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Current Knowledge on Contralateral Prophylactic Mastectomy Among Women with Sporadic Breast Cancer

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LEARNING OBJECTIVES

After completing this course, the reader will be able to:

1. Identify situations in which contralateral prophylactic mastectomy may be appropriate in breast cancer patients.
2. Describe epidemiological data on the clinical benefits of contralateral prophylactic mastectomy for patients with breast cancer.

ABSTRACT

The use of contralateral prophylactic mastectomy (CPM) in the U.S. among patients with unilateral invasive breast cancer increased by 150% from 1993 to 2003. Although CPM has been shown to reduce the risk for developing contralateral breast cancer, there is conflicting evidence on whether or not it reduces breast cancer mortality or overall death. The increase in the CPM rate is especially concerning among women with early-stage sporadic breast cancer who have a minimal annual risk for developing contralateral breast cancer, and for many of these women the risk for distant metastatic disease outweighs the risk for contralateral breast cancer. The lack of information about the clinical value of CPM in women with sporadic breast cancer is an important public health problem. This review evaluates current data on the clinical indications for CPM and long-term patient satisfaction and psychosocial outcomes. Gaps in knowledge about the clinical value of CPM, including patient- and physician-related psychosocial factors that influence the decision-making process of CPM among women with sporadic breast cancer, are highlighted. ***The Oncologist*** 2011;16:935–941

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Introduction

The use of contralateral prophylactic mastectomy (CPM) in the U.S. among patients with unilateral invasive breast cancer increased by 150% from 1993 to 2003, with no evidence of a plateau effect [1]. Although CPM has been shown to reduce the risk for developing contralateral breast cancer, there is conflicting evidence on whether or not it reduces breast cancer mortality or overall death in women with sporadic breast cancer [2]. The lack of definitive clinical evidence is particularly relevant for women with early-stage sporadic breast cancer who have a minimal (0.5%–0.75%) annual risk for developing contralateral breast cancer [3–6] and lifetime risks of 13% and 3.5% for women aged <50 years and ≥ 50 years at diagnosis, respectively [7]. Patients with inflammatory breast cancer have a higher risk for contralateral breast cancer than comparably staged patients with noninflammatory breast cancer [8]. Despite evidence supporting the efficacy of adjuvant endocrine therapy in reducing the risk for contralateral breast cancer [9–11], a growing proportion of women with early-stage sporadic breast cancer undergo CPM, and their reasons for doing so are not well understood. Most studies regarding decision making for prophylactic mastectomy have focused on high-risk women, for example, *BRCA1* and *BRCA2* mutation carriers, who have a 40%–65% lifetime risk for developing breast cancer and, once diagnosed, an approximately 40% risk for contralateral breast cancer over 10 years [12, 13]. CPM has substantial risk-reduction benefits for this subset of women, but at a potential cost to quality of life, because studies have shown long-lasting emotional and self-image distress after CPM, albeit in a minority of women [14, 15]. Thus, the lack of information about the clinical benefits of CPM for women with sporadic breast cancer and the factors that influence the CPM decision-making process are important clinical problems and a critical area of public health concern.

