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Contralateral prophylactic mastectomy for unilateral breast cancer in women at average risk: Systematic review of patient reported outcomes

Amilee Srethbhakdi

Meagan E. Brennan

The University of Notre Dame Australia, meagan.brennan@nd.edu.au

Geaty Hamid

Kathy Flitcroft

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A Systematic Review of Psychosocial Outcomes following Contralateral Prophylactic Mastectomy in Average Risk Women

Running title

Contralateral prophylactic mastectomy patient-reported outcomes

Authors

Amilee Srethbhakdi

School of Medicine, Faculty of Medicine and Health, University of Sydney

asre7187@uni.sydney.edu.au

Meagan E. Brennan

School of Medicine, Faculty of Medicine and Health, University of Sydney

School of Medicine, Sydney, University of Notre Dame Australia

Meagan.brennan@sydney.edu.au

Geaty Hamid

Westmead Breast Cancer Institute, Westmead Hospital, Westmead, Australia

Geaty.hamid@health.nsw.gov.au

Kathy Flitcroft

School of Medicine, Faculty of Medicine and Health, University of Sydney

Kathy.flitcroft@melanoma.org.au

Abstract

Objective

The rate of contralateral prophylactic mastectomy (CPM) in women with early, unilateral cancer is relatively high and is increasing world-wide^{1,2}. Women choose this option for many reasons other than reducing their risk of future cancer, including symmetry, breast reconstruction-related reasons and attempting to manage fear of recurrence. This systematic review evaluated patient-reported quality of life outcomes following CPM.

Methods

A literature search of MEDLINE, PubMed and PsycINFO was performed to February 2019. Abstracts and full-text articles were assessed for eligibility according to pre-determined criteria. Data were extracted into evidence tables for analysis.

Results

19 articles met eligibility criteria for inclusion in analysis. These included patient-reported data from 6088 women undergoing CPM. They reported high levels of satisfaction with the decision for surgery, low levels of decisional regret and high satisfaction with cosmesis and reconstruction. Breast-specific and general quality of life was high overall but was even better in women choosing breast reconstruction after surgery. Fear of cancer recurrence was high after CPM. Depression, distress and a negative impact on body image were evident; however, levels were high in both CPM and non-CPM groups.

Conclusions

This study provides information that can be used by surgeons and psychologists when counselling women about the potential benefits and harms of CPM. This process must include discussion about the trade-offs such as body image issues and ongoing fear of recurrence in addition to the positive aspect of cancer risk reduction. Women are unlikely to regret their decision for CPM.

Keywords

cancer, breast neoplasms, patient outcome assessment, prophylactic mastectomy

PROSPERO ID: 148419

Background

For women at average risk of breast cancer with early-stage, unilateral cancer, the risk of a future contralateral breast cancer is low, around 0.13% per year^{1,2}. No survival benefit has been found from contralateral prophylactic mastectomy (CPM) in women without a high hereditary risk of breast cancer^{3,4}. Despite this low risk and a lack of survival benefit, the rate of CPM in women with unilateral cancer is relatively high and is increasing world-wide^{1,2}. In women with a first diagnosis of unilateral breast cancer undergoing mastectomy, the rate of CPM has increased significantly from 4–6% to 13–24% between 2002 and 2012^{1,5}

Women often overestimate their risk of contralateral cancer and this may contribute to the high CPM rates^{6,7}. However, when reasons for CPM have been studied, women have reported that risk is not always the most important factor in their decision-making. Rather, fear of cancer recurrence, the desire for symmetry and reasons related to breast reconstruction (such as limitations on having a second autologous reconstruction in the future) are important factors⁸. A previous systematic review evaluating decision-making found that women who choose CPM are generally satisfied with the decision, although there is a paucity of research examining other patient-reported outcomes.⁸

Current clinical guidelines recommend against the use of CPM except in women at high genetic risk of breast cancer⁹. Clinicians have expressed alarm about the increasing trend towards CPM^{2,10} and this has driven research into decision-making and outcomes⁸. The current study aims to perform a systematic review to evaluate patient-reported outcomes following CPM on general and breast-specific quality of life (QoL) and other outcomes including satisfaction, body image, sexuality, decisional regret, and fear of cancer recurrence. It also aims to provide information to enhance the pre-operative discussion that women considering CPM have with their clinicians.

Methods

A literature search was performed to identify studies that included patient-reported outcomes in women with unilateral breast malignancy undergoing therapeutic mastectomy with CPM. The eligibility criteria and search strategy are shown in online supplemental material (Appendices 1 and 2).

Abstracts and full-text papers were screened for eligibility by one author (AS) and checked by another (MB). Data were extracted from eligible full-text papers and transferred to evidence tables by one author (AS) and checked for accuracy by another (MB or KS). Cases of uncertain eligibility or discrepant data were solved by consensus. The following data were extracted: (a) study characteristics: year of publication, country where study was conducted, prospective or retrospective methodology, number and age of participants, description of participants/population and comparison group, outcomes assessed, method of assessment of outcomes (e.g. questionnaire, focus group, interview), outcome measure type (scales/subscales used), description and validation of outcome tools; (b) study results: timing of outcome measures relative to surgery, results of outcome measures and study conclusion; (c) Breast-Q data: as this was the most frequently used measurement tool, additional detail about subscales and results was collected for studies using Breast-Q. All data were examined for common themes and presented in summary tables.

Each study was allocated a quality score by two authors using an adaptation of the QualSyst score which was described by Kmet et al¹¹ and adapted for use in a previous systematic review of patient-reported outcomes in breast cancer by Flitcroft et al^{12,13}. Studies were scored on 12 items on a 0–2 scale for a total possible score of 24 and a mean score was calculated.

Results

The outcomes from the search strategy are shown in the PRISMA flowchart in Figure 1. The search identified 1612 abstracts (earliest date searched to February 2019). 81 abstracts met eligibility criteria. 81 full-text articles were reviewed, 63 were subsequently deemed ineligible, and 1 article was added following review of reference lists of eligible studies. 19 studies were eligible for inclusion in the analysis.^{7,14-32}

Study characteristics

The 19 studies included patient-reported outcomes from 6088 women. The study characteristics are shown in Table 1. The studies were published between 1999 and 2018. 17 studies were performed in the United States and 2 across both the US and Canada. There were 2 prospective and 17 retrospective studies. Participants provided information by questionnaire (15 studies), interview (2 studies) or a combination of both (2 studies).

