



Contralateral prophylactic mastectomy: A narrative review of the evidence and acceptability



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ABSTRACT

The uptake of contralateral prophylactic mastectomy (CPM) has increased steadily over the last twenty years in women of all age groups and breast cancer stages. Since contralateral breast cancer is relatively rare and the breast cancer guidelines only recommend CPM in a small subset of patients with breast cancer, the drivers of this trend are unknown. This review aims to evaluate the evidence for and acceptability of CPM, data on patient rationales for choosing CPM, and some of the factors that might impact patient preferences. Based on the evidence, future recommendations will be provided. First, data on contralateral breast cancer risk and CPM rates and trends are addressed. After that, the evidence is structured around four main patient rationales for CPM formulated as questions that patients might ask their surgeon: Will CPM reduce mortality risk? Will CPM reduce the risk of contralateral breast cancer? Can I avoid future screening with CPM? Will I have better breast symmetry after CPM? Also, three different guidelines regarding CPM will be reviewed. Studies indicate a large gap between patient preferences for radical risk reduction with CPM and the current approaches recommended by important guidelines. We suggest a strategy including shared decision-making to enhance surgeons' communication with patients about contralateral breast cancer and treatment options, to empower patients in order to optimize the use of CPM incorporating accurate risk assessment and individual patient preferences.

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Breast cancer is the most frequently diagnosed malignancy in women in the United States of America (USA). With an incidence of 127.5 new cases per 100,000 women per year, approximately 12.8% of women overall will be diagnosed with breast cancer during their lifetime [1]. Surgical treatment options for primary breast cancer include lumpectomy, which is called breast conservation therapy if combined with radiation, and mastectomy [2]. If the patient has no contraindication to breast conservation therapy, ultimately patients decide if breast conservation or mastectomy is preferred, given the absence of survival difference between the two options [3]. While some will choose to undergo unilateral mastectomy for treatment of the primary tumor, others will also undergo contralateral prophylactic mastectomy (CPM); CPM, which is sometimes referred to as contralateral risk-reducing mastectomy, is removal of the

unaffected breast, often performed to prevent contralateral breast cancer [3]. In women with breast cancer, the average risk of contralateral breast cancer is around 0.4% per year with a cumulative incidence of 1.9% after five years [4,5]. Many studies indicate that CPM rates in the USA have increased substantially during the last two decades [6–8].

The current guidelines by the National Comprehensive Cancer Network (NCCN) and the American Society of Breast Surgeons (ASBrS) state that CPM should be considered in patients at high risk of contralateral breast cancer, such as patients with a BRCA1/2 mutation or a strong family history [9–11]. However, Hawley et al. [12] found that only 31% of all women undergoing CPM have a BRCA1/2 mutation or a strong family history (defined as ≥ 2 first-degree relatives with breast or ovarian cancer). These factors suggest that a high risk of developing contralateral breast cancer may not be the reason why patients choose CPM and that the guidelines are not consistently followed in the decision-making process. Contrarily, the European Manchester guidelines [13] do not

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prescribe who should be allowed or refused CPM, but instead focus on the decision-making process.

The decision to undergo CPM is preference-sensitive. Good decision-making requires the best available evidence about CPM combined with well-considered patient preferences. Studies [14–17] have identified several rationales that patients might have for CPM, which we formulated as questions that patients could ask their surgeon. The identified patient rationales include the following:

- Will CPM reduce mortality risk?
- Will CPM reduce the risk of contralateral breast cancer?
- Can I avoid future screening with CPM?
- Will I have better breast symmetry after CPM?

The aim of this review is to evaluate the evidence and acceptability of CPM, data describing patient rationales for CPM, and some of the factors that might impact patient preferences.

First, data on contralateral breast cancer risk and CPM rates and trends will be addressed to provide background on the current situation. Afterwards, the evidence regarding each of the rationales, surgeons' influence on patient decisions, and guidelines regarding CPM will be reviewed. Based on the findings, future recommendations will be provided. This narrative review focuses on all types of CPM in women with stage I to stage III breast cancer.

1. Search methodology

First, the PubMed database was searched on the topics of interest. Search terms used were ""Prophylactic Mastectomy""[-Mesh]; ""Prophylactic Mastectomy""[Mesh] contralateral"; "Contralateral Prophylactic Mastectomy"; ""Prophylactic Mastectomy/trends""[Majr]; ""Breast Neoplasms/genetics""[MAJR] AND Contralateral Prophylactic Mastectomy"; "contralateral prophylactic mastectomy AND (attitudes OR opinion)"; "Risk Factors AND Contralateral Breast Cancer"; "Contralateral Breast Cancer AND Trends".

Articles were saved in RefWorks based on title, year of publication, country, and the full abstract. Abstracts were reviewed, and articles were included if the main subject was related to one of the following topics: contralateral breast cancer risk, mastectomy rates and trends, risks and benefits of CPM, opinions and rationales of patients and surgeons. The snowball method was used to further search based on the forward and backward citations of collected articles, and studies from the 'Related Articles' section in PubMed were reviewed and included if relevant. A total of 259 articles were reviewed and used for the narrative review.

2. Results

2.1. Risk of contralateral breast cancer

In the literature, the risk of contralateral breast cancer is less well defined than the risk of a primary breast cancer. Recent review articles consistently quote the annual risk of contralateral breast cancer in the general breast cancer patient population to be 0.5–0.75% [18–21]. However, many of the population-based studies from which these estimates were derived were conducted decades ago [22–24]. Only a few articles with recent data are published. One recent population-based study found a 5-year cumulative contralateral breast cancer incidence of 1.9%, a 10-year cumulative incidence of 4.6%, and a 20-year cumulative incidence of 10.5% [5]. A Dutch population-based cohort study found a cumulative contralateral breast cancer incidence of 1.9% and 3.8% at 5 and 10 years, respectively; The annual contralateral breast cancer

risk was 0.4% [4]. The contralateral breast cancer risk is 1.3–1.9 times higher than the risk of primary breast cancer in the general population [5]. However, for most patients with primary breast cancer the risk of distant metastases exceeds the risk of developing contralateral breast cancer. 10–12% of women treated for primary breast cancer developed distant recurrence during a mean follow-up of just over 5 years [25,26]. The overall rate of first distant metastasis was 1.94% per year [25], and receipt of CPM has not been shown to improve distant metastases-free survival [27]. A study based on SEER data found a 3% per year decrease in contralateral breast cancer incidence between 1985 and 2006 and attributed this to the increased use of adjuvant hormonal therapies, but increased use of CPM has likely confounded these outcomes [28].

Carrying a BRCA1 or BRCA2 mutation is the strongest known predictor for contralateral breast cancer risk in patients with a history of breast cancer [11]. The annual risk of contralateral breast cancer in these mutation carriers is 2–3%, with a 5-year cumulative risk of contralateral breast cancer of 13% in BRCA1 and 8% in BRCA2 mutation carriers. At 10-years, the cumulative risk is 40% and 26%, respectively [11]. A very strong family history, classified as two or more first degree relatives with breast or ovarian cancer, also puts women at high risk of contralateral breast cancer. Having any first-degree relative with breast cancer doubles the risk of contralateral breast cancer in mutation negative women, but the underlying genetic element in these situations is not yet completely understood [29,30].

Other factors that increase the risk of contralateral breast cancer to a smaller extent include younger age at primary breast cancer diagnosis, lobular histology, higher grade and size of the tumor, ER/PR negative primary breast cancer, higher breast density, and/or a high Body Mass Index (BMI) at primary breast cancer diagnosis; a combination of these characteristics may be associated with an even further increase in risk [18,31,32]. Polygenic risk (based on single nucleotide polymorphisms) might also influence the risk of contralateral breast cancer occurrence. In women with high polygenic risk scores, contralateral risk may approach that of BRCA carriers [33].