Trends in CPM

Data from the population-based Surveillance, Epidemiology, and End Results (SEER) Cancer Registry indicate that, over the period 1993–2003, the CPM rate among patients with unilateral invasive breast cancer increased from 1.8% to 4.5% (150% increase), with no evidence of a geographic difference in practice or plateau effect [1]. A similar increasing trend in CPM was reported among women diagnosed with unilateral ductal cancer in situ using the SEER Registry [16]. McLaughlin et al. [17] used the New York state cancer registry and reported on trends in bilateral prophylactic mastectomy (BPM) among healthy women and CPM among women with breast cancer in 1995–2005. Although the rate of BPM among healthy women increased only slightly, the number of patients with breast cancer undergoing CPM doubled over the study period [17]. Several hospital-based studies also described increasing rates of CPM. Arrington et al. [18] evaluated the rate of CPM among an unselected group of women with unilateral breast cancer in a Minnesota metropolitan-based hospital system over the period 2005–2006 and found that 28.9% of women underwent CPM. Among women who underwent a mastectomy for unilateral breast cancer, 55.9% also underwent CPM [18]. Jones et al. [19] used the National Comprehensive Cancer Network database to evaluate the rate of CPM among women undergoing mastectomy for unilateral breast cancer at the James Cancer Hospital at The Ohio State University. The rates of CPM among this unselected group of women were 6.5% in 1999 and 16.1% in 2007. Stucky et al. [20] found that from 2000 to 2008 the rate of CPM increased from 0% to 20% at the Mayo Clinic, Arizona. In that hospital-based cohort ($n = 1{,}391$) only 11 patients tested positive for a mutation in *BRCA1* or *BRCA2*. The reason for the higher than average annual national rates of CPM at centers that offer multidisciplinary care is unclear and may be partially explained by the availability of breast reconstruction, more genetic testing, or unique patient and physician decision-making characteristics. These percentages from population- and hospital-based studies, however, potentially translate into substantial numbers of women with sporadic breast cancer undergoing CPM, because it is expected that approximately 192,000 women will be diagnosed with breast cancer this year in the U.S. and the majority will have operable disease [21].

Clinical Impact of CPM

Several studies have shown that CPM reduces the incidence of contralateral breast cancer by about 95% among women with a personal history of unilateral breast cancer, but its impact on breast cancer survival and overall survival is unclear [22]. Boughey et al. [23] reported a 95% lower incidence of contralateral breast cancer at a median follow-up of 17.1 years among 385 breast cancer patients with a family history of breast cancer who underwent CPM than in a cohort of patients matched by age and stage who did not have CPM. In that study, with significant long-term follow-up, CPM was also associated with statistically significant superior disease-free and overall survival results. In a population of breast cancer patients with *BRCA1* and *BRCA2* mutations, Van Spundal et al. [24] showed that CPM led to a 91% lower incidence of contralateral breast cancer, but there was no association with longer overall survival after adjusting for prophylactic oophorectomy. A retrospective study of an unselected population of 1,072 breast cancer patients found that CPM was associated with a lower con-

Table 1. Epidemiological studies evaluating the association between CPM and breast cancer outcomes

Study	Sample size	Study design	Follow-up	Study population	Study endpoints	Confounders adjusted
Boughey et al. (2010) [23]	385	Hospital-based cohort with CPM group matched with no CPM group by age, tumor stage, nodal status, and year of diagnosis	Median, 17.3 yrs	Patients with family history of breast cancer	DFS: HR, 0.66; $p < .001$. OS: HR, 0.77; $p = .03$	Age, tumor stage, nodal status, ER/PR status, family history, diagnosis year, oophorectomy, adjuvant treatment
Bedrosian et al. (2010) [27]	107,106	Population-based retrospective cohort	Median, 47 mos	Unselected	Breast mortality: HR, 0.84; 95% CI, 0.76–0.92	Age, race, stage, lymph node status, histology grade, ER status
Van Sprundel et al. (2005) [24]	148	Hospital-based retrospective cohort	Mean, 3.5 yrs	*BRCA1* and *BRCA2* mutation carriers	Breast cancer mortality: log rank $p = .11$. OS: HR, 0.35; $p = .14$	Oophorectomy, chemotherapy, time between first breast cancer and start of follow-up, and chemotherapy
Herrinton et al. (2005) [25]	1,072	Hospital-based retrospective case-cohort	Median, 5.7 yrs	Unselected	Breast cancer mortality: HR, 0.57; 95% CI, 0.45–0.72. OS: HR, 0.60; 95% CI, 0.50–0.72	Age, year of diagnosis, stage, tumor size, type of surgery, chemotherapy, radiation therapy, hormonal therapy
Peralta et al. (2000) [26]	246	Hospital-based cohort with CPM group matched to no CPM group by age, stage at diagnosis, decade of treatment, presence of LCIS, chemotherapy, and tamoxifen use	Median, 6.2 yrs in CPM group and 6.8 yrs in no CPM group	Unselected	15-yr DFS: 55% in CPM group versus 28% in no CPM group; $p = .01$. 15-yr OS: 49% in CPM group versus 58% in no CPM group; $p = .26$	Frequency of LCIS, opposite breast abnormality, affected first-degree relatives
Lee et al. (1995) [28]	404	Hospital-based retrospective cohort	Median, 5.3 yrs	Patients with invasive lobular carcinoma	OS: advantage for CPM versus no CPM; $p = .01$	Age

