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Full title: The psycho-social impact of contralateral risk reducing mastectomy (CRRM) on non-high risk women: a rapid review

Short title: The psycho-social impact of contralateral risk reducing mastectomy

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Abstract

Objectives: For women who have been diagnosed with unilateral breast cancer there is an increasing trend for them to request removal of the contralateral healthy breast, so called contralateral risk reducing mastectomy (CRRM). Although indicated in a minority of patients for whom the risk of contralateral breast cancer is high (family history, genetic mutation carriage), this group of women represents fewer than one-third of women currently undergoing CRRM. The current literature is only just beginning to identify patient-reported reasons for undergoing CRRM and associated patient reported outcomes. It is unclear whether women at high**/moderate** risk of developing a subsequent primary contralateral breast cancer report similar outcomes to those considered to be at **low/average** risk. This lack of knowledge provides the rationale for this review.

Methods: A rapid review methodology was undertaken to identify and explore the published research literature focused on the longer term (>5 years) psychosocial impacts on women (specifically those at low/average risk of developing a future contralateral breast cancer) who undergo CRRM.

Results: 15 studies were identified. No UK studies were identified. High satisfaction rates were reported across all the studies. Dissatisfaction was associated with adverse effects such as poor cosmesis, body image changes, femininity, sexual relationships, reoperations and reconstructive problems.

Conclusions: Although studies reported high satisfaction and psycho-social wellbeing following CRRM, these primarily focused on women at high familial/genetic risk of developing a future contralateral breast cancer and it is therefore unclear whether these findings can be extrapolated to women at low/average risk.

Keywords: Cancer, oncology, rapid review, contralateral, risk reducing, mastectomy, satisfaction, outcomes

The psycho-social impact of contralateral risk reducing mastectomy (CRRM) on non high risk women: a rapid review

Background

Breast cancer is the most common cancer in women in the UK, with over 53,000 new cases being diagnosed in the UK each year[1].Although there is overwhelming evidence of the efficacy of breast conservation surgery in achieving excellent local disease control, there has been a controversial recent trend towards bilateral mastectomy, not for oncological benefit, but for future risk reduction. Over the past decade the total number of women in England who had a bilateral mastectomy doubled[2]. For women without cancer, but at high risk of subsequent primary cancer development (such as BRCA gene carriers), there is a well-established benefit both in terms of reducing the risk of cancer by 90+% AND improving survival[3]. However for women who have been diagnosed with a unilateral breast cancer there is a trend for them to request removal of the contralateral healthy breast, so called contralateral risk reducing mastectomy (CRRM). Although indicated in a minority of patients for whom the risk of contralateral breast cancer (CBC) is high (family history, genetic mutation carriage)[4-6], there are no significant survival benefits of undergoing CRRM among average risk women (0.1%-0.6 % per year)[2,4,7-9].

Within Europe, neither EUSOMA (the European Society of Breast Cancer Specialists) nor EUROPA DONNA (the European Breast Cancer Coalition) have published guidelines on CRRM. The 14th St. Gallen International Breast Cancer Consensus Conference in 2015[10] also made little mention of this. The European Society for Medical Oncology (ESMO) breast cancer guidelines[11] acknowledge that this is an increasingly prevalent option and advise that women considering CRRM must be carefully counselled. Within the UK specifically, the National Institution for Health and Care Excellence (NICE) has yet to publish any recommendations about CRRM, however guidelines are due for review during 2017. In the USA, a consensus statement about RRM and guidelines for how it should be managed have recently been published by the American Association of Breast Surgeons which state that for the majority of average risk women with unilateral breast cancer CRRM should be discouraged as it has no oncological benefit.

Although there are a plethora of studies that have focused on womens' experiences and outcomes of bilateral risk reducing mastectomy[12,13], to date, research focused on CRRM has tended to focus on the oncologic outcomes (risk of CBC, risk reduction with CRRM, lack of survival benefit) and on factors impacting on patients' decisions to pursue CRRM[4,14]. The current literature is only just beginning to identify patient-reported reasons for CRRM [4]. Several recent studies that have reported satisfaction following CRRM[4,20], however these have been based on groups of women at high risk of developing a contralateral breast cancer. It is unclear whether low to average risk women report similar patient reported outcomes. This lack of knowledge provides the rationale for this review.

Aim

The aim of this rapid review was to identify and explore the published research literature focused on patient reported psychosocial impacts of CRRM on women (specifically low to average risk women). Specifically the review aimed to answer the following research question:

What psycho-social impact does a CRRM have on women (specifically low to average risk women)?