Three different contralateral breast cancer risk prediction models have been described in the literature, including the Manchester formula (part of the Manchester guidelines for contralateral risk-reducing mastectomy), CBCrisk, and PredictCBC [13,34–36]. These models calculate an individual's risk of contralateral breast cancer in different ways using patient and tumor characteristics such as age at first primary breast cancer diagnosis, family history, ER status, breast density, first breast cancer type, and adjuvant treatments. However, these models are not widely used yet [37]. Giardiello et al. [37], who used individual patient data from a number of studies with a long follow-up, evaluated the accuracy of the three models. They found only moderate discrimination of all three models and considerable heterogeneity between studies, and concluded that careful re-calibration is required before these models could be used in clinical decision-making [37].

2.2. Contralateral prophylactic mastectomy rates and trends

Between 2004 and 2012 in the USA the proportion of women undergoing CPM showed a nearly three-fold increase in all age groups, with the largest increase in women under the age of 40.7,38,39 The proportion of patients choosing CPM has an inverse relationship with age, ranging from 2.4% in patients 70 years or older to 29.3% in patients between 20 and 29 years old [7,39]. Other factors associated with undergoing CPM include having lobular (compared to ductal) tumor histology, ER+/PR+ cancer, Caucasian race, and having private insurance [6–8]. Non-Hispanic whites had almost double the CPM uptake rate across all age groups and tumor

characteristics compared to Asian/Pacific Islanders and non-Hispanic blacks [6]. Previous studies suggested that disparities in healthcare access could partially explain racial/ethnic differences in CPM, which is often followed by breast reconstruction [6,40]. However, although health insurance is associated with reconstruction after CPM, racial/ethnic disparities remained after controlling for health insurance coverage, suggesting that other factors might also be involved [41,42].

Although having a high risk of contralateral breast cancer is associated with CPM, high-risk patients choosing CPM only explains part of the increasing CPM uptake. The prevalence of genetic predispositions such as BRCA1/2 in the breast cancer population is very low, and therefore other patients who are at low risk are driving the increased use of CPM [12,43,44]. Only 31% of all women undergoing CPM have a BRCA1/2 mutation or a strong family history [12]. Interestingly, breast cancer patients who get tested for BRCA1/2 mutations are more likely to undergo CPM than patients who do not get tested, regardless if the test result was positive or negative [12,45,46]. This likely reflects family history and the fear of developing a second cancer. In a study at one institution [47], young age and increasing number of first degree relatives, regardless of mutation status, drove the choice of CPM. The absence of a known mutation, given their young age (and often young children) and family history, did not deter patients from choosing CPM, nor did it change their perception of risk of developing a contralateral breast cancer. All patients regardless of breast cancer stage increasingly choose CPM if they are choosing mastectomy instead of breast conservation for their primary local therapy, as the upward trend ranges from patients with stage I to stage III breast cancer [8]. Patients with stage III breast cancer choosing CPM may be counter-intuitive, as with increasing stage there is an increasing risk of distant recurrence, which makes the preventative benefit of CPM less pronounced. It is important to note, however, that local and distant risk of recurrence for women with stage III disease is determined by response to therapy and residual disease, which is why neoadjuvant therapy is an important strategy for helping women make decisions about local therapy [48]. The evidence regarding 'Risk of contralateral breast cancer' and CPM rates and trends' is summarized in Table 1.

2.3. Patient rationales for choosing contralateral prophylactic mastectomy

Will CPM reduce mortality risk? One of the main rationales reported for undergoing CPM is improving survival [15,16,49,50]. In a semi-structured interview study of 29 breast cancer patients, patients expressed their belief that contralateral breast cancer would inevitably lead to metastases and then to death [15]. Whereas only 18% of women with breast cancer surveyed in the study by Rosenberg et al. [16] who underwent CPM believed that CPM increased their survival, 94% still hoped that it would prolong their life.

Table 1
CPM context.

Risk of contralateral breast cancer	CPM rates and trends	Surgeons' influence on patient decisions
<ul style="list-style-type: none"> • Patients with breast cancer: annual risk 0.4% [4,5]. • 1.3–1.9 times the risk of first breast cancer in general population [5]. • Strongest risk factor: BRCA1/2 mutation [11]. • Annual risk 2–3%. • Other risk factors: family history, younger age, certain tumor characteristics [18,29–32]. 	<ul style="list-style-type: none"> • Nearly threefold increase in CPM uptake 2004–2012 [7,38,39] • All age groups [7,39] • Breast cancer stage I–III [8]. • Especially younger women, non-Hispanic whites, privately insured [6–8]. • Patients with low risk of contralateral breast cancer contribute to upward trend [12,43,44]. 	<ul style="list-style-type: none"> • Surgeon's opinion may have a large influence.16,85–87 • Surgeons' knowledge vary widely.88,89 • Wide variation between surgeons in recommendations and approaches to the discussion with the patient [16,64,70,87].

Contralateral breast cancer tends to present at a more favorable stage, which means earlier stage, smaller tumor size and more node-negative disease, compared to primary breast cancer [51–54]. Studies provide contradictory results regarding survival after contralateral breast cancer compared to unilateral breast cancer. Xiong et al. [5] and Schaapveld et al. [55] found worse survival after contralateral breast cancer, whereas Verkooijen et al. [56] found no difference. Other studies found more or less favorable or comparable survival rates after contralateral breast cancer and unilateral cancer depending on the stage of the index cancer, the stage of contralateral breast cancer or the follow-up time at which the contralateral breast cancer occurred [52,54,55]. The large study by Liederbach et al. [52] based on SEER data found that overall and disease-specific survival was lower if contralateral breast cancer developed < 4 years after the primary cancer, whereas contralateral breast cancers ≥ 6 years after the primary cancer had more favorable survival than the primary cancer. Several large cohort studies found no significant improvement in breast cancer-specific and overall survival in CPM compared to breast-conserving surgery [8,31,57]. On the other hand, a meta-analysis of studies comparing CPM and non-CPM recipients found an absolute overall survival benefit from CPM of 7.4% [58]. The benefit observed by this meta-analysis might be influenced by selection bias, as CPM recipients are more likely to have characteristics associated with improved survival, such as early-stage tumors and adequate health insurance. This is likely, because no absolute contralateral breast cancer risk reduction was found in the study. Strikingly, the same study found no survival benefit in patients with elevated family or genetic risk, despite an absolute contralateral breast cancer risk reduction. A study [53] which used the Markov model to simulate survival outcomes in non-BRCA carriers after CPM and no CPM, found a less than 1% 20-year overall survival benefit after CPM. Other studies found between 45% and 48% improved 15 to 20-years survival rates in patients with BRCA1/2 mutations who got CPM compared to patients who got unilateral mastectomy or breast conserving surgery [51,59].

Will CPM reduce the risk of contralateral breast cancer?

Concern about contralateral breast cancer is another reason that patients with breast cancer undergo CPM [15,16,49,50]. Misconceptions about contralateral breast cancer and CPM benefit may contribute to these decisions, since patient-perceived risk of contralateral breast cancer consistently overestimates actual calculated risk [15,16,60,61]. In a recent study [61] breast cancer patients without a BRCA mutation perceived their 10-year risk of contralateral breast cancer to be 22%, nearly four times the actual 10-year risk. On the other hand, a study using in-depth interviews with 45 patients [62] found that patients knew of their low risk of contralateral breast cancer, but they still wanted CPM. Similarly, another study of 60 patients found that patients found any risk intolerable [63]. Greater worry about cancer recurrence is associated with receipt of CPM [12,64].