Abbreviations: CI, confidence interval; CPM, contralateral prophylactic mastectomy; DFS, disease-free survival; ER, estrogen receptor; HR, hazard ratio; LCIS, lobular carcinoma in situ; OS, overall survival; PR, progesterone receptor.

tralateral breast cancer incidence and a 3% absolute disease-free survival benefit but no difference in overall survival [25]. A smaller study by Peralta et al. [26] also showed that CPM was significantly associated with longer disease-free survival but had no effect on overall survival. A recently updated Cochrane review of six observational studies concluded that CPM resulted in a lower risk for contralateral breast cancer but did not convey a survival benefit [2].

The overall lack of translation in benefit of a lower contralateral breast cancer incidence to disease-specific survival is not unexpected. For many women with early-stage sporadic breast cancer, the risk for distant metastatic disease outweighs the annual (0.5%–0.75%) and 30-year (5.3%–7.6%) risks for contralateral breast cancer [8]. It is possible that the marginal benefit of CPM in terms of disease-free survival will be observed only among certain subgroups of patients. Indeed, Bedrosian et al. [27] used the population-based SEER database to identify outcomes of CPM patients stratified by estrogen receptor (ER) and progesterone receptor (PR) tumor status. The study found that, in patients with an ER^+ breast cancer, CPM was not associated with longer breast cancer–specific survival (hazard ratio, 0.88; $p = .4$). A 3% statistically significant higher breast cancer–specific survival rate was observed in patients with ER^- breast cancer [27]. The lack of survival benefit for CPM in women with ER^+ tumors in that study may be attributed to the additional benefit of adjuvant endocrine therapy in reducing the risk for contralateral breast cancer. Lee et al. [28] evaluated a cohort of 404 women diagnosed with unilateral invasive lobular cancer and found a survival advantage for women who underwent CPM, but the results were adjusted only for age at diagnosis [28]. Limitations of epidemiological studies include small sample sizes, short-term follow-up, and incomplete information on tumor characteristics, treatment, and comorbidities. It is unlikely that a randomized study will ever be conducted to evaluate the risks and benefits of CPM. The collective experience with CPM in observational studies is summarized in Table 1.

Clinical Factors Associated with CPM

In 2007, the Society of Surgical Oncology updated its position statement to indicate the situations under which CPM may be appropriate in patients with a personal history of breast cancer [29]. The situations under which it was deemed appropriate to consider CPM included the following: (a) to reduce contralateral breast cancer risk in high-risk patients, (b) for patients in whom surveillance with mammograms or ultrasound is difficult because of dense

breast tissue or diffuse indeterminate calcifications, and (c) to improve symmetry in patients undergoing reconstruction for the index tumor or to maintain balance in women undergoing unilateral mastectomy. The statement advised that, because of the unclear benefit of CPM in terms of mortality and because breast cancer patients may overestimate their risk for developing contralateral breast cancer, physicians should counsel patients appropriately [29]. In a series of 2,505 patients treated at the MD Anderson Cancer Center who underwent mastectomy for their primary tumor, the clinical factors associated with the decision to have CPM included age <50 years, white race, having a family history of breast cancer, undergoing *BRCA1* and *BRCA2* testing, a higher clinical stage, and invasive lobular histology. However, the strongest clinical predictor of CPM was having breast reconstruction [30]. Several other hospital-based and registry studies have found similar clinical factors to be associated with CPM among patients with a personal history of breast cancer [1, 20, 31].