Methods

Rapid review methodology

A rapid review methodology was undertaken to enable identification and synthesis of published research evidence in a timely and resource-efficient manner[15-17].This rapid review differs from a full systematic review in three ways. Firstly, searches were restricted to bibliographic databases: grey literature was not searched. Secondly, during the study selection stage, not all papers were double-screened. Thirdly, in relation to data extraction and synthesis, only key variables of relevance to the review question were extracted. No meta-analysis was planned.

Searches

Electronic searches were conducted in the Cochrane Library (Wiley), Medline (EBSCOHost), CINAHL (EBSCOHost), PsycINFO (ProQuest), Scopus (Elsevier), and Web of Science (Thomson Reuters), on 19 February 2016. The search strategy included search terms in the title/abstract and relevant database subject headings relating to CRRM, combined with search terms and subject headings relating to psychosocial outcomes of interest (including quality of life, satisfaction, body image, sexuality, self-esteem, and relationships). See Table 1 for an indicative search strategy in Medline. No language or date restrictions were applied to the searches, although non-English language results were excluded at the screening stage. Reference-checking and citation searching were performed in respect of relevant papers, to identify additional relevant papers not returned by the searches. Duplicates were removed prior to study selection, and the references were managed in a RefWorks database[18].

Study selection

Original empirical studies of women (>18 years) with breast cancer who had undergone CRRM, and which reported on psycho-social outcomes of interest (including quality of life, satisfaction, body image, sexuality, self-esteem and relationships) were included. Studies of males, women without breast cancer, women undergoing unilateral mastectomy or bilateral risk reducing mastectomy only (or where data relating to CRRM patients could not be distinguished), or studies focusing only on physical outcomes were excluded. Books, editorials and letters were excluded.

A screening tool incorporating the above inclusion/exclusion criteria was developed and piloted on the same 20 papers, by three reviewers (AC, KC, MG). Following this, the lead reviewer (AC) undertook the remainder of the title and abstract screening and all the full text screening. Two other reviewers (KC, MG) each spot-checked 10 random papers for full-text inclusion/exclusion and confirmed agreement. Where there was any doubt regarding study inclusion, a consensus was taken.

Data extraction and synthesis

A data extraction sheet was developed and piloted using the same four included studies, by two reviewers (AC, MG), to ensure consistency. Data from each of the remaining studies was extracted by one of these reviewers and checked by the other. Extracted fields included country, study design, study methodology, sample size, outcomes of interest, measurement instruments (if applicable), and key findings related to the outcomes of interest. The findings were synthesised thematically, in tabular and narrative format, classified according to the outcomes of interest.

Results

See Figure 1 for a flow chart summarising the search and screening processes. The database searches identified 361 records, resulting in 206 records after the removal of duplicates and non-English publications. Following title/abstract screening, 70 full papers were examined, from which 15 were included in this review. Reference and citation searches (including checking the reference lists of any literature reviews returned in the original searches) yielded no further relevant records. Thus in total 15 records[19-33], relating to 13 studies, are included in this review.

The main characteristics of the included studies are shown in Table 2.

Three of the papers[20,22,23] relate to the same population followed up at two different time points (first time point was at median FU of 10.7 years, range 1.9-34.4 years) and second FU was at a median of 20.2 years (range 11.4-44.5 years) post CRRM. Two papers [20,23] report on both surveys but one of these[23] reports only in respect of those women who responded to both surveys, and has a focus on reconstruction and reoperation on long term satisfaction. The third[22] paper reports on the first survey only. As these three papers report on different data they have been treated as separate (but related) entities in the presentation of the results.

The studies identified were undertaken in the United States[19,20,22-25,28-32], Canada[21], Hong Kong[27], and Sweden [26,33]. No UK studies were identified. Findings have been grouped into the following headings: satisfaction with the decision to undergo CRRM, overall satisfaction with CRRM, impact on psychological health and perceived impact on partners. The key findings from the papers in relation to each of these outcomes are presented below.

Satisfaction with the CRRM procedure

Five papers[20,22-24,27]were identified. None of the papers focused on low or average risk women so it is not possible to sub group analyse according to risk level. Satisfaction was typically measured using Likert scales, with one study[22] supplementing this with open-ended questions.

Within these studies, womens' satisfaction with the procedure (either 'satisfied' or 'very satisfied') ranged from 67% from a survey[27] of 12 women (follow-up at mean 20 months after CRRM) to 90% from a survey[23] of 269 women (mean 20.2 years post CRRM).