Study quality

All studies were rated for quality by two authors against a standardised checklist¹¹⁻¹³. There was good concordance between raters, with a mean difference in scores of 1.6 (range 0–3) on the 24-point scale. There were differences in quality scores between included studies, with the lowest score 14 and the highest score 22 out of 24. Studies were most likely to be rated lower if they did not adequately describe the study sample, sampling strategy or outcome measures, or did not connect the study to the wider body of knowledge. The higher-quality studies tended to be larger (with over 100 participants), to have well-described methodology and to use validated measurement tools. The more recent studies (2013 onwards) also tended to have higher quality scores. The mean study score was 19.1 (median 19.5). Of the 19 studies, 8 had a quality score over 20, indicating a high quality.

Patient-reported outcomes (PROs) evaluated in studies

The studies reported a range of PROs, as shown in Tables 1–3 and online supplemental material (Appendix 3). These were grouped into 10 main domains: breast-related QoL (reported in 5 studies^{18,24-27}, satisfaction with decision for CPM (12 studies)^{7,14-16,20-23,28-31}, satisfaction with reconstruction and cosmesis (4 studies)^{15,16,30,31}, overall QoL (3 studies)^{21,22,32}, fear of cancer recurrence (5 studies)^{16,21,22,29,30}, body image (4 studies)^{15,21,22,30}, sexuality (4 studies)^{16,19,22,30}, distress (3 studies)^{21,22,32}, combined body image/sexuality (2 studies)^{14,20} and other outcomes (5 studies)^{21,22,29,30}.

Breast-related QoL

Five studies reported breast-specific QoL using Breast-Q^{18,24-27} (Table 2) and all of these had a quality score of 19 or higher (moderate to high quality). The largest study (Hwang et al²⁴) had almost 1600 women in the CPM group. It compared Breast-Q results between women who chose CPM and those who did not and reported results in reconstruction and no-reconstruction groups. In women who did not choose reconstruction, there was no difference in scores for any domain between CPM and no-CPM groups. Reconstruction was associated with better QoL than no reconstruction regardless of choice for CPM. Scores in the 'satisfaction with breast' domain were higher in the CPM group compared to the unilateral mastectomy group, however the scores for psychosocial and physical well-being domains were lower in the CPM group²⁴. Two studies showed better satisfaction in the CPM groups compared to unilateral mastectomy groups^{25,27} and the remaining two studies showed better QoL scores in the no-CPM group^{18,26}.

Overall quality of life

Three studies reported overall QoL^{21,22,32} (Table 3). One reported good QoL (8.7 out of 10) at 20 year follow-up on a single-item question in a CPM cohort without a comparison group²¹.

Another found good QoL and no difference between CPM and no-CPM groups evaluated by a single-item²². The third used FACT-B and found good QoL with no difference in CPM and no-CPM groups 12 months after surgery³².

Satisfaction with the decision for CPM

Twelve studies evaluated at least one aspect of satisfaction or regret with the decision for CPM^{7,14-16,20-23,28-31} (Table 3). The majority of these assessed satisfaction and regret with a single-item closed question. Among 10 studies exploring satisfaction with CPM^{14-16,20-23,28-30}, 82–98% of participants undergoing CPM expressed satisfaction. Satisfaction with the decision for CPM was lower in women who had surgical complications²⁰, a poor cosmetic result, a diminished sense of sexuality or lack of information about surveillance versus CPM²⁸. Satisfaction was higher in women choosing simple mastectomy with no reconstruction in one study²⁰. Two studies compared satisfaction with the decision in women undergoing CPM and women choosing against CPM^{15,23}. One showed no difference between the groups²³ and the other showed higher satisfaction in the CPM group (97%) compared to the no-CPM group (89%, no p-value reported). One study that used closed- and open-ended questions found that satisfaction was 85% in a CPM cohort on the closed question but the open-ended question showed responses that were positive in 30%, negative in 33% and disparate in 35% of the sample¹⁴. Six studies asked a CPM cohort if they would make the same decision again or recommend the procedure to other women; 83–97% responded that they would do the same again or recommend it^{7,16,20,21,30,31}. One study comparing a CPM to a no-CPM group reported that 98% of the CPM group and 77% of the no-CPM group would make the same decision again²³.

Two studies used validated questionnaires to assess decisional regret. One study of 269 women undergoing CPM with 10 and 20 year follow-up used the Decision Conflict Scale and found a mean score of 1.4 (scale 1–4), representing very low decisional conflict and stable findings across both time periods²¹. The other used the SURE scale and found 87% of women undergoing CPM scored 4/4 indicating no decisional conflict³⁰.

Satisfaction with reconstruction and cosmesis

Four studies reported satisfaction with reconstruction and cosmesis^{15,16,30,31} (Table 3). In two studies, satisfaction was high^{15,31}. One reported 94% overall satisfaction³¹ and in another there was no difference between bilateral (CPM) and unilateral mastectomy groups in satisfaction with reconstruction (80% vs 79%, no p-value reported)¹⁵. However, another interview study of 45 women reported that 89% of women choosing reconstruction after CPM said the reconstruction did not live up to their expectations regarding sexuality,

reconstruction feeling like part of their body and risk of surgical complications. Despite this, 91% said they would make the same decision again¹⁶. Another study in women <40 years reported that 45% felt the cosmetic result was as expected, 34% worse than expected and 25% better than expected; 90% would make the same decision again and SURE scores showed low decisional conflict³⁰. Breast reconstruction methods have improved over time, however no change satisfaction levels were seen in studies across different study years. Time since surgery also did not change satisfaction.

Fear of cancer recurrence

Five studies reported fear of cancer recurrence^{16,21,22,29,30} (online supplemental material Appendix 3). All studies reported ongoing moderate to high levels of cancer or health worry following CPM. One study used a validated questionnaire (Health Concern Score) and found moderate levels of concern in a cohort of 269 women at 20 years²¹. The remaining studies used questionnaires developed for the individual studies that included an item about fear of recurrence. Current concern about cancer was reported by 49, 53, 82 and 90% of CPM patients in these studies^{16,22,29,30}. Only one of these studies compared the CPM to no-CPM group and this reported concern about cancer to be higher in the non-CPM group (74% reporting worry) compared to the CPM group (50%, $p < 0.05$)²².