The increase in the use of preoperative breast magnetic resonance imaging (MRI) has changed the surgical treatment of patients with unilateral breast cancer, and in one study it appears to have resulted in higher rates of CPM. Sorbero et al. [32] compared the rates of therapeutic mastectomy and CPM among 3,606 women with stage I–III breast cancer during two time periods, 1998–2000 and 2003–2005. The rate of CPM increased by 50% from the early to the later period (4.1% to 6.4%; $p < .002$), whereas the rate of therapeutic mastectomy increased from 28% to 30% ($p > .05$) [32]. Women diagnosed with breast cancer who received breast MRI were nearly twice as likely to undergo CPM than women who did not receive breast MRI [32]. Although the reasons for the greater use of CPM caused by MRI screening is unclear, studies examining the impact of MRI on the surgical management of patients with breast cancer found that it changes treatment management from breast-conserving surgery to mastectomy in 25% of cases [33–35]. It is therefore possible that women requiring more aggressive treatment of their primary breast cancer may be more likely to opt for CPM in order to have more reconstructive options or to reduce anxiety about their future risk for breast cancer.

Patient-Related Psychosocial Factors and the Decision-Making Process for CPM

To the best of our knowledge, there are no published studies that have prospectively evaluated the decision-making process for CPM among women with a personal history of breast cancer. A few retrospective studies have evaluated long-term satisfaction and quality of life in women who underwent CPM. Spear et al. [36], for example, conducted a retrospective analysis of clinical outcomes and satisfaction of women who had undergone prophylactic mastectomy and breast reconstruction. They found that 81% were "highly" or "very" satisfied and 98% indicated that they were willing to undergo the procedure again. This study included both women who had CPM and those who had BPM, and likely included women at varying levels of risk for breast cancer. In another retrospective study, Frost et al. [14] found that, 10 years after their surgery, 83% of women were either satisfied or very satisfied with their decision to have CPM. Another limitation of that study and similar studies is the lack of a control group, which limits our ability to ascertain whether CPM is associated with better or worse psychosocial outcomes [37]. Most studies of decision making about CPM have been conducted among high-risk women and *BRCA1* and *BRCA2* mutation carriers who have an approximately 40% risk for developing contralateral breast cancer over 10 years [14, 38, 39]; thus, findings from these studies may not reflect the experiences of breast cancer patients without familial risk. Nonetheless, prior research suggests that a small proportion of women who undergo CPM experience less satisfaction with their appearance or adverse effects on their sexuality despite overall high satisfaction with their decision [14, 15]. On the other hand, Geiger et al. [37] found that 50% of breast cancer patients who elected CPM experienced greater cancer concerns, versus 74% who did not have CPM, suggesting that CPM may confer some quality of life improvements among breast cancer patients. Based on retrospective studies of women who underwent CPM and BPM [14, 40, 41], and on models of decision making [42, 43], there are several psychosocial predictors that may influence a woman's decision to have CPM, including: cancer-related distress, cancer worry and fear of recurrence, knowledge about treatment options, perceived risk, trust in the physician, anxiety, body image, and illness uncertainty. Future studies are needed to comprehensively evaluate the range of factors that may impact the decision-making process for women considering CPM.