In the cohort study[22] of 583 women who had undergone CRRM (mean 10.3 years post CRRM) 83% (n=471) of women reported that they were satisfied with their CRRM, similarly 83% (n=471) stated that they would choose to have a CRRM again. Having 'peace of mind' knowing the risk of breast cancer in the unaffected breast (contralateral breast) was reduced and satisfaction with cosmesis were the main reasons explaining satisfaction. Only 9% (n=52) of women stated they were dissatisfied with their CRRM. Dissatisfaction with cosmetic results, adverse symptoms, complications or diminished body image were reasons given for this[22]. Strong associations were made between dissatisfaction with CRRM and decreased satisfaction with body appearance, and increased levels of stress in life after CRRM[22].

A second survey[23] was undertaken with the same cohort of women 10 years later (mean 20.2 years post CRRM). Of the 269 women (mean 20.2 years post CRRM), 90% (n=243) stated they were satisfied with their CRRM. Perception of making an informed choice and current quality of life was moderately associated with higher satisfaction with CRRM (r=0.37 and 0.37, respectively)[23].

Dissatisfaction with CRRM was significantly associated with the need for reoperation due to complications with the reconstruction[20,22]. Similarly, in a smaller study[27] which sampled just 12 women, 6 of whom had reconstructive surgery, only one woman who experienced flap failure stated her overall satisfaction with the CRRM was unsatisfactory[27].

Satisfaction with decision

Five papers[20,22,23,26,27], relating to three studies investigated womens' satisfaction with their decision to undergo CRRM, and whether or not they would choose CRRM again. None of the studies focused on low or average risk women. A combination of Likert scales, study specific measurement tools, and open ended questions were used within the reported studies. No study used a validated tool such as the decision regret scale[34].

Most women reported that they were satisfied with their decision and would choose CRRM again, with responses ranging from 75% from a survey[27] of 12 women (follow-up at mean 20 months after CRRM) to 100% in a survey[26] of 21 women (follow-up at median 42 months). In two large surveys[22,23] of 269 women, 90% and 92% of women at a median of 10.3 and 20.2 years post CRRM respectively reported that, knowing what they do now, they probably or definitely would choose CRRM again.

Impact of CRRM on body image

Nine papers [19-24,27-29] relating to seven studies explored the impact of CRRM (with and without reconstruction) on womens' body image using a range of validated and non-validated tools in the short, medium or long term. None of the studies focused on low or average risk women. Among the quantitative studies, perceptions of body image were typically measured using ordinal scales or Likert scales. One study[23] used a validated Body Image Scale.

Womens' overall perceptions of their body image and general satisfaction with their appearance were measured by two studies[20,22,23,27]. More specifically, studies explored women's feelings of femininity[20,22], sexuality and sexual attractiveness[23,28,29], self-consciousness about their appearance[23,24], and satisfaction with the cosmetic result of CRRM/reconstruction[29].

Body image and cosmesis post-CRRM emerged as an important theme within these studies[19,21]. Women expressed positive views of enhanced breast size or pertness, pride in survivorship, acceptance of the trade-off of survival at the expense of sub-optimal cosmesis and regret at the loss of femininity[19].

Two papers relating to the same large study reported long term follow-up of women with a personal and family history of breast cancer (FU median 10.3 years[22] (n=583) and median 20.2 years[23](269 women) post CRRM). At first and second follow-up, body image was negatively affected in 33% (n=192) and 31%(n=89) of women respectively. At a median FU of 10.3 years post CRRM[22], 33% (n=192) of women reported decreased satisfaction with their body appearance, and 26% (n=70) reported adverse effects of CRRM on their sense of femininity. At a median FU of 20.3 years post CRRM[23], 11% (n=29) of women reported that they felt less physically attractive, and 15% (n=41) reported feeling less sexually attractive since undergoing their CRRM. Feelings of femininity were found to correlate with sexual relationships in this study[22]. In another study, immediate CRRM was found to have a significant negative impact on sexuality compared to delayed or no CRRM[28]. A diminished sense of sexuality was reported as a reason for decision regret [29]. Self-consciousness about their appearance was reported by between 10- 21% of women in another study[24]. In a further study [27] 90% (n=11) of women reported their initial impression of their appearance after surgery as being acceptable. Successful reconstruction was significantly associated with increased satisfaction with physical appearance and with increased feelings of femininity[20].

Body image was an important factor influencing whether or not women would choose CRRM/reconstruction again[20]. Of 583 women that were surveyed 10 years post CRRM, 69% (n=403) underwent CRRM/reconstruction, 84%(n=338) stated that they would choose CRRM again, and 73% (n=296) would make the same choice regarding reconstruction. Most commonly, women cited positive effects on body image and self-esteem.[20] However, 17% (n=68) stated that they would not choose reconstruction again, with adverse body image/poor cosmetic outcomes as being the main factors underlying this[20].