Body image and sexuality

Four studies reported body image^{15,21,22,30} (online supplemental material Appendix 3), four reported sexuality^{16,19,22,30} and two studies reported these two outcomes together^{14,20}. Three studies used the validated Body Image Scale, either in full or in part, and two compared a CPM group to a no-CPM group. These all showed that women reported concerns about their body image, however there was no significant difference between CPM and no-CPM groups^{15,22} with the exception of women who underwent CPM without reconstruction who had slightly lower body image scores¹⁵. When asked if body image was as expected, 49% said yes, 31% said it was worse than expected and 23% said it was better than expected³⁰. Similarly, in studies examining sexuality, there was no difference in score between the CPM and no-CPM groups^{19,22}. In an interview study, women reported feeling emotionally closer to partners after the surgery compared to before the surgery, however sexually more distant, with chest numbness related to CPM being a major factor (no comparison group)¹⁶.

One study that examined global psychological issues found that women reported CPM to have a greater adverse effect on body image than other domains such as femininity, sexuality, relationships and self-esteem²⁰. Another study found that women had generally positive comments about the impact of CPM on body image, sexuality and emotional

domains; this was compared to generally negative comments from high-risk women without cancer undergoing bilateral prophylactic mastectomy¹⁴.

Distress

Distress was reported in three studies^{21,22,32} (online supplemental material Appendix 3). Two studies used the Impact of Events Scale and found that cancer related distress was moderately high but there was no difference between CPM and no-CPM groups. The remaining study used a general Health Distress Score and found low distress in the CPM group (no comparison group) at 20 years²¹.

Other outcomes (5 studies).

Several other outcomes were reported (online supplemental material Appendix 3). These included depression (two studies, prevalence of depression 27% in both, with no difference between CPM and no-CPM groups^{22,29}. There was also no difference between groups for general health perception²². There were low levels of anxiety and high levels of optimism in a CPM group (no comparison group)²¹ and pain and numbness were 'about the expected level' in 40 and 51%³⁰.

Discussion

This review includes patient-reported outcomes from 19 studies of 6,088 women with unilateral cancer undergoing CPM (bilateral mastectomy). Significant heterogeneity was noted among studies. Different methodology, outcomes and measurement tools were used in different studies and outcomes were measured at varying time intervals. Study quality also varied and fewer than half the studies had a quality score >20 (out of 24).

Most studies focused on how women felt about the decision to undergo CPM. Overall, these showed that women were very comfortable with their decision. Satisfaction with the decision was 82–98% across 10 studies, levels of decisional regret were low, and despite many women being disappointed with their cosmetic outcome (up to 89% in one study), most women reported they would make the same decision again and/or recommend CPM to other women¹⁶. This evidence can provide clinicians with reassurance that women who are taking control of their cancer and requesting CPM despite low risk of contralateral cancer are unlikely to regret their decision.

The impact of surgery on body image was significant in women undergoing CPM. However, in studies comparing the CPM group with a no-CPM group, there was no difference between

groups^{15,22}. This implies that it is the cancer surgery overall, not specifically the removal of the contralateral breast, that is the cause. This is consistent with previous studies showing that body image is dramatically and adversely affected by breast cancer surgery, even when surgery is unilateral and the breast is conserved³³. This is a strong and consistent finding and was noted particularly in the higher-quality studies in this review such as those that used Breast-Q.

A previous systematic review examining reasons for women choosing CPM found that fear of cancer recurrence was the most important factor in the decision⁸. Other research has shown that fear of recurrence was higher in women having breast conservation rather than mastectomy on their ipsilateral side³³. In this review, fear of cancer recurrence was still prevalent among women who had undergone CPM. This shows that CPM probably does not reduce fear of recurrence even though women may expect it to at the time they make the decision. This has important implications for pre-operative counselling and informed consent. It also demonstrates that psychological strategies, not surgery, should be used to manage fear of cancer recurrence.

The previous review identified the desire for good cosmesis, symmetry and/or reconstructive reasons as the second most important factor in the decision to undergo CPM⁸. The present study did not find that satisfaction with the cosmetic outcome was any different for women undergoing CPM compared to unilateral surgery^{15,31}. However, only two studies examined this issue. It is also possible that there is significant selection bias as women who are most likely to experience asymmetry (such as those with larger breasts) may be more likely to undergo CPM.

Clinical Implications

A patient requesting CPM from her surgeon may present an ethical dilemma. Patient-centred care is the aim, and the operation of CPM is associated with high levels of patient satisfaction. It is, however, a major operation with significant potential complications especially when performed with immediate breast reconstruction. The competing principles of 'autonomy' and 'non-maleficence' are challenging for surgeons to balance, particularly at a time of heightened distress typically associated with a cancer diagnosis.

However, dismissing a woman's request to discuss CPM may be viewed as paternalistic and limiting her right to fully informed decision-making. There is a significant body of literature that reports benefits to CPM with bilateral reconstruction, as seen in this review. Unilateral mastectomy may lead to post-surgical psychological distress due to asymmetry and poor

body image. Weighing up the benefits and risks of unilateral versus bilateral surgery is something that only the informed patient can do, based on her personal situation and values.

These ethical dilemmas underline the importance of providing each patient with as much pre-operative information and support as she requires. Discussion about CPM, several consultations and the input of a clinical psychologist may be required to fully inform the patient about the risks of the surgery, the potential outcomes and importantly, the lack of impact on fear of recurrence. Given that decisions regarding CPM usually need to be made within a limited timeframe, decision-making aids may be beneficial. The role of decision aids in this situation has recently been explored and shows promising results, especially in facilitating a realistic (and usually reassuring) assessment of the true risk of contralateral cancer as well as crucial (and often concerning) information about the additional surgical risks^{34,35}. Support is required as a woman makes this important and complex decision which is likely to have long-term consequences for her QoL and psychological well-being.