The Physician's Role in the Decision-Making Process for CPM

At the time of diagnosis, many breast cancer patients lack the knowledge and information necessary to make informed decisions about treatment [44]. How physicians communicate with patients regarding treatment options is an important determinant of patients' treatment decisions and satisfaction [45, 46]. In retrospective studies, patients' most frequently cited reasons for choosing CPM included physician advice and a family history of breast cancer [14, 47]. Prior research has suggested that patient regret may be

a more prevalent consequence after surgery when CPM or BPM was discussed or recommended by physicians [48], although this finding was not replicated in other studies [40]. In a survey evaluating perceived roles in decision making of women having CPM, Nekhlyudov et al. [40] found that the majority of women reported having a more active role than or a role equal to that of their surgeon in the decision-making process regarding the surgical management of their breast cancer. Interestingly, a recent study found that surgeon gender was one significant predictor of whether women had CPM [18]. They found that the rate of CPM among female surgeons was significantly higher than among male surgeons. However, the study was limited in that it had few female surgeons. It is clear that communication with surgeons and other physicians is important when deciding on CPM and other surgical treatment decisions for breast cancer. Studies are needed to evaluate how CPM is discussed with breast and plastic surgeons preoperatively and how it impacts CPM decision making.

Cost-Effectiveness of CPM

Although BPM has been shown to be cost-effective in cancer-free *BRCA1* and *BRCA2* mutation carriers, compared with breast cancer surveillance [49–51], to our knowledge, there are no studies to date that have evaluated the cost-effectiveness of CPM in women with a personal history of breast cancer. The lack of economic information on CPM represents a significant gap in the literature because cost is becoming a major component of the medical decision-making process. From a societal perspective, costs associated with CPM include both direct and indirect medical costs (also known as productivity loss) [52, 53]. Direct medical costs are the costs of the surgical procedure and the associated downstream costs such as those involved in the treatment of surgical complications or breast reconstruction following the surgery. In addition to the cost of mastectomy, CPM with immediate reconstruction has surgical morbidity. Frost et al. [14] reported that 27% of women had at least one unanticipated reoperation after the CPM and Barton et al. [54] reported that 66% of women had at least one complication. Indirect costs include days absent from work and usual daily activities when patients are undergoing CPM and its downstream medical events [55, 56]. They also capture impaired work productivity (i.e., presenteeism). Whereas direct medical costs are most likely to be greater with CPM, indirect costs may be lower for some patients. For example, a woman's productivity may be impaired prior to CPM because of heightened anxiety from her constant worry of breast cancer recurrence, but her productivity may be substantially greater after CPM because the surgery has lowered her anxiety. When considering the cost-effectiveness of CPM, there are also noneconomic factors, such as cancer worry, that will affect patients' health utility, which is a key determinant in the construction of quality-adjusted life year (QALY), which is a commonly used effectiveness measure in cost-effectiveness analyses. Currently, there is a lack of information regarding health utilities for patients with sporadic breast cancer for both those who do and do not choose to have CPM. It is possible that patients who are risk averse are more likely to elect CPM than those who are risk neutral or risk seeking. The underlying risk attitude may affect patients' decision making about CPM and changes in health utilities as a result of CPM, and consequently the cost-effectiveness of CPM may differ by patients' risk attitudes. Information on the economic burden of CPM and patient health utility as a component of cancer treatment and cancer survivorship is necessary for determining the cost-effectiveness of the procedure and is a high priority given the unsustainable growing cost of cancer care [57].

Conclusion

Although CPM has clear benefits in reducing the risk for contralateral breast cancer, there remains considerable uncertainty about its impact on disease-specific and overall survival outcomes. Epidemiological studies investigating the clinical value of CPM have had significant limitations, including small sample size, short follow-up time, lack of data on receipt of adjuvant treatment, failure to stratify by important prognostic clinical variables such as ER and PR tumor status, and the inability to reduce selection bias [58]. Important limitations of retrospective studies evaluating patient-related psychosocial factors involved in the decision-making process for CPM are the inclusion of primarily high-risk women and the lack of documentation of the physician–patient communication process about CPM, including any discussion of the expected benefits and drawbacks of CPM [38]. Ideally, the decision to proceed with CPM should be guided by genetic counseling, and patients with sporadic breast cancer should be informed of alternative options, such as more rigorous breast surveillance options with MRI and effective adjuvant treatment options with tamoxifen or aromatase inhibitors for reducing the risk for developing contralateral breast cancer. Studies are needed to improve knowledge of the clinical outcome and economic impact of CPM and to prospectively evaluate the factors that contribute to the decision-making process between patients and their providers.