Women in the no reconstruction group who said they would still opt for no reconstruction gave the most frequently cited reason that they felt comfortable with their body without reconstruction (42% n=170).

At 20 years post CRRM, a smaller percentage of women compared to 10 years said they would change their decision: 10%, (n=26) of reconstruction patients and 16% , (n=40) of no reconstruction patients said they would change their decision. Successful reconstruction and use of implants also contributed to better adjustment towards surgical outcomes[20].

Impact on psychological health

Ten papers relating to eight studies specifically examined the impact of CRRM on mental health[19,20,22-25,30-33]. None of the papers reported on differences between low, average or high risk women. Psychological health was measured in the short-, medium- and long-term. A combination of Likert and unspecified ordinal scales were used. A number of validated instruments were also used to measure symptoms related to mental health conditions including: the Hospital Anxiety and Depression scale[33], the 15-item Impact of Events Scale[25,32], the 17-item Multidimensional Impact Cancer Risk assessment[32], the Functional Assessment of Cancer Therapy(FACT)-Breast Cancer quality of Life Instrument[24], the Centre for Epidemiologic Studies-Depressions (CES-D) scale[24,30], and the Short-form of the Hopkins Symptom Checklist (HSCL-25)[25].

In one survey[20] of 583 women (at median FU of 11.9 years post CRRM), CRRM followed by reconstruction was significantly associated with positive feelings of self-esteem (32% (n= 125) with and 12% (n=21) without reconstruction – P=0.00002). Whilst in a survey follow up of 269 women (median of 20.2 years post CRRM) this was 26% (n=52) and 16 % (n=9) respectively. Differences between reconstruction and non-reconstruction patients was not statistically significant[20].

The same large study examined emotional stability following CRRM. Emotional stability was reported to be adversely affected in 23% (n= 65) of women in the first survey (median 10.7 years post CRRM) [23].Whilst in the second survey (mean 20.2 years post CRRM) only 14% (n=19) reported an adverse emotional effect[23]. In both the first and the second survey there was no statistically significant difference in emotional stability between those who underwent reconstruction following CRRM compared to those with no reconstruction[20].

One study[22] reported perceived stress following CRRM with 17% (n=100) of women reporting that they experienced stress in life following CRRM. Stress was negatively correlated with self-esteem (r=0.33) and emotional stability (r=0.21).

Three studies reported on anxiety following CRRM[19,31,33]. In surveys[33] of 60 women at different time points, prior to CRRM, 30% (n=18) of patients scored above the cut off point for clinically relevant levels of anxiety (>8) on the anxiety subscale and at 6-month and 2-year post CRRM, 37% (n=22) and 22% (n=13) respectively. In another study[19] 4% (n=25) of women post CRRM commented on feelings of relief from breast cancer worry or anxiety since having the surgery (median follow-up 9 years (range 3-22). A further study[31] reported no significant difference in levels of anxiety in women who chose CRRM compared to those having breast-conserving surgery or unilateral mastectomy only.

Four studies focused on depression following CRRM[24,30,31,33]. In one study, albeit with very small numbers precluding statistical analysis, rates of depression varied very little before and after CRRM[33]. They found 13% (n=8) of patients at baseline, 12% (n=7) at 6 months and 8% (n=5) at 2 years post CRRM had evidence of depression, using a threshold of >8 on the depression subscale as indicative of clinically relevant depression. In another study[24] of 519 women who had undergone CRRM between 1979-1999, 27% (n=14) of women studied had met the Centre for Epidemiologic Studies-Depression (CES-D) threshold for depression. In another study[30] 25% (n=114) of women who had undergone CRRM in the past had depressive symptoms at the time of the survey (the mean time since CRRM was not reported but 60% women had CRRM within the last 10 years).

Two studies[25,32] found that CRRM was not associated with, or a predictor of, cancer specific distress.

One study[24] focused on contentment with life following CRRM and found that of the 580, women who had CRRM between 1979-1999, 76.3% (n=396) reported significant contentment with their life post CRRM, and only 7.3%(n=38) reported poor levels of contentment. There were no differences between those having CRRM and those having CRRM/reconstruction[24]. This rather historic time period largely predated clinical gene testing so few women will have had risk assessment and counselling according to modern standards.