Studies demonstrate that CPM effectively reduces the risk of

contralateral breast cancer, with a relative risk reduction of approximately 90–96% in women with or without genetic predisposition [58,65,66]. No mastectomy could reduce the relative risk of contralateral breast cancer by 100%, as it is impossible to remove all breast tissue. Based on this fact, the most recent Cochrane review used the term risk-reducing mastectomy instead of prophylactic mastectomy, which implies an elimination of risk [67]. A study [31] including almost 250,000 patients with breast cancer with a median follow-up time of 6.7 years calculated the absolute reduction of contralateral breast cancer risk as the number of observed breast cancer cases minus the expected number of incident breast cancers for the general California population, which was then divided by the person-years at risk; The study found 43 fewer cases of contralateral breast cancer per 10,000 patient years after bilateral mastectomy compared to unilateral mastectomy, and 34 fewer cases per 10,000 patient years in bilateral mastectomy as compared to breast-conserving therapy, although patients with BRCA1/2 and other genetic mutations were not excluded from this analysis [31]. Interestingly, a meta-analysis found a reduction of absolute risk (i.e. risk difference) of contralateral breast cancer in CPM receivers compared to non-CMP receivers in patients with elevated family risk or BRCA1/2 carriers, but not in the general breast cancer population. This could be explained by the lower contralateral breast cancer incidence in the general population [58].

Can I avoid future screening with CPM? The use of pre-operative breast magnetic resonance imaging (MRI) has increased over the last two decades, similar to the use of CPM [27,68]. Women who get breast MRI at diagnosis are more likely to receive CPM than women who do not receive MRI; it is unknown if the correlation between pre-operative MRI and CPM is due to MRI findings or other factors [12,17,27,34,43,68]. Still, patients' wish to avoid screening as a reason for CPM has been suggested in several articles [8,27,62,69]. Two studies using interviews [62,70] found that anxiety towards mammograms and no trust in screening to detect future cancers were reasons why patients chose CPM. Also, patients who choose CPM believe that it has more benefits than harms [62,71].

Although some providers might recommend imaging surveillance after mastectomy, in most situations such routine imaging is unnecessary and has not been shown to improve outcomes. One analysis of local recurrence after mastectomy with autologous reconstruction [72] found that 3.9% of patients experienced local recurrence, all occurring in women previously treated for breast cancer, and none occurring in the setting of prophylactic mastectomy. Current NCCN guidelines [10] do not recommend routine breast imaging after CPM, but do recommend history and physical examination at least annually.

Complications might occur after CPM. Undergoing bilateral mastectomy nearly doubles the risk of postoperative complications compared to unilateral mastectomy without reconstruction [73,74]. On the other hand, one study which only included complications requiring reoperation [75] found no significant difference in complication rates between the groups regardless of whether reconstruction was performed. In the studies that only included surgery followed by reconstruction, bilateral mastectomy showed significantly higher complication rates than unilateral mastectomy, but the differences were smaller than without reconstruction [76,77]. Bilateral surgery also required a longer hospital stay than unilateral mastectomy [75,77].

Will I have better breast symmetry after CPM? A desire for breast symmetry is also a common reason to choose CPM, usually secondary to avoiding the risk of a contralateral breast cancer [15,16,50,70]. This is a consideration both for those who do and do not want to get reconstruction after CPM [15,70].

Breast symmetry and other subjective outcomes. Despite the lack of demonstrated clinical advantage and the risk of

complications, studies show that most women are happy with their choice to undergo CPM. Approximately 90% of women are satisfied about CPM and would choose it again [16,62,78,79]. Factors influencing satisfaction with the surgery include peace of mind, satisfaction with the cosmetic results, body image, risk reduction, and the feeling to be 'prevailing over cancer' [78,80,81]. Despite high satisfaction in those studies, 45% or more patients report adverse effects on aspects such as body image, cosmetic results, and sexuality [15,78,80]. Parker et al. [82] compared body image concerns in patients before and after CPM and unilateral mastectomy using the Body Image Scale. This is a self-report measure with 10 items such as 'dissatisfied with appearance,' 'body less whole' and 'dissatisfied with body,' in which a higher score reflects more body image disturbances [83]. It was found that CPM patients had significantly higher body image concerns than unilateral mastectomy patients pre-surgery [82]. Eighteen months post-surgery, concern scores had nearly doubled in both groups. Body image was significantly more disturbed in CPM compared to unilateral mastectomy patients. The Breast-Q breast satisfaction domain includes questions related to satisfaction with breast symmetry, appearance, feel, fit in a bra, and look in and out of clothing, which are scored using a 0 to 100 scale [84]. A study [84] including 5500 patients found no statistically significant difference in breast satisfaction between unilateral mastectomy and CPM without reconstruction. The four patient rationales for CPM are summarized in Fig. 1.

Surgeons' influence on patient decisions. The surgeon's opinion may largely influence the patient's decision whether to undergo CPM [16,85–87]. In one study [87], when surgeons recommended against CPM, only 6.1% of the patients underwent the procedure compared to 57.5% of those whose surgeons did not recommend against it. In another study [86], only 4% of patients whose surgeon was reluctant to perform CPM and strongly in favor of breast conservation had CPM, compared to 34% of patients whose surgeon had the opposite view.

Whereas patients seem to rely on the surgeon's opinion in their decision, surgeons may not have fully informed opinions. Also, there is a wide variation in surgeon recommendations regarding CPM and surgeons' approaches to the discussion with the patient. Just 25.7% of all sampled surgeons always used the ASBrS guidelines, whereas 42.5% used them not very often and 12.3% never [88]. In a large study based on surveys [89], only 55% of breast surgeons had high knowledge regarding contralateral breast cancer, and low knowledge was significantly associated with favoring CPM. Despite the higher risk of distant metastasis, surgeons were more likely to recommend CPM to patients with stage III disease compared to stage I [88]. Katz et al. [87] found that in almost one third of the cases (32.3%), surgeons had no substantial discussion about CPM with their patients before a decision was made. In the study by Rosenberg et al. [16], only half of participants responded that their doctors discussed the reasons not to have CPM. On the other hand, a study [64] found that of 117 breast cancer patients surveyed, 50% were moderately to extremely interested in CPM before their first surgery visit, whereas only 10% ultimately had CPM with their primary breast cancer surgery, which suggests that surgeons had made patients more reluctant towards CPM. In a semi-structured interview study [70], many women characterized the process of requesting CPM to their surgeon as a challenging process or a 'battle', and they felt not understood by their surgeon in their wish for CPM. The surgeon's influence on patient decisions is summarized in Table 1.

2.4. Guidelines

Several organizations have created clinical guidelines and recommendations for CPM. Two trusted resources in the USA are the