Study Limitations

This review has several limitations. Significant heterogeneity of the studies was noted: a large variety of different outcomes, time points, measures and comparison groups were used in the studies, making conclusions difficult to draw. Study quality was highly variable, and the majority of studies were retrospective. These limitations are true of many systematic reviews. All of the studies were performed in the United States and Canada, so the generalisability to other countries with different health systems and cultures (such as Europe and Australia) is uncertain and there were no studies in non-English-speaking countries, so no information is available about more culturally diverse populations. Future research in this area would be facilitated by using more standardised methodology and validated measurement tools and including a comparison group who did not undergo CPM. Moreover, the role of combining evidence-based strategies to address fear of cancer recurrence with pre-operative decision-making regarding CPM should be explored. A further area of potential research could address the ethical issues around the provision of surgical procedures that could be viewed as potentially hazardous and 'medically unnecessary' by surgeons but 'valued' by patients, using CPM as an example.

Conclusion

In conclusion, this review has built on previous research and added more depth to the understanding of this area by presenting a detailed evaluation of studies of patient-reported outcomes following CPM. Significant heterogeneity was found, presenting challenges for synthesis of the data. Women undergoing surgery reported high levels of satisfaction with

the decision, low levels of decisional regret and high satisfaction with cosmesis and reconstruction. General and breast-specific QoL were high. Depression, distress and a negative impact on body image were evident; however, levels were high in both CPM and non-CPM groups. Fear of cancer recurrence was high after surgery. Women must be informed about the potential benefits and harms of surgery, and the decision process must include counselling about these factors in addition to the discussion about risk of future cancer.

Table 1: Characteristics of eligible studies (ordered by year of publication)

Author	Publication year	Country	Study years	Study Design	Methodology	Participants (N CPM)	Age (years, mean or median)	Population	Outcomes reported	Outcome measures	Quality score (mean)
Montgomery ²⁸	1999	USA	1954-1998	R	Mail questionnaire and interview	296	53.8 (mean) at CPM	CPM (bilateral mastectomy) with or without reconstruction in patients with unilateral BC. No comparison group.	Satisfaction with CPM decision, Satisfaction with reconstruction.	Study-specific questionnaire and follow-up interview with some participants.	18.5
Frost 2005 ²⁰	2005	USA	1960-1993	R	Mail questionnaire	583	48 at CPM	CPM for unilateral BC, surveyed 10 years after BC. Family history of BC. Overlap with population in Frost (2011).	Satisfaction with CPM, self-esteem, feelings of femininity, sexual relationships, level of stress, emotional stability, complications.	Study-specific questionnaire; closed and open questions	17
Nekhlyudov ²⁹	2005	USA	1979-1999	R	Mail questionnaire	431	71% <55yrs at CPM	CPM (bilateral mastectomy) with or without reconstruction in patients with unilateral BC. No comparison group.	Past and current satisfaction with CPM (single items), current fear of recurrence (single item), current depression (CES-D), current perception of general health (single item from SF-36). Focused on role in decision-making; also reported long-term outcomes.	Study-specific questionnaire plus validated measures- single item from SF-36 and full CES-D.	20
Geiger ²²	2006	USA	1979-1990	R	Mail questionnaire	519	30% <55yrs at survey	CPM (bilateral mastectomy) vs no CPM (unilateral mastectomy or BCS) for unilateral BC.	Contentment with QoL, satisfaction with CPM, experience of BC thoughts, body image, sexual satisfaction, depression and health perception.	Study-specific questionnaire and adapted items from validated scales; closed questions	19.5
Tercyak ³²	2007	USA	1997-2003	P	Telephone interview	167	45 at diagnosis	CPM (bilateral mastectomy) with or without reconstruction in patients with unilateral BC. No comparison group. All had BRCA testing 15% positive.	QoL (FACT-B); psychological distress (Impact of Events Scale; Multidimensional Impact of Cancer Risk Assessment)	Validated scales: FACT-B, IES, MICRA	21
Spear ³¹	2007	USA	2000-2005	R	Mail questionnaire	47	NR	CPM (bilateral mastectomy) with immediate reconstruction in patients with unilateral BC. Comparison bilateral risk-reducing.	Satisfaction with reconstruction (rating scale)	Study-specific questionnaire.	14

Altschuler¹⁴	2008	USA	1979-1999	R	Mail questionnaire	567	18-80 at survey	CPM vs bilateral prophylactic mastectomy.	QoL, satisfaction with CPM decision, BC risk-related worry, body image, sexual satisfaction and overall health perception	Study-specific mail questionnaire; closed and open questions. Responses classified as 'positive,' 'negative' or 'disparate'	20.5
Frost 2011²¹	2011	USA	1960-1993	R	Mail questionnaire	269	47.4 at CPM	CPM for unilateral BC, surveyed 10 years and 20 years after cancer. Family history of BC. Overlap with population in Frost (2005).	Decision conflict scale, LOT-R optimism scale, Trait anxiety, Health concern and Health distress scales, QoL (single item), body image scale (validated)	Standardised scales with additional study-specific items	19
Han²³	2011	USA	2005-2007	R	Mail questionnaire	101	Range 20-89	CPM vs no CPM (unilateral mastectomy) for unilateral BC. Includes some bilateral BC patients.	Satisfaction with choice of CPM and choice of reconstruction	Study-specific questionnaire.	15.5
Koslow²⁵	2013	USA	2000-2007 (+2008-2012)	R	Questionnaire	121	46.6 at CPM	CPM (bilateral reconstruction) vs no CPM (unilateral reconstruction) in patients with unilateral BC undergoing implant reconstruction	Breast-related QoL (BREAST-Q, 5 domains)	BREAST-Q	21
Rosenberg³⁰	2013	USA + Canada	NR	R	Mail questionnaire	123	37 at diagnosis	CPM (bilateral mastectomy) with or without reconstruction in patients with unilateral BC. No comparison group.	BC worry (CPM survey), Decisional conflict (SURE scale=items from Decisional Conflict Scale). Focused on knowledge and role in decision making; also reported long term satisfaction.	Study-specific questionnaire 'CPM survey' 23 items, SURE scale.	20.5
Soran⁷	2015	USA	2000-2010	R	Mail questionnaire	206		CPM (bilateral mastectomy) with or without reconstruction in patients with unilateral BC. No comparison group.	Satisfaction with surgical procedure and overall decision (Single-item questions)	Study-specific questionnaire.	18.5
Buchanan¹⁸	2016	USA	2011-2012	R	Phone interview and mail questionnaire	17	45.2 at CPM	CPM (bilateral reconstruction) vs no CPM (unilateral reconstruction) in patients with unilateral BC; comparing fear of recurrence in different groups	Breast-related QoL (BREAST-Q, 5 domains), Fear of cancer recurrence (Concerns About Recurrence Scale), Interview	BREAST-Q, Concerns About Recurrence Scale, Semi-structured interview exploring decision-making	19
Hwang²⁴	2016	USA	NR	R	E-mail questionnaire	1598	53.7 at survey	CPM (bilateral mastectomy) vs no CPM (unilateral mastectomy) in patients with unilateral BC; comparing reconstruction vs no reconstruction	Breast-related QoL (BREAST-Q, 4 domains)	BREAST-Q	19.5