Another study[33] used the Short Form 36 Health Survey (SF-36, validated Swedish version) to report on health status following CRRM and found no statistically significant differences between preoperative and postoperative (both at 6-months and 2-years) assessments for any of the SF-36 subscales. At 6 months post CRRM, patients scored lower on emotional domains when compared to preoperative values. This was considered clinically significant, although this may have reflected the emotional impact of the end of the cancer treatment spell, which is often associated with depression, rather than the CRRM itself, although this was not specified[33]. However, two years after CRRM, a positive clinical difference (an increase in SF-36 score of >5) in social functioning and mental health was found[33]. It should be noted that the SF36 is a generic health status instrument and more sensitive tools are available to specifically measure breast cancer and breast surgery related outcomes.

Impact of CRRM on relationships with partners

Nine papers[19-24,27,31,33] relating to seven studies explored the impact of CRRM on personal relationships in the short-, medium- and long-term using a variety of validated and non-validated tools. One study[33] used a specific sexual activity questionnaire (SAQ - Swedish version).

Three studies[20,22-24,27] reported specifically on the extent to which sexual relationships had been affected post CRRM. In two studies[22,23] 24% (n=143) and 23% (n=138) respectively , stated that sexual relationships had been adversely affected 10 and 20 years post CRRM. Changes in satisfaction with body appearance were correlated with changes in sexual relationships (r=0.46), feelings of femininity correlating with sexual relationships (r=0.33) and levels of stress significantly correlated with sexual relationship(s) (r = -0.23)[23]. In the same study, significantly more women who had undergone reconstruction reported adverse effects on sexual relationships at the first follow-up, than those who had not (24% and 21% respectively; p=0.03), however at the second follow-up time point the difference was not statistically significant (23% and 18% respectively)[20]. One study found that, of those who had undergone CRRM, 41% (n=213) reported satisfaction with their sex life[24]. In another study[33]exploring sexual activity using a self-assessment questionnaire of 60 women 2 years post CRRM, over half of the women reported problems/dissatisfaction with their body appearance, scars, femininity and attractiveness across 2 of the body image domains[33]. One study reported on perceived strained personal relationships prior to and following CRRM and found no statistically significant differences between pre and post-operative scores [31]. Three studies[19,21,27] reported that women were sensitive to the reaction of their partners following CRRM. Two of these studies[19,27] reported that spouses' attitudes and support contributed to the overall adjustment of women. They also reported that among those who were married but sexually inactive (50% n=3/6), lack of sexual activity predated the CRRM and simply persisted afterwards. Reasons included decreased libido after cancer treatment, menopause and fatigue. They also found that the sexually inactive single participants appeared to adjust better to the cosmetic results of the surgery[21].

Conclusions and recommendations made within the reviewed studies

Conclusions from each of the reviewed studies have been grouped into 5 broad categories:

1. Additional decision support and education aids are needed not only relating to whether to have CRRM but also to what type of reconstructive surgery (if any) to select (6/15 studies)
2. Women should be informed of the potential risks and adverse outcomes (specific consideration given for sexuality, psycho-social outcomes and body image changes) (9/15 studies)

3. The role of the health professional (surgeon, specialist nurse, psychologist) was emphasised in supporting informed decision making and guidance may be helpful to optimise informed decision making. (4/15 studies)
4. Psycho-social and counselling support should be provided both before and after such surgery (5/15 studies)

Discussion

This review has synthesised the current evidence from 15 studies focused on the psychosocial impact of CRRM. All studies reported high levels of satisfaction following CRRM. Two studies reporting on the same cohort of women (mean 10.3 and 20.2 years post CRRM) found satisfaction to be consistently stable over a 10 year period[22,23]. Reducing the risk of a CBC in the future and therefore reducing cancer related anxiety, and satisfaction with cosmesis, were key themes running across all studies explaining satisfaction among this group. Dissatisfaction was associated with adverse effects, with poor cosmesis, body image changes, femininity, sexual relationships, reoperations for acute and longer term complications and reconstructive problems cited as significant concerns[19-24,29].

Of the 15 papers included in the review, 13 focused exclusively on women who were considered to be at high risk (family history, genetic mutation carriers) of developing a subsequent contralateral breast cancer. Only 3[19], [29, 30] of the studies included women that were at low to average risk of developing a subsequent breast cancer. None of the studies reported any differences between these groups.

Since undertaking this review, a systematic review focusing on factors and predictors influencing choice and satisfaction with CRRM has been published. This review primarily focuses on factors influencing decisions to undergo CRRM and rather than longer term outcomes. The review reported that overall, women appeared satisfied with their decision to undergo CRRM, and similar to our findings, adverse/diminished body image, poor cosmetic result, complications, diminished sense of sexuality, emotional issues and perceived lack of education regarding alternative surveillance/CRRM efficacy were cited as reasons for dissatisfaction[4].