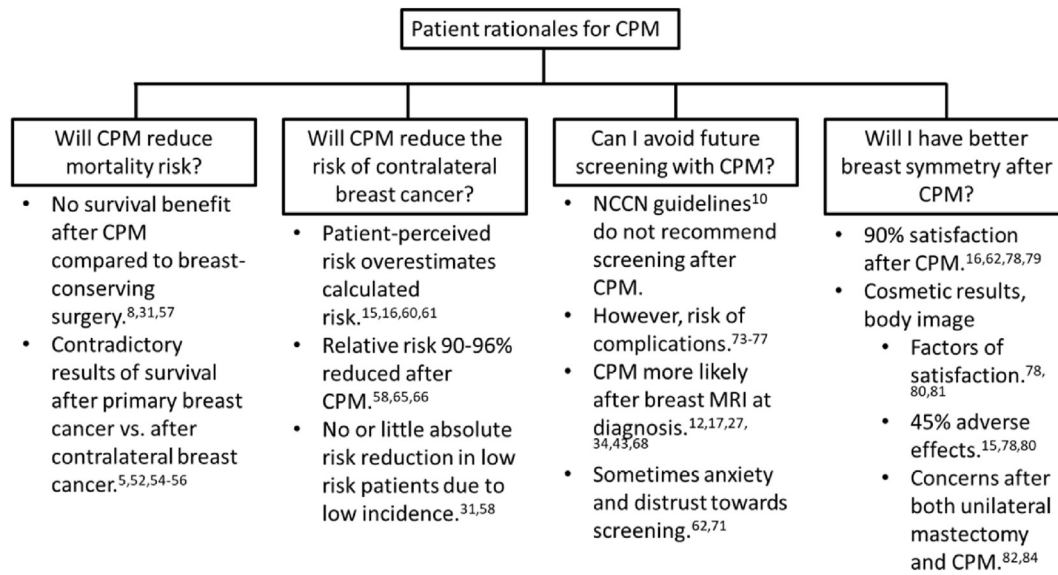


Fig. 1. Patient rationales for CPM

NCCN guidelines and the ASBrS consensus statement [9,10,90]. These state that CPM is not recommended except in certain high-risk situations. The NCCN provides an overview of high-risk situations, which include the genetic predispositions BRCA1 and BRCA2 [10]. Patients without known mutations may be eligible for genetic testing. If a woman is not a mutation carrier or is ineligible for testing, a risk score is calculated using the Gail model incorporating other risk elements such as family history, atypical hyperplasia, and higher breast density. In women with a $\geq 1.7\%$ 5-year risk of first primary breast cancer combined with a life expectancy of ≥ 10 years, CPM should be considered [10]. The ASBrS also lists a strong family history as a condition under which CPM could be an option, which is formulated as “a greater than 25% lifetime risk of breast cancer primarily due to family history in the absence of deleterious mutations”.^{9(p.3103)} The NCCN and the ASBrS both recommend that options for risk reduction be discussed in a shared decision-making environment; they stress the importance of patient counseling and informed discussion regarding personal preferences, values, and the risks and benefits of the procedure with eligible women [9,10,90,91]. Above that, the ASBrS specifically states that the surgeon should make a direct recommendation for or against CPM to each patient [9].

In contrast with the NCCN and the ASBrS, the European Manchester guidelines for contralateral risk-reducing mastectomy [13] state that “it is not possible to be prescriptive in terms of who should be allowed or refused contralateral risk reducing mastectomy.”^{13(p.5)} Instead they describe a five step process of preoperative assessment and counseling for patients who have requested CPM as a tool for clinicians involved in the shared-decision making process. In step (1), taking a history, it is stated that the reasons behind a patient’s request to discuss CPM should be determined first, followed by the clinical history. In (2), calculating the risk of contralateral breast cancer, the Manchester formula are used to provide patients an estimation of their individual risk. The step (3) “cooling off period” means that patients should not make a decision regarding CPM until their primary cancer treatment has been completed to avoid making a too quick decision when they are emotionally vulnerable. Step (4) is a multi-disciplinary team discussion, in which a breast care nurse, breast surgeon, oncologist, radiologist and pathologist discuss the patient’s CPM request based on the information from the previous steps, the risks and benefit of

the procedure, and alternative options. In the final step, the patient signs a formal consent form to confirm her decision. An overview of the three guidelines is provided in Table 2.

3. Discussion

CPM rates have risen steadily over the last two decades in all patients of all age groups and breast cancer stages, but most notably in women under the age of 40. Although the NCCN and ASBrS guidelines recommend CPM only in high contralateral breast cancer risk patients such as BRCA1/2 carriers and those with a strong family history, the increase of CPM in women without genetic predispositions is mainly responsible for the overall increased uptake of CPM. These data suggest that women without a BRCA1/2 mutation or a family history may be at risk for being overtreated with CPM.

This review provides insight into why patients without a genetic predisposition or a strong family history would choose CPM. The main reasons are to reduce risk of mortality and contralateral breast cancer. Based on the presented evidence, a patient should be discouraged to undergo CPM if her main drive is to reduce the risk of mortality. Although the risk of contralateral breast cancer in the general breast cancer population is relatively low (about 0.4% per year), and much lower than the risk of distant metastasis in most cases, most patients overestimate their risk of contralateral breast cancer. Other patients are aware of their low risk, but still want to eliminate all risk. This shows that patients’ feelings about the data also play a role in their preference for CPM. The growing attention around breast cancer prevention, screening and testing in the public might be a factor explaining the overestimation of contralateral breast cancer risk. Additionally, some patients with breast cancer may pursue CPM to avoid the need for ongoing screening. As the NCCN guidelines do not recommend screening after CPM, this might be a good reason to undergo CPM, although patients need to be aware that CPM does not eliminate all contralateral breast cancer risk. Screening is an area that warrants future study, particularly as recommendations for screening have recently increased [92]. Patients who choose CPM believe that the benefits are greater than the harms. Studies also identify breast symmetry as a reason for patients to choose CPM. The surgeon’s opinion plays a major role in patients’ choice for CPM. Satisfaction after CPM is

Table 2
Guidelines.

NCCN (USA) [10,90]	ASBrS (USA) [9,91]	Manchester Guidelines (UK) [13]
<ul style="list-style-type: none"> • CPM only recommended in high-risk situations, including BRCA1/2. • Gail model used to identify non-mutation carriers at high risk. • Options for risk reduction should be discussed in a shared decision-making environment. • Patient counseling and informed discussion are important. 	<ul style="list-style-type: none"> • CPM only recommended in high-risk situations, including BRCA1/2 and a strong family history. • Options for risk reduction should be discussed in a shared decision-making environment. • Patient counseling and informed discussion are important. • Surgeons should make a direct recommendation for or against CPM to each patient. 	<ul style="list-style-type: none"> • Five step process of pre-operative assessment and counseling: <ol style="list-style-type: none"> 1. Reasons and clinical history 2. Calculating CBC risk 3. Giving the patient time for the decision 4. Multi-disciplinary team discussion 5. Patient decision and consent form

very high (around 90%), although adverse effects related to body image, cosmetic results, and sexuality are also common.

Despite high patient satisfaction, professional societies are concerned that the benefits of CPM in low-risk patients do not outweigh the risks. CPM does not impact mortality and has only a very small impact on the chance of developing a contralateral cancer. Above that, the risk of complications after CPM is evident. Still, it is important to note that the decision to undergo CPM is preference-sensitive and should reflect the values of the patient, which has been more adequately emphasized in the Manchester guidelines than in the NCCN and the ASBrS guidelines. If a patient really wants to avoid screening or take away all worry about future breast cancer, CPM might be a good option for that patient despite the risks.

3.1. Recommendations

While action to disrupt the rise of CPM rates is warranted, patient preference should be the major factor in the decision whether to perform CPM. Clinicians have an ethical role to facilitate good decision making based on the best available evidence and well-considered patient preferences. Surgeons need to make sure that patients understand the impact of CPM on the chance of dying of breast cancer, the chance of experiencing another cancer diagnosis and treatment, the chance of avoiding screening, and the chance to gain breast symmetry. We recommend that breast surgeons have a conversation about the option of CPM and patient preferences with every patient considering any type of mastectomy. In this conversation, surgeons should adopt shared decision-making and other decision aids.

Shared decision-making has been acknowledged as important in the literature regarding cancer care and breast surgery [91,93,94]. It is a four-step process, which starts with the professional informing the patient that a decision needs to be made and that the patient’s opinion is important [95]. Next, the professional explains the available options and the pros and cons. After discussion of the patient’s preferences and deliberation, they discuss the patient’s wish to make a decision, make or defer the decision, and discuss follow-up. However, these steps are not yet widely implemented in clinical practice [95]. Alston et al. [96], who surveyed a representative sample of over a thousand adults from the USA, found that the majority of people desire the shared decision-making steps in their communication with the healthcare provider. The finding by Katz et al. [87] that lack of discussion between patient and surgeon was associated with dissatisfaction with the surgery decision suggests that patients also desire shared decision-making on CPM specifically.