Anderson¹⁵	2017	USA	2004-2012	R	Mail question naire	262	55 at diagnosis	CPM (bilateral mastectomy) vs no CPM (unilateral mastectomy) with or without reconstruction in patients with unilateral BC; comparing satisfaction and body image in different groups. Included BCS patients.	Satisfaction with CPM decision (single item), Satisfaction with reconstruction (single item), body image (Body Image Scale, adapted, 5 items)	Study-specific questionnaires and adapted validated body image scale	20
Cornell¹⁹	2017	USA	2010-2015	R	Mail question naire	67	56 at diagnosis	CPM (bilateral mastectomy) vs no CPM (unilateral mastectomy) for unilateral BC. Included BCS patients.	Sexual function, reported pre-op, and post-op at regular intervals	Female sexual functioning index (FSFI)-validated questionnaire (19 items)	19.5
Momoh²⁷	2017	USA + Canada	2012-2014	P	In-person question naire	604	43% 40-49 yrs	CPM (bilateral reconstruction) vs no CPM (unilateral reconstruction) in patients with unilateral BC; comparing implant vs autologous reconstruction	Breast-related QoL (BREAST-Q, 4 domains), Health-related QoL (GAD), Anxiety (PROMIS)	BREAST-Q, GAD-7, PROMIS	22
Kuykendall²⁶	2017	USA	2011-2015	R	Mail question naire	65	Not reported	CPM (bilateral reconstruction) vs no CPM (unilateral reconstruction) in patients with unilateral BC; comparing implant vs autologous reconstruction	Breast-related QoL (BREAST-Q, 10 domains)	BREAST-Q	21
Bloom¹⁶	2019	USA	NR	R	In-person interview	45	45 at interview	CPM for unilateral, early-stage BC and low genetic risk. Interview exploring decision and effects.	Decision-making, short term and long-term impacts of CPM	Semi-structured interview; open questions	16.5

CPM: Contralateral prophylactic mastectomy; P: Prospective; R: Retrospective; NR: not reported; QoL: quality of life; BC=breast cancer

Table 2: Results of studies assessing breast-related quality of life using Breast-Q, ordered by number of participants

Author	N (CPM group)	Timing of measurement	Groups assessed	Results for women undergoing CPM						Results/ Conclusions
				Breast-Q satisfaction with breast	Breast-Q satisfaction with outcome	Breast-Q physical well-being abdomen	Breast-Q psychosocial well-being	Breast-Q physical well-being chest/upper body	Breast-Q sexual well-being	
Hwang ²⁴	1598	1.6 years (median) post-surgery	CPM with reconstruction	62	nr	nr	71.7	74.5	50	CPM (bilateral reconstruction) higher satisfaction with breast compared with no CPM (unilateral reconstruction) at the expense of lower psychosocial and physical well-being
			CPM without reconstruction	54	nr	nr	69.1	75	39.9	No differences in any domain scores in women not having reconstruction
			CPM with and without reconstruction	60.4	nr	nr	71.2	74.6	46.9	Reconstruction better QoL than no reconstruction regardless of choice for CPM
Momoh ²⁷	604	1 year post-surgery	CPM with implant reconstruction	50.25	nr	n/a	63.05	66.22	50.65	CPM with bilateral reconstruction associated with better satisfaction than no CPM with unilateral reconstruction
			CPM with autologous reconstruction	82.96	nr	79.98	65.57	67.76	52.41	No differences in satisfaction between groups
Koslow ²⁵	121	52 months (median) post-surgery	CPM with implant reconstruction	64.4	74.8	nr	75.4	77.4	55.1	CPM significantly better satisfaction with breast and satisfaction with outcome.
Kuykendall ²⁶	65	nr	CPM with implant reconstruction	62.7	69.3	nr	71.6	69.5	51.6	No significant differences between CPM and no-CPM in group with implant reconstruction.
			CPM with autologous (DIEP) reconstruction	69	61	nr	71.2	66.5	49.5	No-CPM group better satisfaction with outcome and sexual well-being in women undergoing DIEP
			CPM with implant or autologous reconstruction	64.3	67.4	nr	71.5	68.7	51	Overall, no-CPM (unilateral reconstruction) significantly better satisfaction with outcome, psychosocial well-being and sexual well-being
Buchanan ¹⁸	17	22 months (mean) post-surgery	Overall- CPM	82.2	89.9	nr	88†	74.4	71†	CPM associated with better satisfaction with breast and outcome (non-significant); No CPM (unilateral reconstruction) associated with better physical well-being (chest, significant)

†Result estimated from figure

N: number; CPM: Contralateral prophylactic mastectomy; NR: not reported

Table 3: Results of studies assessing satisfaction with decision and satisfaction with reconstruction, ordered by number of participants