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References

1 Tuttle TM, Habermann EB, Grund EH et al. Increasing use of contralateral prophylactic mastectomy for breast cancer patients: A trend toward more aggressive surgical treatment. J Clin Oncol 2007;25:5203–5209.

2 Lostumbo L, Carbine NE, Wallace J. Prophylactic mastectomy for the prevention of breast cancer. Cochrane Database Syst Rev 2010;11:CD002748.

3 Kollias J, Ellis IO, Elston CW et al. Clinical and histological predictors of contralateral breast cancer. Eur J Surg Oncol 1999;25:584–589.

4 Robbins GF, Berg JW. Bilateral primary breast cancer: A prospective clinicopathological study. Cancer 1964;17:1501–1527.

5 Healey EA, Cook EF, Orav EJ et al. Contralateral breast cancer: Clinical characteristics and impact on prognosis. J Clin Oncol 1993;11:1545–1552.

6 Rosen PP, Groshen S, Kinne DW et al. Contralateral breast carcinoma: An assessment of risk and prognosis in stage I (T1N0M0) and stage II (T1N1M0) patients with 20-year follow-up. Surgery 1989;106:904–910.

7 Adami HO, Bergström R, Hansen J. Age at first primary as a determinant of the incidence of bilateral breast cancer. Cumulative and relative risks in a population-based case-control study. Cancer 1985;55:643–647.

8 Schairer C, Brown LM, Mai PL. Inflammatory breast cancer: High risk of contralateral breast cancer compared to comparably staged non-inflammatory breast cancer. Breast Cancer Res Treat 2011 Mar 9. [Epub ahead of print].

9 Forbes JF, Cuzick J, Buzdar A et al. Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 100-month analysis of the ATAC trial. Lancet Oncol 2008;9:45–53.

10 Thürlimann B, Keshaviah A, Coates AS et al. A comparison of letrozole and tamoxifen in postmenopausal women with early breast cancer. N Engl J Med 2005;353:2747–2757.

11 Tamoxifen for early breast cancer: An overview of the randomised trials. Early Breast Cancer Trialists' Collaborative Group. Lancet 1998;351:1451–1467.

12 Metcalfe K, Lynch HT, Ghadirian P et al. Contralateral breast cancer in BRCA1 and BRCA2 mutation carriers. J Clin Oncol 2004;22:2328–2335.

13 Easton DF, Ford D, Bishop DT. Breast and ovarian cancer incidence in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. Am J Hum Genet 1995;56:265–271.

14 Frost MH, Slezak JM, Tran NV et al. Satisfaction after contralateral prophylactic mastectomy: The significance of mastectomy type, reconstructive complications, and body appearance. J Clin Oncol 2005;23:7849–7856.

15 Montgomery LL, Tran KN, Heelan MC et al. Issues of regret in women with contralateral prophylactic mastectomies. Ann Surg Oncol 1999;6:546–552.

16 Tuttle TM, Jarosek S, Habermann EB et al. Increasing rates of contralateral prophylactic mastectomy among patients with ductal carcinoma in situ. J Clin Oncol 2009;27:1362–1367.

17 McLaughlin CC, Lillquist PP, Edge SB. Surveillance of prophylactic mastectomy: Trends in use from 1995 through 2005. Cancer. 2009;115:5404–5412.

18 Arrington AK, Jarosek SL, Virnig BA et al. Patient and surgeon characteristics associated with increased use of contralateral prophylactic mastectomy in patients with breast cancer. Ann Surg Oncol 2009;16:2697–2704.

19 Jones NB, Wilson J, Kotur L et al. Contralateral prophylactic mastectomy for unilateral breast cancer: An increasing trend at a single institution. Ann Surg Oncol 2009;16:2691–2696.