To practice optimal shared decision-making, both surgeons and patients need to be informed with the latest evidence regarding

CPM and contralateral breast cancer risk. High knowledge is predictive of surgeon recommendation against CPM, but currently almost half of the US surgeons lack this knowledge. Only a quarter of the surgeons always use the ASBrS guidelines. In order to avoid the misperceptions that increasingly drive low-risk women towards CPM, it is essential that surgeons help clarify what women want to achieve with the decision to undergo CPM and make sure patients are aware of the “price to pay” and the consequences of surgery. Therefore, we need to develop better ways to get the evidence to the patients in a clear, understandable way.

Decision aids, tools that present evidence-based, objective information to the patient on all treatment options, might be useful in this context [93,97]. A large systematic review found that patient decision aids were associated with more accurate risk perceptions and improved decisional conflict scores [98]. In CPM decision-making, decision aids were acceptable and feasible to patients and healthcare professionals and associated with higher levels of knowledge [14,99,100]. An online interactive breast cancer in-visit decision aid (BIDA) has been used successfully by patients during breast surgery decision-making; under ‘Evaluation’, this tool showed published estimates using pictograms of 100 women for outcomes such as the risk of getting a new cancer in the other breast stratified by the three procedures—lumpectomy, unilateral mastectomy, and bilateral mastectomy—to compare those options [14,101]. Patients who had used the BIDA during the consultation estimated the 5-year contralateral breast cancer risk of women with breast cancer significantly more accurate than patients after usual care [101]. If valid contralateral breast cancer risk prediction models are established, individual risk information calculated with these models could be incorporated in the decision aids for each patient.

Also, as recommended by the ASBrS, after the first three steps in the shared decision-making process surgeons should give a strong recommendation in favor of or against CPM to each patient, informed by the best available evidence and the patient’s preferences. This consultation as a whole should provide breast cancer patients with all the requirements to make good decision whether to undergo CPM. However, this decision is not an emergency and patients should get enough time to consider their choices. Giving patients additional time, if desired, to discuss options and do anxiety management with a psychologist might be useful and may in the end change the patient’s mind on CPM. If this strategy becomes widely used in clinical practice, it may lead to reduction in potentially harmful overtreatment.

4. Conclusion

In a time where breast cancer patients increasingly choose CPM regardless of contralateral breast cancer risk, we suggest a strategy

including shared decision-making and discussion of patients' rationales for CPM. This should enhance surgeons' communication with patients about contralateral breast cancer risk and treatment options to make sure that patients are empowered to make a well-informed decision. Given the fact that patients' current preference for CPM may be driven by misperceptions about contralateral breast cancer and the risks and benefits of CPM, this strategy, if widely implemented, might contribute to closing the gap between patients' choice for CPM and the more conservative approach that the guidelines prescribe for patients without high contralateral breast cancer risk.

Declaration of competing interest

None.