Author	n (CPM group)	Timing of measurement	Outcome and measurement tool	Groups assessed	Results/ Conclusions
Overall Quality of Life					
Frost (2011) ²¹	269	10 & 20 years	Multiple outcomes assessed at two follow-up times; Validated questionnaires	CPM (bilateral mastectomy)	Overall QoL high; 10-point scale single item (Range 0-10, higher score better qol). 20 year follow-up: 8.7 mean.
Geiger ²²	519	nr	Multiple outcomes assessed at follow-up. Study-specific questionnaire.	CPM (bilateral mastectomy) vs No CPM (unilateral mastectomy or BCS)	Contentment with QoL good (single item from FACT-B). CPM group 76.3 satisfied 'quite a bit' or 'very much' No difference between groups.
Tercyak ³²	167	1 and 12 months after CPM	CPM (bilateral mastectomy) with or without reconstruction in patients with unilateral BC. Comparison group Non-CPM: unilateral mastectomy or BCS (combined)	CPM (bilateral mastectomy). 81% had reconstruction. Scores at 12 months.	FACT-B score (mean). CPM 115.9; Non-CPM 116.9 (Non-significant difference at 12 months)
Satisfaction with decision					
Frost (2005) ²⁰	583	10 years	Multiple outcomes relating to decision and satisfaction assessed at 10 years follow-up; study-specific questionnaire	CPM (bilateral mastectomy)	Overall satisfaction with decision high. 83% satisfied or very satisfied. Lower satisfaction in women with surgical complications and subcutaneous mastectomy compared to simple mastectomy. Higher satisfaction for no reconstruction vs reconstruction. Would choose CPM again: 83%
Altschuler ¹⁴	567	3-22 years	Satisfaction with CPM decision (Single item closed question)	CPM (bilateral mastectomy)	Satisfaction with decision (closed question n=223): satisfied 85.2% not satisfied 14.8%. Better satisfaction expressed for CPM compared to bilateral prophylactic mastectomy.
					Satisfaction with decision (open question n=280): positive 30.1%, negative 33.9%, disparate 35.8% Despite high satisfaction levels, around 1/3 of women expressed disparate comments.
Geiger ²²	519	nr	Multiple outcomes assessed at follow-up. Study-specific questionnaire.	CPM (bilateral mastectomy) vs No CPM (unilateral mastectomy or BCS)	Satisfaction with CPM decision high (single item, developed for study). CPM group 86.5% 'satisfied' or 'very satisfied.'
Nekhlyudov ²⁹	431	60% had CPM within the past 10 years	Focused on decision-making roles (alone or shared with doctor); also reported psychosocial outcomes.	CPM (bilateral mastectomy)	Satisfaction with choice for CPM (6 months). 352/431 (81.7%) satisfied. Active decision-making roles more likely to be satisfied at 6 months.
			Focused on decision-making roles (alone or shared with doctor); also reported psychosocial outcomes.	CPM (bilateral mastectomy)	Satisfaction with choice for CPM (current). 367/431 (85.2%) satisfied. Decision-making roles not related to current satisfaction.

Montgomery²⁸	296	Median 4.9 years; 53% > 10 years	Assessed satisfaction with decision (regret) with study-specific questionnaire. Follow-up phone interview with women who expressed regret to assess reasons.	CPM (bilateral mastectomy)	Satisfaction with choice for CPM. Low level of regret. 278/296 (94%) satisfied. Reasons for regret: poor cosmetic result (CPM or recon), diminished sense of sexuality, lack of education regarding alternative surveillance methods or CPM efficacy.
			Assessed satisfaction with decision (regret) with study-specific questionnaire. Follow-up phone interview with women who expressed regret to assess reasons.	CPM (bilateral mastectomy)	Satisfaction with choice for reconstruction. 37.5% had reconstruction; 12/111 (10.8%) with CPM and reconstruction had regrets. 6/185 (3.2%) with CPM and no reconstruction had regrets. CPM and no recon (3.2%) had lower regret than CPM with recon (10.8%).
Frost (2011)²¹	269	10 & 20 years	Multiple outcomes assessed at two follow-up times; Collection of validated questionnaires	CPM (bilateral mastectomy)	Decision-conflict scale (Range 1-5, high score= greater conflict) 20 year follow-up: 1.4 mean; 95% satisfied with their decision. Very low decisional conflict score. Stable findings between 10 and 20 year surveys.
					Overall satisfaction with decision high: 20 year follow-up: 90% satisfied or very satisfied.
					Would choose CPM again: 20 year follow-up: 92% would choose CPM again. Stable between 10 and 20 year surveys.
Anderson¹⁵	262	3.6 years (mean)	Satisfaction with CPM decision (single item)	CPM (bilateral mastectomy) vs No CPM (unilateral mastectomy)	Satisfaction with decision for CPM: CPM group 97% satisfied with decision; No-CPM group 89% satisfied with decision. Satisfaction slightly higher in CPM compared to no-CMP group (p-value nr)
Soran⁷	207	93% >1 year	Focused on decision-making role and reasons; also reported satisfaction with decision.	CPM (bilateral mastectomy)	Would recommend to other women (single item). 191/200 (92.7%) would recommend to others. High level of satisfaction.
			Focused on decision-making role and reasons; also reported satisfaction with decision.	CPM (bilateral mastectomy)	Satisfaction with surgical procedure of CPM (single item). 200/206 (91.7%) satisfied. High satisfaction levels.
					(Single item). 199/206 (96.6%) would choose CPM again.
Rosenberg³⁰	123	2.1 years mean	Focused on decision-making role and reasons; also reported psychosocial outcomes.	CPM (bilateral mastectomy) with or without recon	Decisional conflict about choice for CPM low (SURE scale). 87% of respondents scored 4/4, indicating no decisional conflict
					Satisfaction with choice for CPM high. 80% of women were extremely confident in their decision to undergo CPM and 90% of respondents would definitely choose CPM if deciding again.
Han²³	101	nr	Assessed satisfaction with decision for CPM and for reconstruction. Study-specific mailed questionnaire.	CPM (bilateral mastectomy) vs No CPM (unilateral mastectomy)	Satisfaction with choice for reconstruction high. 125/242 52% (CPM and no-CPM combined) had reconstruction; 89% of patients satisfied with their decision for or against reconstruction; no difference between CPM/no-CPM groups.