Although satisfaction rates were high, the reasons for dissatisfaction seem to suggest that there is a need for additional information resources to support informed decision making regarding the decision to have CRRM and/or immediate/delayed reconstruction (or not) and the provision of evidence based information on the risks and benefits of CRRM may be warranted. Women need to be more fully informed of the impact of CRRM on long term survival, recurrence risk, post-operative complications and possible quality of life and psychological outcomes[6,12,14]. This seems imperative among low/average risk women where there are no significant survival benefits of undergoing CRRM.

Although not part of this review, the role and influence of health professionals and partners on treatment decisions became apparent and further investigation is warranted.

Limitations of this study

In common with all rapid reviews, this review has limitations compared with a full systematic review. By limiting the search to English language publications and not contacting authors for additional relevant research, relevant unpublished reports, grey literature, and papers published in other languages, some data may have been missed. By performing a light-touch quality assessment there was a risk of over-reliance on and misinterpretation of poor research. The disadvantage of single-screening some of the papers by the lead author was mitigated against by piloting the screening tool by three authors, and two authors further checking a sample of screened papers. All data extractions were also double-checked by a different reviewer.

Conclusion

Although satisfaction with CRRM was consistently reported across all studies, the focus of these studies was largely high familial/genetic risk women rather than low/average risk women and it is therefore unclear from this review whether such findings can be extrapolated to low/average risk women. Given the growing numbers of CRRM being performed in women considered to be at low/average risk of developing a new primary CBC for whom there will be no significant survival benefit of undergoing a CRRM, there is a need for improved decision support in order to ensure women are fully aware of the risks and benefits of CRRM (specifically long terms survival, recurrence risk, post-operative complications and short/medium and longer term quality of life/psychological outcomes) in order to make informed decisions regarding this complex decision. However the evidence from this review is that the psychological outcomes are largely positive, even in the long term, and this should be considered when supporting women in informed decision making.

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Table 1. Indicative search strategy in Medline

TI = title words; AB = abstract words; MH = database subject heading

S1	TI "contralateral risk reducing mastectom*" OR AB "contralateral risk reducing mastectom*" OR TI "contralateral surger*" OR AB "contralateral surger*"	230
S2	TI "contralateral risk reduc* mastectom*" OR AB "contralateral risk redu* mastectom*"	17
S3	S1 OR S2	247
S4	(MH "Quality of Life")	131,267
S5	TI "quality of life" OR AB "quality of life"	178,080
S6	TI "patient reported outcome measures" OR AB "patient reported outcome measures"	1,013
S7	TI "patient reported experience measures" OR AB "patient reported experience measures"	14
S8	TI psychological OR AB psychological	148,789

S9	TI psychosocial OR AB psychosocial	67,719
S10	(MH "Patient Satisfaction+")	67,044
S11	TI satisfaction OR AB satisfaction	90,107
S12	TI wellbeing OR AB wellbeing	7,516
S13	(MH "Body Image")	13,976
S14	TI "body image" OR AB "body image"	7,428
S15	(MH "Emotions+")	184,009
S16	TI regret* OR AB regret*	2,917
S17	TI relationship* OR AB relationship*	971,697
S18	TI partner* OR AB partner*	119,789
S19	TI "sexual function*" OR AB "sexual function*" OR TI sexuality OR AB sexuality	20,342
S20	(MH "Mental Disorders+")	1,012,537
S21	TI mental* OR AB mental*	255,405
S22	TI depress* OR AB depress*	349,415
S23	TI anxiet* OR AB anxiet*	130,565
S24	TI stress OR AB stress	512,998
S25	TI self-esteem OR AB self-esteem	15,311
S26	TI (behaviour* OR behavior*) OR AB (behaviour* OR behavior*)	886,130
S27	TI emotion* OR AB emotion*	133,613
S28	S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30	3,728,026
S29	S3 AND S28	66

Figure 1. Document flow diagram

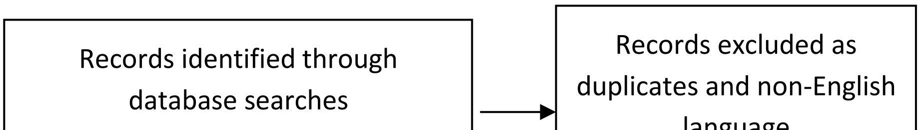

Table 2.Main characteristics and outcomes of the papers reviewed

Study, country, design	Study aim(s) (relevant to this review)	Sample size, study population, time of follow-up (if given) (relevant to this review)	Outcome categories of findings relevant to this review
Altschuler *et al.* (2008)[19]	To assess and compare the multidimensional and psychosocial	For the qualitative element: n=327 women (of whom n=249	Satisfaction with decision