20 Stucky CC, Gray RJ, Wasif N et al. Increase in contralateral prophylactic mastectomy: Echoes of a bygone era? Surgical trends for unilateral breast cancer. Ann Surg Oncol 2010;17(suppl 3):330–337.

21 Jemal A, Siegel R, Ward E et al. Cancer statistics, 2009. CA Cancer J Clin 2009;59:225–249.

22 Recht A. Contralateral prophylactic mastectomy: Caveat emptor. J Clin Oncol 2009;27:1347–1349.

23 Boughey JC, Hoskin TL, Degnim AC et al. Contralateral prophylactic mastectomy is associated with a survival advantage in high-risk women with a personal history of breast cancer. Ann Surg Oncol 2010;17:2702–2709.

24 Van Sprundel TC, Schmidt MK, Rookus MA et al. Risk reduction of contralateral breast cancer and survival after contralateral prophylactic mastectomy in BRCA1 or BRCA2 mutation carriers. Br J Cancer 2005;93:287–292.

25 Herrinton LJ, Barlow WE, Yu O et al. Efficacy of prophylactic mastectomy in women with unilateral breast cancer: A cancer research network project. J Clin Oncol 2005;23:4275–4286.

26 Peralta EA, Ellenhorn JD, Wagman LD et al. Contralateral prophylactic mastectomy improves the outcome of selected patients undergoing mastectomy for breast cancer. Am J Surg 2000;180:439–445.

27 Bedrosian I, Hu CY, Chang GJ. Population-based study of contralateral prophylactic mastectomy and survival outcomes of breast cancer patients. J Natl Cancer Inst 2010;102:401–409.

28 Lee JS, Grant CS, Donohue JH et al. Arguments against routine contralateral mastectomy of undirected biopsy for invasive lobular breast cancer. Surgery 1995;118:640–647.

29 Giuliano AE, Boolbol S, Degnim A et al. Society of Surgical Oncology: Position statement on prophylactic mastectomy. Approved by the Society of Surgical Oncology Executive Council, March 2007. Ann Surg Oncol 2007;14:2425–2427.

30 Yi M, Hunt KK, Arun BK et al. Factors affecting the decision of breast cancer patients to undergo contralateral prophylactic mastectomy. Cancer Prev Res (Phila) 2010;3:1026–1034.

31 Polednak AP. Frequency of prophylactic contralateral mastectomy among breast cancer patients. J Am Coll Surg 2001;192:804–805.

32 Sorbero ME, Dick AW, Beckjord EB et al. Diagnostic breast magnetic resonance imaging and contralateral prophylactic mastectomy. Ann Surg Oncol 2009;16:1597–1605.

33 Biglia N, Bounous VE, Martincich L et al. Role of MRI (magnetic resonance imaging) versus conventional imaging for breast cancer presurgical staging in young women or with dense breast. Eur J Surg Oncol 2011;37:199–204.

34 Bedrosian I, Mick R, Orel SG et al. Changes in the surgical management of patients with breast carcinoma based on preoperative magnetic resonance imaging. Cancer 2003;98:468–473.

35 Bilimoria KY, Cambic A, Hansen NM et al. Evaluating the impact of preoperative breast magnetic resonance imaging on the surgical management of newly diagnosed breast cancers. Arch Surg 2007;142:441–445.

36 Spear SL, Schwarz KA, Venturi ML et al. Prophylactic mastectomy and

reconstruction: Clinical outcomes and patient satisfaction. Plast Reconstr Surg 2008;122:1–9.

37 Geiger AM, West CN, Nekhlyudov L et al. Contentment with quality of life among breast cancer survivors with and without contralateral prophylactic mastectomy. J Clin Oncol 2006;24:1350–1356.

38 Schwartz MD. Contralateral prophylactic mastectomy: Efficacy, satisfaction, and regret. J Clin Oncol 2005;23:7777–7779.