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References

- [1] Surveillance epidemiology [SEER] ERP. Cancer Stat Facts: Female breast cancer. 2020(March/10). <https://seer.cancer.gov/statfacts/html/breast.html>.
- [2] Gradishar WJ, Balassanian R, Blair SL, et al. NCCN invasive breast cancer version 1.2016 clinical practice guidelines in oncology. *J Natl Compr Cancer Netw* 2016;14(3):324–54. <https://jncn.org/view/journals/jncn/14/3/article-p324.xml>.
- [3] Gradishar WJ, Anderson BO, Abraham J, et al. Breast cancer NCCN evidence blocks: version 3.2020. 2020. https://www.nccn.org/professionals/physician_gls/pdf/breast_blocks.pdf.
- [4] Kramer I, Schaapveld M, Oldenburg HSA, et al. The influence of adjuvant systemic regimens on contralateral breast cancer risk and receptor subtype. *J Natl Cancer Inst*. Published online January 2019. <https://doi.org/10.1093/jnci/djz010> [doi].
- [5] Xiong Z, Yang L, Deng G, et al. Patterns of occurrence and outcomes of contralateral breast cancer: analysis of SEER data. *J Clin Med* 2018;7(6):10.3390/jcm7060133. doi:E133 [pii].
- [6] Brown D, Shao S, Jatoi I, Shriver CD, Zhu K. Trends in use of contralateral prophylactic mastectomy by racial/ethnic group and ER/PR status among patients with breast cancer: a SEER population-based study. *Cancer Epidemiol* 2016;42:24–31. <https://doi.org/10.1016/j.canep.2016.02.011> [doi].
- [7] Nash R, Goodman M, Lin CC, et al. State variation in the receipt of a contralateral prophylactic mastectomy among women who received a diagnosis of invasive unilateral early-stage breast cancer in the United States, 2004–2012. *JAMA Surg* 2017;152(7):648–57. <https://doi.org/10.1001/jamasurg.2017.0115> [doi].
- [8] Wong SM, Freedman RA, Sagara Y, Aydogan F, Barry WT, Golshan M. Growing use of contralateral prophylactic mastectomy despite no improvement in long-term survival for invasive breast cancer. *Ann Surg* 2017;265(3):581–9. <https://doi.org/10.1097/SLA.0000000000001698> [doi].
- [9] 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* 2016;23(10):3100–5. <https://doi.org/10.1245/s10434-016-5443-5> [doi].
- [10] Daly MB, Pal T, Berry MP, et al. Genetic/Familial high-risk assessment: breast, ovarian, and pancreatic, version 2.2021, NCCN clinical practice guidelines in oncology. *J Natl Compr Cancer Netw* 2021;19(1):77–102. <https://doi.org/10.6004/jncn.2021.0001>.
- [11] Kuchenbaecker KB, Hopper JL, Barnes DR, et al. Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. *Jama* 2017;317(23):2402–16. <https://doi.org/10.1001/jama.2017.7112> [doi].
- [12] Hawley ST, Jagsi R, Morrow M, et al. Social and clinical determinants of contralateral prophylactic mastectomy. *JAMA Surg* 2014;149(6):582–9. <https://doi.org/10.1001/jamasurg.2013.5689> [doi].
- [13] Basu NN, Ross GL, Evans DG, Barr L. The Manchester guidelines for contralateral risk-reducing mastectomy. 237-y *World J Surg Oncol* 2015;13. <https://doi.org/10.1186/s12957-015-0638-y> [doi].
- [14] Yao K, Belkora J, Bedrosian I, et al. Impact of an in-visit decision aid on patient knowledge about contralateral prophylactic mastectomy: a pilot study. *Ann Surg Oncol* 2017;24(1):91–9. <https://doi.org/10.1245/s10434-016-5556-x> [doi].
- [15] Covelli AM, Baxter NN, Fitch MI, McCready DR, Wright FC. "Taking control of cancer": understanding women's choice for mastectomy. *Ann Surg Oncol* 2015;22(2):383–91. <https://doi.org/10.1245/s10434-014-4033-7> [doi].
- [16] Rosenberg SM, Tracy MS, Meyer ME, et al. Perceptions, knowledge, and satisfaction with contralateral prophylactic mastectomy among young women with breast cancer: a cross-sectional survey. *Ann Intern Med* 2013;159(6):373–81. <https://doi.org/10.7326/0003-4819-159-6-201309170-00003> [doi].
- [17] Houssami N, Turner RM, Morrow M. Meta-analysis of pre-operative magnetic resonance imaging (MRI) and surgical treatment for breast cancer. *Breast Cancer Res Treat* 2017;165(2):273–83. <https://doi.org/10.1007/s10549-017-4324-3> [doi].
- [18] Akdeniz D, Schmidt MK, Seynaeve CM, et al. Risk factors for metachronous contralateral breast cancer: a systematic review and meta-analysis. *Breast* 2019;44:1–14. doi:S0960-9776(18)30322-9 [pii].
- [19] Boccardo C, Gentilini O. Contralateral risk reducing mastectomy in patients with sporadic breast cancer. Benefits and hazards. *Eur J Surg Oncol* 2016;42(7):913–8. <https://doi.org/10.1016/j.ejso.2016.04.054> [doi].
- [20] Mamtani A, Morrow M. Why are there so many mastectomies in the United States? *Annu Rev Med* 2017;68:229–41. <https://doi.org/10.1146/annurev-med-043015-075227> [doi].
- [21] Murphy JA, Milner TD, O'Donoghue JM. Contralateral risk-reducing mastectomy in sporadic breast cancer. *Lancet Oncol* 2013;14(7):262. [https://doi.org/10.1016/S1470-2045\(13\)70047-0](https://doi.org/10.1016/S1470-2045(13)70047-0) [doi].
- [22] Healey EA, Cook EF, Orav EJ, Schnitt SJ, Connolly JL, Harris JR. Contralateral breast cancer: clinical characteristics and impact on prognosis. *J Clin Oncol* 1993;11(8):1545–52. <https://doi.org/10.1200/JCO.1993.11.8.1545> [doi].
- [23] Kollias J, Ellis IO, Elston CW, Blamey RW. Clinical and histological predictors of contralateral breast cancer. *Eur J Surg Oncol* 1999;25(6):584–9. <https://doi.org/10.1053/ejso.1999.0711> [doi].
- [24] Rosen PP, Groshen S, Kinne DW, Hellman S. 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(5):904–10. doi:0039-6060(89)90164-5 [pii].
- [25] Colzani E, Johansson AL, Liljegren A, et al. Time-dependent risk of developing distant metastasis in breast cancer patients according to treatment, age and tumour characteristics. *Br J Canc* 2014;110(5):1378–84. <https://doi.org/10.1038/bjc.2014.5> [doi].
- [26] Fung F, Cornacchi SD, Vanniyasingam T, et al. Predictors of 5-year local, regional, and distant recurrent events in a population-based cohort of breast cancer patients. *Am J Surg* 2017;213(2):418–25. doi:S0002-9610(16)30290-2 [pii].
- [27] Chung A, Huynh K, Lawrence C, Sim MS, Giuliano A. Comparison of patient characteristics and outcomes of contralateral prophylactic mastectomy and unilateral total mastectomy in breast cancer patients. *Ann Surg Oncol* 2012;19(8):2600–6. <https://doi.org/10.1245/s10434-012-2299-1> [doi].
- [28] Nichols HB, de Gonzalez Jr AB, Jvl, Rosenberg PS, Anderson WF. Declining incidence of contralateral breast cancer in the United States from 1975 to 2006. *J Clin Oncol* 2011;29(12):1564–9. <https://doi.org/10.1200/JCO.2010.32.7395> [doi].
- [29] Kenny R, Reed M, Subramanian A. Mastectomy for risk reduction or symmetry in women without high risk gene mutation: a review. *Int J Surg* 2018;50:60–4. doi:S1743-9191(17)31501-7 [pii].
- [30] Reiner AS, Sisti J, John EM, et al. Breast cancer family history and contralateral breast cancer risk in young women: an update from the women's environmental cancer and radiation epidemiology study. *J Clin Oncol* 2018;36(15):1513–20. <https://doi.org/10.1200/JCO.2017.77.3424> [doi].
- [31] Kurian AW, Canchola AJ, Ma CS, Clarke CA, Gomez SL. 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* 2020;126(5):958–70. <https://doi.org/10.1002/cncr.32618> [doi].
- [32] Reiner AS, Lynch CF, Sisti JS, et al. Hormone receptor status of a first primary breast cancer predicts contralateral breast cancer risk in the WECARE study population. *Breast Cancer Res* 2017;19(1):83–x. <https://doi.org/10.1186/s13058-017-0874-x> [doi].
- [33] Sawyer S, Mitchell G, McKinley J, et al. A role for common genomic variants in the assessment of familial breast cancer. *J Clin Oncol Off J Am Soc Clin Oncol* 2012;30(35):4330–6. <https://doi.org/10.1200/JCO.2012.41.7469>.
- [34] Chowdhury M, Euhus D, Onega T, Biswas S, Choudhary PK. A model for individualized risk prediction of contralateral breast cancer. *Breast Canc Res Treat* 2017;161(1):153–60. <https://doi.org/10.1007/s10549-016-4039-x> [doi].
- [35] Chowdhury M, Euhus D, Arun B, Umbricht C, Biswas S, Choudhary P. Validation of a personalized risk prediction model for contralateral breast cancer. *Breast Canc Res Treat* 2018;170(2):415–23. <https://doi.org/10.1007/s10549-018-4763-5> [doi].
- [36] Giardiello D, Steyerberg EW, Hauptmann M, et al. Prediction and clinical utility of a contralateral breast cancer risk model. *Breast Cancer Res* 2019;21(1):141–4. <https://doi.org/10.1186/s13058-019-1221-1> [doi].
- [37] Giardiello D, Hauptmann M, Steyerberg EW, et al. Prediction of contralateral breast cancer: external validation of risk calculators in 20 international cohorts. *Breast Canc Res Treat* 2020;181(2):423–34. <https://doi.org/10.1007/s10549-020-05611-8> [doi].
- [38] Kurian AW, Lichtensztajn DY, Keegan THM, Nelson DO, Clarke CA, Gomez SL. Use of and mortality after bilateral mastectomy compared with other surgical treatments for breast cancer in California, 1998–2011. *J Am Med Assoc* 2014;312(9):902–14. <https://doi.org/10.1001/jama.2014.10707>.
- [39] Marmor S, Altman AM, Mayleben WT, et al. The use of contralateral prophylactic mastectomy among elderly patients in the United States. *Breast Canc Res Treat* 2019;177(1):175–83. <https://doi.org/10.1007/s10549-019-05288-8> [doi].