United States Qualitative/Quantitative (Qualitative element relevant to this review) Survey	effect of risk reducing mastectomy (bilerateral and contralateral) in women with and without a personal history of breast cancer	had CRRM and n=78 had bilateral prophlyactic mastectomy) Women who had had risk reducing mastectomy between 1979 and 1999, aged 18-80 years Follow-up post CRRM: 3-22 years (median 9 years)	Body image Relationships Mental health
Boughey**et al.* (2015)[20] United States Quantitative Two surveys	To evaluate the long-term satisfaction with CRRM and compare satisfaction between those with/without breast reconstruction; to examine the adverse aspects that patients attribute to reconstruction and the subsequent effect on psychosocial consequences.	First survey: n=583 women (of whom n=403 underwent reconstruction) Second survey: n=269 women (of whom n=210 underwent reconstruction) Women with unilateral breast cancer and a family history of breast cancer who underwent CRRM. Age at first survey 28-92 years Follow-up post CRRM, first survey: 1.9-35.4 years (mean 11.9 years)** Follow-up post CRRM, second survey: 11.4-44.5 years (mean 20.2 years)	Satisfaction with procedure Satisfaction with decision Body image Relationships Mental health
Frost**et al.* (2005)[22] United States Quantitative Survey	To investigate: satisfaction with CRRM and factors associated with satisfaction/dissatisfaction; factors associated with satisfaction/dissatisfaction after CRRM; how reconstruction affects satisfaction after CRRM; how does CRRM affect women's long-term psychological and social function, and stress levels	n=583 women Women with unilateral breast cancer and a family history of breast cancer who underwent CRRM. Age at first survey 28-92 years Follow-up post CRRM: mean 10.3 years**	Satisfaction with procedure Satisfaction with decision Body image Relationships Mental health
Frost**et al.* (2011)[23] United States Quantitative Survey	To evaluate the long-term consistency of satisfaction with CRRM and adverse psychological and social effects; to explore the effect of informed decision-making, personality traits, and quality of life (QOL) on satisfaction.	n=269 women (who responded to first and second surveys) Women who with unilateral breast cancer and a family history of breast cancer who underwent CRRM. Age at CRRM 24.1-75.3 years; age at first survey 31.7-84.3 years; age at second survey 41.8-94.0 years. Follow-up post CRRM, first survey: 1.9-35.4 years (mean 10.7 years) Follow-up post CRRM, second survey: 11.4-44.5 years (mean 20.2 years)	Satisfaction with procedure Satisfaction with decision Body image Relationships Mental health
Covelli *et al.* (2015)[21] Canada Qualitative Semi-structured interview	To explore patients' perspectives on decision making for early stage breast cancer and women's choice for mastectomy	n=14 women (who had unilateral mastectomy + CRRM) Women who had undergone either UM or UM + CRRM within the previous 9-12 months. Of the UM+CRRM patients, age range 37-69 years, median 46 years.	Body image Relationships

		Follow-up post CRRM: 9-12 months	
Geiger *et al.* (2006)[24] United States Quantitative Survey	To understand the psychosocial outcomes after CRRM; to determine long-term contentment with quality of life and to examine factors associated with less contentment with quality of life	n=519 women (who had CRRM) Women who had been diagnosed with breast cancer from 1979-1999, aged 18-80 at diagnosis. Follow-up post CRRM: not reported	Satisfaction with procedure Body image Relationships Mental health
Graves *et al.* (2007)[25] United States Quantitative Interview	To determine the predictors and impact of CRRM on psychological outcomes	n=89 women (who had CRRM by the 12-month follow-up, from n=435 women affected with unilateral breast cancer who received positive uninformative BRCA1/2 genetic test results) Participants (N = 435) were women affected with unilateral breast cancer who received BRCA1/2 test results through the Lombardi Comprehensive Cancer Center's Cancer Assessment and Risk Evaluation (CARE) program from 1995 to 2000. Follow-up post CRRM: <12 months	Mental health
Isern *et al.* (2008)[26] Sweden Quantitative Survey	To investigate the long-term aesthetic outcome, patient satisfaction, health related quality of life and complication rates among women undergoing CRRM and immediate reconstruction	n=21 women (who underwent CRRM) Women who underwent CRRM with immediate breast reconstruction, all with a previous ipsilateral cancer. 16 of these women had a previous cancer treated with mastectomy. 5 had a previous breast cancer and nonradical breast conserving surgery. Follow-up post CRRM: 7-99 months (median 42 months)	Satisfaction with decision
Kwong & Chu (2012)[27] Hong Kong Qualitative/Quantitative Semi-structured interview	To explore the impact of CRRM from the subjective account of high-risk unilateral breast cancer survivors following a genetic BRCA1 or BRCA2 diagnosis	n=12 women (comprising n=11 confirmed BRCA 1/2 mutated gene carriers and n=6 had reconstructive surgery with CRRM) Women who had CRRM after BRCA1/2 genetic testing. Age 34-55 years. Follow-up post CRRM: 11-34 months (mean 21 months)	Satisfaction with procedure Satisfaction with decision Body image Relationships
Lee *et al.* (2013)[28] United States Quantitative Survey	To examine short-term QOL impairment in premenopausal patients with breast cancer (diagnosed before the age of 50 years), including self-perception, views of their sexuality, impact of surgical and oncologic treatment,	n=143 women of whom n=67 women had undergone CRRM (n=54 underwent immediate CRRM, n=13 underwent delayed CRRM) Women diagnosed between the	Body image