					Satisfaction with choice for CPM high. CPM group 99/101 (98%), No-CPM group 90/117 76.9% would make the same decision again. CPM significantly more likely to make same decision again
Spear³¹	47	Mean 31 months	CPM (bilateral mastectomy) with immediate reconstruction in patients with unilateral BC. Comparison bilateral risk-reducing.	CPM (bilateral mastectomy)	High satisfaction; 31/32 (98%) would choose again.
Bloom¹⁶	45	1-10 years	Decisional regret (Semi-structured interview; open questions)	CPM (bilateral mastectomy)	Satisfaction with decision 41/45 (91%) would make the same decision again.
Satisfaction with reconstruction and cosmesis					
Anderson¹⁵	262	3.6 years (mean)	Satisfaction with reconstruction (single item)	CPM (bilateral mastectomy with reconstruction) vs No CPM (unilateral mastectomy with reconstruction)	Satisfaction with breast reconstruction high: CPM group 80% satisfied; No-CPM group 79% satisfied. Young women, all <40 yrs. >90% reconstruction rate.
Rosenberg³⁰	123	2.1 years (mean)	Focused on decision-making role and reasons; also reported psychosocial outcomes.	CPM (bilateral mastectomy) with or without reconstruction	Cosmetic result. Worse than expected 34%; about what expected 45%; better than expected 25%
Spear³¹	47	31 months (mean)	CPM (bilateral mastectomy) with immediate reconstruction in patients with unilateral BC. Comparison bilateral risk-reducing.	CPM (bilateral mastectomy)	Satisfaction with reconstruction. Overall 30/32 (94%) satisfied. Highly satisfied 30/32 (53%); Very satisfied 8/32 (25%); Mod satisfied 4/32 (13%); Satisfied 1/32 (3%); Disappointed 2/32 (6%); Very disappointed 0/32 (0%)
Bloom¹⁶	45	1-10 years	Semi-structured interview; open questions	CPM (bilateral mastectomy)	Satisfaction with reconstruction. 38/45 had reconstruction; 89% said reconstruction did not live up to expectations; reported that their expectations were unrealistic for sexuality, feeling like part of their body and potential surgical complications

N=number; CPM: Contralateral prophylactic mastectomy; NR: not reported; QoL= quality of life; BC=breast cancer

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Conflict of interest statement

None

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Figure 1. PRISMA flowchart of search strategy outcomes

Appendix 1: Study inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none">• Studies of women with breast malignancy (DCIS or invasive cancer) AND• Studies of women who have previously undergone CPM AND• Original research articles from peer-reviewed journals AND• Studies reporting patient-reported outcomes following CPM such as, quality of life, cosmetic outcome, decisional regret AND• Quantitative or qualitative study design AND• Retrospective or prospective study design	<ul style="list-style-type: none">• Studies of women without a breast cancer diagnosis• Studies not including patient reported outcomes• Studies of women at high-risk of breast cancer such as BRCA1/2 mutation carriers• Studies of women planning future CPM• Studies of women with bilateral breast cancer• Studies of women with a past history of breast cancer and new contralateral breast cancer• Review papers, Editorials, Case reports and Abstract-only presentations• Papers published in languages other than English

CPM=contralateral prophylactic mastectomy

Appendix 2: Search terms for MEDLINE, PubMed and PsycINFO

English language, human studies

Double mastectomy OR bilateral mastectomy OR contralateral prophylactic mastectomy
OR prophylactic mastectomy OR preventive mastectomy

AND

Breast neoplasms OR early stage breast cancer

AND

Patient reported outcomes OR patient reported outcome measures OR patient outcome
assessment OR self report OR patient satisfaction OR patient acceptance OR quality of life
OR well-being OR stress, psychological OR morbidity OR regret OR postoperative
complications OR adverse effects OR cosmetic outcome OR anxiety OR depression OR
self-esteem OR self-concept OR body image OR body appearance OR femininity OR
sexuality OR sexual relationships OR relationship

Appendix 3: Results of studies assessing various patient-reported outcomes, ordered by number of participants

Study	n (CPM group)	Timing of measurement	Outcome and measurement tool	Groups assessed	Results/ Conclusions
Fear of cancer recurrence					
Geiger ¹	519	nr	Multiple outcomes assessed at follow-up. Study specific questionnaire.	CPM (bilat mastectomy) vs No CPM (unilat mastectomy or BCS)	Concern about BC (single item, developed for study). CPM group 50.3% 'concerned' or 'very concerned.' No-CPM group 73.8%; p=0.004. CPM group significantly less concern about BC
Nekhlyudov ²	431	60% had CPM within the past 10 years	Focused on decision making roles (alone or shared with doctor); also reported psychosocial outcomes.	CPM (bilat mastectomy)	Fear of recurrence (current). 210/431 (48.7%)
Frost (2011) ³	269	10 & 20 years	Multiple outcomes assessed at two follow-up times; Collection of validated questionnaires	CPM (bilat mastectomy)	Health concern score moderate (Range 1-100, higher score greater concern) 20 year follow-up: 55.8 mean
Rosenberg ⁴	123	2.1 years mean	Focused on decision making role and reasons; also reported psychosocial outcomes.	CPM (bilat mastectomy) with or without recon	Fear of recurrence high (current). 87% said they had been very worried about contralateral cancer at the time of CPM; 90% reported 'at least a little' worry about cancer at follow-up.
			Focused on decision making role and reasons; also reported psychosocial outcomes.	CPM (bilat mastectomy) with or without recon	Worry/anxiety about cancer. Worse than expected 23%; about what expected 51%; better than expected 24%
Bloom ⁵	45	1-10 years	Semi-structured interview; open questions	CPM (bilat mastectomy)	Fear of recurrence/ 'peace of mind': 82% did not report peace of mind; continued to worry about metastatic disease.
Body image					
Geiger ¹	519	nr	Multiple outcomes assessed at follow-up. Study specific questionnaire.	CPM (bilat mastectomy) vs No CPM (unilat mastectomy or BCS)	Self-conscious about appearance (single item from Body Image Scale). CPM group 21.1% self-conscious. No difference between groups; included BCS patients.
			Multiple outcomes assessed at follow-up. Study specific questionnaire.	CPM (bilat mastectomy) vs No CPM (unilat mastectomy or BCS)	Satisfied with appearance when dressed (single item from Body Image Scale). CPM group satisfied 59.3%. No difference between groups; included BCS patients)
Frost (2011) ³	269	10 & 20 years	Multiple outcomes assessed at two follow-up times; Collection of validated questionnaires	CPM (bilat mastectomy)	Body image scale (Range 0-30, high score more distress). 20 year follow-up: 5.0 mean total score; Items: feeling less attractive 11%, less feminine 8%, self-conscious 10%, less whole 8%, dissatisfied with appearance 7%. Significant impact of surgery on body image.