- [40] Enewold LR, McGlynn KA, Zahm SH, et al. Breast reconstruction after mastectomy among Department of Defense beneficiaries by race. *Cancer* 2014;120(19):3033–9. <https://doi.org/10.1002/cncr.28806> [doi].
- [41] Shippee TP, Kozhimannil KB, Rowan K, Virnig BA. Health insurance coverage and racial disparities in breast reconstruction after mastectomy. *Wom Health Issues* 2014;24(3):261. <https://doi.org/10.1016/j.whi.2014.03.001> [doi].
- [42] Sisco M, Du H, Warner JP, Howard MA, Winchester DP, Yao K. Have we expanded the equitable delivery of postmastectomy breast reconstruction in the new millennium? Evidence from the national cancer data base. *discussion* 666 *J Am Coll Surg* 2012;215(5):658–66. <https://doi.org/10.1016/j.jamcollsurg.2012.07.008> [doi].
- [43] King TA, Sakr R, Patil S, et al. Clinical management factors contribute to the decision for contralateral prophylactic mastectomy. *J Clin Oncol* 2011;29(16):2158–64. <https://doi.org/10.1200/JCO.2010.29.4041> [doi].
- [44] Malone KE, Daling JR, Doody DR, et al. Prevalence and predictors of BRCA1 and BRCA2 mutations in a population-based study of breast cancer in white and black American women ages 35 to 64 years. 2006. p. 1538–7445 (Electronic); 0008-5472 (Linking).
- [45] Tynan M, Peshkin BN, Isaacs C, et al. Predictors of contralateral prophylactic mastectomy in genetically high risk newly diagnosed breast cancer patients. *Breast Canc Res Treat* 2020;180(1):177–85. <https://doi.org/10.1007/s10549-019-05515-2> [doi].
- [46] Yi M, Hunt KK, Arun BK, et al. Factors affecting the decision of breast cancer patients to undergo contralateral prophylactic mastectomy. *Canc Prev Res* 2010;3(8):1026–34. <https://doi.org/10.1158/1940-6207.CAPR-09-0130> [doi].
- [47] Wang F, Amara D, Peled AW, et al. Negative genetic testing does not deter contralateral prophylactic mastectomy in younger patients with greater family histories of breast cancer. *Ann Surg Oncol* 2015;22(10):3338–45. <https://doi.org/10.1245/s10434-015-4745-3> [doi].
- [48] Cureton EL, Yau C, Alvarado MD, et al. Local recurrence rates are low in high-risk neoadjuvant breast cancer in the I-SPY 1 Trial (CALGB 150007/150012; ACRIN 6657). *Ann Surg Oncol* 2014;21(9):2889–96. <https://doi.org/10.1245/s10434-014-3721-7>.
- [49] Fisher CS, Martin-Dunlap T, Ruppel MB, Gao F, Atkins J, Margenthaler JA. Fear of recurrence and perceived survival benefit are primary motivators for choosing mastectomy over breast-conservation therapy regardless of age. *Ann Surg Oncol* 2012;19(10):3246–50. <https://doi.org/10.1245/s10434-012-2525-x> [doi].
- [50] Baptiste DF, MacGeorge EL, Venetis MK, et al. Motivations for contralateral prophylactic mastectomy as a function of socioeconomic status. *BMC Wom Health* 2017;17(1):10–2. <https://doi.org/10.1186/s12905-017-0366-2> [doi].
- [51] Heemskerk-Gerritsen BA, Rookus MA, Aalfs CM, et al. Improved overall survival after contralateral risk-reducing mastectomy in BRCA1/2 mutation carriers with a history of unilateral breast cancer: a prospective analysis. *Int J Cancer* 2015;136(3):668–77. <https://doi.org/10.1002/ijc.29032> [doi].
- [52] Liederbach E, Wang CH, Lutfi W, et al. Survival outcomes and pathologic features among breast cancer patients who have developed a contralateral breast cancer. *Ann Surg Oncol* 2015;22(Suppl 3):412. <https://doi.org/10.1245/s10434-015-4835-2> [doi].
- [53] Portschy PR, Kuntz KM, Tuttle TM. Survival outcomes after contralateral prophylactic mastectomy: a decision analysis. *Print* 2014 Aug *J Natl Cancer Inst* 2014;106(8). <https://doi.org/10.1093/jnci/dju160> [doi].
- [54] Quan G, Pommier SJ, Pommier RF. Incidence and outcomes of contralateral breast cancers. *discussion* 650 *Am J Surg* 2008;195(5):645–50. <https://doi.org/10.1016/j.amjsurg.2008.01.007> [doi].
- [55] Schaapveld M, Visser O, Louwman WJ, et al. The impact of adjuvant therapy on contralateral breast cancer risk and the prognostic significance of contralateral breast cancer: a population based study in The Netherlands. *Breast Canc Res Treat* 2008;110(1):189–97. 9709 [pii].
- [56] Verkooyen HM, Chatelain V, Fioretta G, et al. Survival after bilateral breast cancer: results from a population-based study. *Breast Canc Res Treat* 2007;105(3):347–57. <https://doi.org/10.1007/s10549-006-9455-x> [doi].
- [57] Lazow SP, Riba L, Alapati A, James TA. Comparison of breast-conserving therapy vs mastectomy in women under age 40: national trends and potential survival implications. *Breast J* 2019;25(4):578–84. <https://doi.org/10.1111/tbj.13293> [doi].
- [58] Fayanzu OM, Stoll CR, Fowler S, Colditz GA, Margenthaler JA. Contralateral prophylactic mastectomy after unilateral breast cancer: a systematic review and meta-analysis. *Ann Surg* 2014;260(6):1000–10. <https://doi.org/10.1097/SLA.0000000000000769> [doi].
- [59] Metcalfe KA, Retrouvey H, Kerrebijn I, et al. Predictors of uptake of contralateral prophylactic mastectomy in women with nonhereditary breast cancer. *Cancer*; 2019. <https://doi.org/10.1002/cncr.32405> [doi].
- [60] Abbott A, Rueth N, Pappas-Varco S, Kuntz K, Kerr E, Tuttle T. Perceptions of contralateral breast cancer: an overestimation of risk. *Ann Surg Oncol* 2011;18(11):3129–36. <https://doi.org/10.1245/s10434-011-1914-x> [doi].
- [61] Kaiser K, Cameron KA, Beaumont J, et al. What does risk of future cancer mean to breast cancer patients? *Breast Canc Res Treat* 2019;175(3):579–84. <https://doi.org/10.1007/s10549-019-05182-3>.
- [62] Bloom DL, Chapman BM, Wheeler SB, et al. Reframing the conversation about contralateral prophylactic mastectomy: preparing women for postsurgical realities. *Psycho Oncol* 2019;28(2):394–400. <https://doi.org/10.1002/pon.4955>.
- [63] Beesley H, Holcombe C, Brown SL, Salmon P. Risk, worry and cosmesis in decision-making for contralateral risk-reducing mastectomy: analysis of 60 consecutive cases in a specialist breast unit. *Breast* 2013;22(2):179–84. <https://doi.org/10.1016/j.breast.2012.06.005>.
- [64] Parker PA, Peterson SK, Bedrosian I, et al. Prospective study of surgical decision-making processes for contralateral prophylactic mastectomy in women with breast cancer. *Ann Surg* 2016;263(1):178–83. <https://doi.org/10.1097/SLA.0000000000001216>.
- [65] Hartmann LC, Schaid DJ, Woods JE, et al. Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. *N Engl J Med* 1999;340(2):77–84. <https://doi.org/10.1056/NEJM199901143400201> [doi].
- [66] Rebbeck TR, Friebel T, Lynch HT, et al. Bilateral prophylactic mastectomy reduces breast cancer risk in BRCA1 and BRCA2 mutation carriers: the PROSE Study Group. *J Clin Oncol* 2004;22(6):1055–62. <https://doi.org/10.1200/JCO.2004.04.188> [doi].
- [67] Carbine NE, Lostumbo L, Wallace J, Ko H. Risk-reducing mastectomy for the prevention of primary breast cancer. *Cochrane Database Syst Rev* 2018;4:CD002748. <https://doi.org/10.1002/14651858.CD002748.pub4> [doi].
- [68] Killelea BK, Long JB, Chagpar AB, et al. Trends and clinical implications of preoperative breast MRI in Medicare beneficiaries with breast cancer. *Breast Canc Res Treat* 2013;141(1):155–63. <https://doi.org/10.1007/s10549-013-2656-1> [doi].
- [69] Barry M, Sacchini V. When is contralateral mastectomy warranted in unilateral breast cancer? *Expert Rev Anticancer Ther* 2011;11(8):1209–14. <https://doi.org/10.1586/era.11.100> [doi].
- [70] Tollow P, Williams VS, Harcourt D, Paraskeva N. "It felt like unfinished business, it feels like that's finished now": women's experiences of decision making around contralateral prophylactic mastectomy (CPM). *Psycho Oncol* 2019;28(6):1328–34. <https://doi.org/10.1002/pon.5086>.
- [71] Hamilton JG, Genoff MC, Salerno M, et al. Psychosocial factors associated with the uptake of contralateral prophylactic mastectomy among BRCA1/2 mutation noncarriers with newly diagnosed breast cancer. *Breast Canc Res Treat* 2017;162(2):297–306. <https://doi.org/10.1007/s10549-017-4123-x>.
- [72] Noroozian M, Carlson LW, Savage JL, et al. Use of screening mammography to detect occult malignancy in autologous breast reconstructions: a 15-year experience. *Radiology* 2018;289(1):39–48. <https://doi.org/10.1148/radiol.2018172783>.
- [73] Miller ME, Czechura T, Martz B, et al. Operative risks associated with contralateral prophylactic mastectomy: a single institution experience. *Ann Surg Oncol* 2013;20(13):4113–20. <https://doi.org/10.1245/s10434-013-3108-1> [doi].
- [74] Osman F, Saleh F, Jackson TD, Corrigan MA, Cil T. Increased postoperative complications in bilateral mastectomy patients compared to unilateral mastectomy: an analysis of the NSQP database. *Ann Surg Oncol* 2013;20(10):3212–7. <https://doi.org/10.1245/s10434-013-3116-1> [doi].
- [75] Huang J, Chagpar A. Complications in patients with unilateral breast cancer who undergo contralateral prophylactic mastectomy versus unilateral mastectomy. *Surgery* 2018;164(6):1347–50. S0039-6060(18)30297-6 [pii].
- [76] Momoh AO, Cohen WA, Kidwell KM, et al. Tradeoffs associated with contralateral prophylactic mastectomy in women choosing breast reconstruction: results of a prospective multicenter cohort. *Ann Surg* 2017;266(1):158–64. <https://doi.org/10.1097/SLA.0000000000001840> [doi].
- [77] Silva AK, Lapin B, Yao KA, Song DH, Sisco M. The effect of contralateral prophylactic mastectomy on perioperative complications in women undergoing immediate breast reconstruction: a nsqip analysis. *Ann Surg Oncol* 2015;22(11):3474–80. <https://doi.org/10.1245/s10434-015-4628-7> [doi].
- [78] Frost MH, Hoskin TL, Hartmann LC, Degnim AC, Johnson JL, Boughey JC. Contralateral prophylactic mastectomy: long-term consistency of satisfaction and adverse effects and the significance of informed decision-making, quality of life, and personality traits. *Ann Surg Oncol* 2011;18(11):3110–6. <https://doi.org/10.1245/s10434-011-1917-7> [doi].
- [79] Jeevan R, Cromwell DA, Browne JP, et al. Findings of a national comparative audit of mastectomy and breast reconstruction surgery in England. *J Plast Reconstr Aesthetic Surg* 2014;67(10):1333–44. <https://doi.org/10.1016/j.bjps.2014.04.022> [doi].
- [80] Altschuler A, Nekhlyudov L, Roilnick SJ, et al. Positive, negative, and disparate—women's differing long-term psychosocial experiences of bilateral or contralateral prophylactic mastectomy. *Breast J* 2008;14(1):25–32. <https://doi.org/10.1111/j.1524-4741.2007.00521.x> [doi].
- [81] 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(31):7849–56. doi: JCO.2005.09.233 [pii].
- [82] Parker PA, Peterson SK, Shen Y, et al. Prospective study of psychosocial outcomes of having contralateral prophylactic mastectomy among women with nonhereditary breast cancer. *J Clin Oncol Off J Am Soc Clin Oncol* 2018;36(25):2630–8. <https://doi.org/10.1200/JCO.2018.78.6442>.
- [83] Hopwood P, Fletcher I, Lee A, Al Ghazal S. A body image scale for use with cancer patients. *Eur J Canc* 2001;37(2):189–97. [https://doi.org/10.1016/s0959-8049\(00\)00353-1](https://doi.org/10.1016/s0959-8049(00)00353-1).
- [84] Hwang ES, Locklear TD, Rushing CN, et al. Patient-reported outcomes after choice for contralateral prophylactic mastectomy. *J Clin Oncol Off J Am Soc Clin Oncol* 2016;34(13):1518–27. <https://doi.org/10.1200/JCO.2015.61.5427>.
- [85] Soran A, Ibrahim A, Kanbour M, et al. Decision making and factors influencing long-term satisfaction with prophylactic mastectomy in women with

