the risk status of the participants (Kreiger et al., 1999). Outcome measures included incidence of gynecologic or breast cancer. Follow-up times varied from 12 months to over 10 years.

The decision analyses found that prophylactic oophorectomy reduced the risk of both ovarian and gynecological cancer and improved survival, although the magnitude of the protective effect was greatest for women at highest risk, and for younger women and premenopausal women. The basis for the effect on survival was largely due to a reduction in breast cancer incidence, and the impact of prophylactic oophorectomy was enhanced by prophylactic mastectomy. The case-control and cohort studies also found a protective effect associated with prophylactic oophorectomy, particularly for

younger women, premenopausal women, and women with confirmed *BRCA1* or *BRCA2* mutations. This protective effect was most significant in the reduction in breast cancer incidence; several studies reported breast cancer risk reduction of between 40% and 50% (Kreiger et al., 1999; Rebbeck et al., 1999). Limitations of most of these studies included relatively small patient population, lack of information regarding the use of hormone replacement therapy, hysterectomy, *BRCA* status, or other risk factors, inadequate case-matching, and exclusion of women under the age of 35. In addition, some studies lacked sufficient follow-up time to assess incidence of cancer adequately, and none of the cohort or case-control studies evaluated the effect of prophylactic oophorectomy on survival.

The studies evaluating the efficacy of prophylactic oophorectomy in reducing cancer risk are summarized below:

Patient Selection Criteria: No definitive patient selection criteria have been established for prophylactic oophorectomy. However, there is sufficient evidence from cohort and case-control studies and from decision analyses based on cumulative breast and gynecologic cancer incidence rates and survival data to conclude that prophylactic oophorectomy reduces breast cancer and gynecologic cancer risk, and likely improves disease-free survival rates. The available evidence supports the use of prophylactic oophorectomy as a primary breast and ovarian cancer prevention strategy in the following populations:

- Women with confirmed mutations in *BRCA1* or *BRCA2* who are over the age of 35 or have completed childbearing.
- Women with multiple relatives with breast and/or ovarian cancer who are confirmed members of a site-specific ovarian cancer family.

Although there is less evidence to support the following patient selection criteria, there is some medical consensus that prophylactic oophorectomy should also be offered to these women (NIH, 1995; ACOG, 1999):

- Women with multiple relatives with breast and/or ovarian cancer who are not members of confirmed HBOC or site-specific ovarian cancer families.
- Women with confirmed HNPCC associated Lynch II Syndrome.
- Women with no confirmed increase in cancer risk but with one or more relatives with breast or ovarian cancer who are undergoing abdominal surgery may opt for an incidental oophorectomy.
- Postmenopausal women undergoing hysterectomy or other elective nongynecological abdominal surgery.

The records of 204 women with metastatic breast carcinoma treated by oophorectomy were analyzed. Premenopausal women had a response rate of 50 percent. Forty-one percent of postmenopausal women responded. Those who responded had an average duration of response of 22 months and a length of survival twice that of the nonresponders. There was a better than 60 percent correlation between response to oophorectomy and response to further endocrine ablation. Response to endocrine manipulation is more a function of the hormonal sensitivity of the carcinoma than of menopausal status (Peetz, et al 1981).

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Billing Coding/Physician Documentation Information

- 58940** Oophorectomy, partial or total, unilateral or bilateral
58720 Salpingo-oophorectomy, complete or partial, unilateral or bilateral (separate procedure)
58661 Laparoscopy, surgical; with removal of adnexal structures (partial or total oophorectomy and/or salpingectomy)

Additional Policy Key Words

N/A

Policy Implementation/Update Information

- 5/1/09 New policy; may be considered medically necessary.
 5/1/10 No policy statement changes.
 5/1/11 Policy statement revised indicating may be medically necessary for women diagnosed with an estrogen receptor positive breast cancer; women who have two first degree relatives (e.g., mother, sister, daughter) with a history of ovarian cancer; women with a personal history of breast cancer and at least one first degree relative with a history of ovarian cancer; or women with one first degree relative and one or more second degree relatives (e.g., maternal or paternal aunt, grandmother, niece) with ovarian cancer. Removed the investigational policy statement regarding use in patients with one or more relatives with breast and/or ovarian cancer who are not confirmed members of a site-specific ovarian family or who are not confirmed BRCA mutation carriers.
 5/1/12 No policy statement changes.
 5/1/13 No policy statement changes.
 5/1/14 Policy statement revised to add additional medically necessary indications.
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