39 Litton JK, Westin SN, Ready K et al. Perception of screening and risk reduction surgeries in patients tested for a BRCA deleterious mutation. Cancer 2009;115:1598–1604.

40 Nekhlyudov L, Bower M, Herrinton LJ et al. Women's decision-making roles regarding contralateral prophylactic mastectomy. J Natl Cancer Inst Monogr 2005;(35):55–60.

41 Graves KD, Peshkin BN, Halbert CH et al. Predictors and outcomes of contralateral prophylactic mastectomy among breast cancer survivors. Breast Cancer Res Treat 2007;104:321–329.

42 O'Connor AM, Tugwell P, Wells GA et al. A decision aid for women considering hormone therapy after menopause: Decision support framework and evaluation. Patient Educ Couns 1998;33:267–279.

43 O'Connor AM, Jacobsen MJ, Stacey D. An evidence-based approach to managing women's decisional conflict. J Obstet Gynecol Neonatal Nurs 2002;31:570–581.

44 Fagerlin A, Lakhani I, Lantz PM et al. An informed decision? Breast cancer patients and their knowledge about treatment. Patient Educ Couns 2006;64: 303–312.

45 Fox SA, Heritage J, Stockdale SE et al. Cancer screening adherence: Does physician-patient communication matter? Patient Educ Couns 2009;75: 178–184.

46 Chen JY, Tao ML, Tisnado D et al. Impact of physician-patient discussions on patient satisfaction. Med Care 2008;46:1157–1162.

47 Gershenwald JE, Hunt KK, Kroll SS et al. Synchronous elective contralateral mastectomy and immediate bilateral breast reconstruction in women with early-stage breast cancer. Ann Surg Oncol 1998;5:529–538.

48 Borgen PI, Hill AD, Tran KN et al. Patient regrets after bilateral prophylactic mastectomy. Ann Surg Oncol 1998;5:603–606.

49 Anderson K, Jacobson JS, Heitjan DF et al. Cost-effectiveness of preventive strategies for women with a BRCA1 or a BRCA2 mutation. Ann Intern Med 2006;144:397–406.

50 Norum J, Hagen AI, Maehle L et al. Prophylactic bilateral salpingo-oophorectomy (PBSO) with or without prophylactic bilateral mastectomy (PBM) or no intervention in BRCA1 mutation carriers: A cost-effectiveness analysis. Eur J Cancer 2008;44:963–971.

51 Grann VR, Panageas KS, Whang W et al. Decision analysis of prophylactic mastectomy and oophorectomy in BRCA1-positive or BRCA2-positive patients. J Clin Oncol 1998;16:979–985.

52 Gold M. Panel on cost-effectiveness in health and medicine. Med Care 1996;34(12 suppl):DS197–DS199.

53 Cartwright WS. Methods for the economic evaluation of health care programmes, second edition. By Michael F. Drummond, Bernie O'Brien, Greg L. Stoddart, George W. Torrance. Oxford: Oxford University Press, 1997. J Ment Health Policy Econ 1999;2:43.

54 Barton MB, West CN, Liu IL et al. Complications following bilateral prophylactic mastectomy. J Natl Cancer Inst Monogr 2005;(35):61–66.

55 Gold M, Siegel J, Russell L et al. Cost Effectiveness in Health and Medicine. New York: Oxford University Press, 1996:197–199.

56 Drummond MF, Sculpher MJ, Torrance GW, et al. Methods for the Economic Evaluation of Health Care Programmes, Third Edition. New York: Oxford University, 2005:55.

57 Brown ML, Lipscomb J, Snyder C. The burden of illness of cancer: Economic cost and quality of life. Annu Rev Public Health 2001;22:91–113.

58 Helzlsouer KJ. Contralateral prophylactic mastectomy: Quantifying benefits and weighing the harms. J Clin Oncol 2005;23:4251–4253.