Anderson⁶	262	3.6 years (mean)	Body Image Scale, adapted (5 items)	CPM (bilat mastectomy) vs no CPM (unilat mastectomy) with or without recon	Body image scale. CPM (bilat) without recon 14.4; CPM (bilat) with recon 16.4; No CPM (unilat) without recon 16.7; No CPM (unilat) with recon 16.1. Worse body image in CPM no-recon group compared to other 3 groups.
Rosenberg⁴	123	2.1 years mean	Focused on decision making role and reasons; also reported psychosocial outcomes.	CPM (bilat mastectomy) with or without recon	Self-conscious about appearance. Worse than expected 31%; about what expected 49%; better than expected 23%
Sexuality					
Geiger¹	519	nr	Multiple outcomes assessed at follow-up. Study specific questionnaire.	CPM (bilat mastectomy) vs No CPM (unilat mastectomy or BCS)	Satisfied with sex life (single item from FACT-B). CPM group satisfied 40.9%. No difference between groups.
Rosenberg⁴	123	2.1 years mean	Focused on decision making role and reasons; also reported psychosocial outcomes.	CPM (bilat mastectomy) with or without recon	Sense of sexuality. Worse than expected 42%; about what expected 39%; better than expected 14%
Cornell⁷	67	12 months	Female sexual functioning index (FSFI)- validated questionnaire (19 items); 36 max score; 26 indicates sexual dysfunction	CPM (bilat mastectomy) vs no CPM (unilat mastectomy) for unilateral BC. Also included BCS cohort.	FSFI score (baseline and follow-up, p-value) CPM 23.7, 22.8, p=0.74; No CPM 25.2, 17.4, p=0.010; BCS 26.3, 23.5, p<0.001. No difference between three groups in baseline overall scores. All scores reduced at follow-up. Change at follow-up was significant in BCS and unilat mastectomy group but not in CPM group. However, sexual function in CPM group was still low.
Bloom⁵	45	1-10 years	Semi-structured interview; open questions	CPM (bilat mastectomy)	Sexual intimacy. Majority reported feeling emotionally closer but sexually more distant from partner. Sexual dysfunction/ lack of interest in sex reported. Numbness on chest a major factor.
Body image, sexuality and emotional domains (combined)					
Frost (2005)⁸	583	10 years	Multiple outcomes relating to decision and satisfaction assessed at 10 years follow-up; study-specific questionnaire	CPM (bilat mastectomy)	Psychological impacts. Reporting an adverse effect on: femininity 26%, sexual relationships 23%, stress in life 17%, emotional stability 12%, self-esteem 17%, body appearance 33%. Adverse effect on body appearance (33%) is higher than other adverse effects.
Altschuler⁹	567	3-22 years	Study-specific mail questionnaire; closed and open questions	CPM (bilat mastectomy)	General feelings in body image, sexuality and emotional domains (open question n=75): positive 50.7%, negative 32%, disparate 17.3%. Better outcomes in body image, sexuality and emotional domains for CPM compared to bilateral prophylactic mastectomy.
			Study-specific mail questionnaire; closed and open questions	Bilateral prophylactic mastectomy	General feelings in body image, sexuality and emotional domains (open question n=143): positive 26.6%, negative 47.6%, disparate 25.9%. More negative than positive comments in body image, sexuality and emotional domains
Distress					

Geiger¹	519	nr	Multiple outcomes assessed at follow-up. Study specific questionnaire.	CPM (bilat mastectomy) vs No CPM (unilat mastectomy or BCS)	Avoiding thoughts about BC moderately high (single item from Impact of Events Scale). CPM group 58.6% 'modest' or 'high' avoidance. No difference between groups.
			Multiple outcomes assessed at follow-up. Study specific questionnaire.	CPM (bilat mastectomy) vs No CPM (unilat mastectomy or BCS)	Experiencing intrusive BC thoughts moderately high (single item from Impact of Events Scale). CPM group 64.9% 'modest' or 'high' intrusiveness. No difference between groups.
Frost (2011)³	269	10 & 20 years	Multiple outcomes assessed at two follow-up times; Collection of validated questionnaires	CPM (bilat mastectomy)	Health distress score low (Range 1-100, higher score greater concern). 20 year follow-up: 14.1 mean
Tercyak¹⁰	167	1 and 12 months after CPM	CPM (bilat mastectomy) with or without reconstruction in patients with unilateral BC. Comparison group Non-CPM: unilat mastectomy or BCS (combined)	CPM (bilat mastectomy). 81% had reconstruction. Scores at 12 months.	Cancer-specific distress: Impact of Events Scale (IES). CPM 14.2; Non-CPM 14.6 (Non-significant difference)
Other					
Geiger¹	519	nr	Multiple outcomes assessed at follow-up. Study specific questionnaire.	CPM (bilat mastectomy) vs No CPM (unilat mastectomy or BCS)	Possible Depression (CES-D>=16). CPM group 27% depression. No difference between groups.
			Multiple outcomes assessed at follow-up. Study specific questionnaire.	CPM (bilat mastectomy) vs No CPM (unilat mastectomy or BCS)	General health perception (single item from Medical Outcomes Study Short Form-36). CPM group 46.7% 'very good' or 'excellent.' No difference between groups.
Nekhlyudov²	431	60% had CPM within 10 years	Focused on decision making roles (alone or shared with doctor); also reported psychosocial outcomes.	CPM (bilat mastectomy)	Depressive symptoms (current) CES-D >=16. 114/431 (26.5%). Depressive symptoms more likely in women who shared decision making.
Frost (2011)³	269	10 & 20 years	Multiple outcomes assessed at two follow-up times; Collection of validated questionnaires	CPM (bilat mastectomy)	LOT-R optimism scale (Range 1-24, high score greater optimism). 20 year follow-up: 18.5 mean- high scores
			Multiple outcomes assessed at two follow-up times; Collection of validated questionnaires	CPM (bilat mastectomy)	Trait anxiety low (Range 20-80, higher score greater anxiety). 20 year follow-up: 32.1 mean
Rosenberg⁴	123	2.1 years mean	Focused on decision making role and reasons; also reported psychosocial outcomes.	CPM (bilat mastectomy) with or without recon	Pain at surgical site. Worse than expected 25%; about what expected 40%; better than expected 30%
			Focused on decision making role and reasons; also reported psychosocial outcomes.	CPM (bilat mastectomy) with or without recon	Numbness/tingling in chest. Worse than expected 28%; about what expected 51%; better than expected 15%

N=number; CPM: Contralateral prophylactic mastectomy; NR: not reported; BC=breast cancer

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