- breast cancer. *Am J Clin Oncol* 2015;38(2):179–83. <https://doi.org/10.1097/COC.0b013e318292f8a7> [doi].
- [86] Katz SJ, Hawley ST, Hamilton AS, et al. Surgeon influence on variation in receipt of contralateral prophylactic mastectomy for women with breast cancer. *JAMA Surg* 2018;153(1):29–36. <https://doi.org/10.1001/jamasurg.2017.3415> [doi].
- [87] Katz SJ, Janz NK, Abrahamse P, et al. Patient reactions to surgeon recommendations about contralateral prophylactic mastectomy for treatment of breast cancer. *JAMA Surg* 2017;152(7):658–64. <https://doi.org/10.1001/jamasurg.2017.0458> [doi].
- [88] Taylor MA, Allen CM, Presson AP, Millar MM, Zurbuchen R, Matsen CB. Exploring surgeon variability in recommendations for contralateral prophylactic mastectomy: what matters most? *Ann Surg Oncol* 2019;26(10):3224–31. <https://doi.org/10.1245/s10434-019-07561-y> [doi].
- [89] Kantor O, Chang C, Bleicher RJ, et al. Physician knowledge of breast cancer recurrence and contralateral breast cancer risk is associated with increased recommendations for contralateral prophylactic mastectomy: a survey of physicians at NAPBC-accredited centers. *Ann Surg Oncol* 2019;26(10):3080–8. <https://doi.org/10.1245/s10434-019-07559-6> [doi].
- [90] Bevers TB, Ward JH, Ahrendt GM, et al. NCCN clinical practice guidelines in oncology (NCCN Guidelines®): breast cancer risk reduction version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/breast_risk.pdf; 2020.
- [91] Boughey JC, Attai DJ, Chen SL, et al. Contralateral prophylactic mastectomy consensus statement from the American society of breast surgeons: additional considerations and a framework for shared decision making. *Ann Surg Oncol* 2016;23(10):3106–11. <https://doi.org/10.1245/s10434-016-5408-8> [doi].
- [92] Monticciolo DL, Newell MS, Moy L, Niell B, Monsees B, Sickles EA. Breast cancer screening in women at higher-than-average risk: recommendations from the ACR. *J Am Coll Radiol* 2018;15(3 Pt A):408–14. <https://doi.org/10.1016/j.jacr.2017.11.034>.
- [93] Levit L, Balogh E, Nass S, Ganz PA. Delivering high-quality cancer care: charting a new course for a system in crisis. National Academies Press (US); 2013. doi:NBK202148 [bookaccession].
- [94] Margenthaler JA, Ollila DW. Breast conservation therapy versus mastectomy: shared decision-making strategies and overcoming decisional conflicts in your patients. *Ann Surg Oncol* 2016;23(10):3133–7. <https://doi.org/10.1245/s10434-016-5369-y> [doi].
- [95] Stiggelbout AM, Pieterse AH, Haes JC De. Shared decision making: concepts, evidence, and practice. *Patient Educ Counsel* 2015;98(10):1172–9. <https://doi.org/10.1016/j.pec.2015.06.022> [doi].
- [96] Alston C, Paget L, Halvorson G, et al. Communicating with patients on health care evidence: discussion paper. 2012. <http://nam.edu/wp-content/uploads/2015/06/evidence>.
- [97] [MedPAC] MPAC. Report to the congress: aligning Incentives in medicare
. 2010. http://www.medpac.gov/docs/default-source/reports/Jun10_Ch07.pdf?sfvrsn=0.
- [98] Stacey D, Legare F, Lewis KB. Patient decision aids to engage adults in treatment or screening decisions. *Jama* 2017;318(7):657–8. <https://doi.org/10.1001/jama.2017.10289> [doi].
- [99] Ager B, Jansen J, Porter D, et al. Development and pilot testing of a Decision Aid (DA) for women with early-stage breast cancer considering contralateral prophylactic mastectomy. *Breast* 2018;40:156–64. doi:S0960-9776(18)30101-2 [pii].
- [100] Squires JE, Stacey D, Coughlin M, et al. Patient decision aid for contralateral prophylactic mastectomy for use in the consultation: a feasibility study. *Curr Oncol* 2019;26(2):137–48. <https://doi.org/10.3747/co.26.4689> [doi].
- [101] Yao K, Belkora J, Lee C, et al. An in-visit decision aid for surgeons to address decision making for bilateral mastectomy for newly diagnosed breast cancer patients. *Ann Surg Oncol* 2019;26(13):4372–80. <https://doi.org/10.1245/s10434-019-07912-9> [doi].