	femininity, and changes in relationships with partners and other family members.	ages of 18 and 49 y with non metastatic breast cancer and ≥ 6 months from last curative treatment (surgery, chemotherapy, radiation) except for ongoing hormone therapy Follow-up post CRRM: ≥6 months (mean not reported)	
Montgomery *et al.* (1999)[29] United States Qualitative Semi-structured interview	To understand which factors may cause a women to regret her decision to undertake CRRM	n=18 women who expressed regret from an overall survey response of n=296 women Women who had undergone CRRM and who reported they regretted their decision to have CRRM (ie would not have a CRRM againnor would recommend it to another woman at similar risk). Mean age for the whole sample (ie those who did or did not regret) at CRRM was 53.8 years (range 27-80, median 53). Follow-up post CRRM: 0.25-43.8 years (mean 10.9 years)	Satisfaction with decision Body image
Nekhlyudov *et al.* (2005)[30] United States Quantitative Survey	To determine women's reported decision making roles regarding CRRM, including trends over time, and to explore the association of decision making roles with psychological outcomes, including satisfaction, long-term concern about breast cancer, and depressive symptoms	n=431 women Women aged 18-80 years with CRRM between 1979 and 1999. Follow-up post CRRM: mean 10.0 years	Satisfaction with decision Mental health
Portschy *et al*. (2015)[31] United States Quantitative Survey	To evaluate contralateral breast cancer risk perception changes over time among breast cancer patients	n=43 women of whom n=11 women had undergone CRRM Women over the age of 18 with Ductal carcinoma in situ or invasive breast cancer (newly diagnosed unilateral breast cancer). Mean age of thosewho had CRRM was 47 years Follow-up post CRRM: 1.8-3.5 years (mean 2.6 years) (reporting on n=43 women)	Satisfaction with decision Relationships Mental health
Tercyak *et al*. (2007)[32] United States Quantitative Interview	To investigate the impact of CRRM during the immediate postdiagnostic period (1 month after BRCA1/2 testing) and after the completion of adjuvant treatment (12 months after testing)	n=29 and n=44 women who had undergone CRRM at 1- and 12-months respectively, from n=147 and n=149 women completing the 1- and 12-month follow-up Women newly diagnosed with ductal carcinoma in situ (DCIS) to stage IIIa breast cancer, who had not received definitive local breast cancer treatment, and had received genetic counselling and testing. Mean age 45 years (range 23-70 years). Follow-up post BRCA 1/2 testing: 1 and 12 months	Mental health

Unukovych *et al.* (2012)[33] Sweden Quantitative Questionnaire	To prospectively (before CRRM, 6 months and 2 years after CRRM) evaluate HRQoL, anxiety and depression, sexuality and body image in breast cancer patients with a family history, undergoing CRRM with immediate breast reconstruction	n=60 women responded to any of the three questionnaires, with n=45 women responding to the pre-CPN survey, n=49 at the 6-month survey, and n=45 at the 24-month survey Women with a confirmed family history of breast cancer who underwent CRRM with immediate breast construction, and who had a consultation with a medical psychologist before CRRM. Age at CRRM 25-65 years. Excluded women who underwent CRRM in conjunction with breast cancer surgery. Majority (57/60) patients had already undergone breast cancer surgery and adjuvant treatment prior to CRRM.	Body image Relationships Mental health

*The papers Boughey *et al.* (2015), Frost *et al.* (2005) and Frost *et al.* (2015) relate to the same large cohort study.

**The papers Boughey *et al.* (2015) and Frost *et al.* (2005), although referring to the same population for the first survey, report different mean times of follow-up since CRRM.