



Patient-reported outcomes in bilateral prophylactic mastectomy with breast reconstruction: A narrative review

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ABSTRACT

In women at high risk of developing breast cancer, bilateral prophylactic mastectomy (BPM)¹ significantly reduces the risk; simultaneously, breast reconstruction preserves body integrity. Given the complex and personal nature of such surgical procedures, patient assessment of satisfaction and health-related quality of life (HRQoL)² is essential in evaluation of surgical outcomes.

With this review, we aim to organize the current knowledge on patient-reported outcomes (PROs)³ in bilateral prophylactic surgery. Literature search was conducted using the databases Google Scholar, PubMed, and Web of Science to address the following questions, which can help clinicians and women undergoing the procedures navigate their healthcare decision-making process: How does BPM with reconstruction influence cancer-related distress? How does the surgery impact patient satisfaction and HRQoL? How do preoperative PROs differ from postoperative outcomes? Does the type of BPM and the type of reconstruction impact patient satisfaction and HRQoL? Furthermore, we summarize available patient-reported outcome measures (PROMs)⁴ that can be administered to women undergoing BPM with reconstruction. In addition, we discuss possible future directions for PRO research in prophylactic breast surgery.

1. Introduction

Hereditary breast cancer is responsible for 5–10 % of all breast cancer cases [1–3]. In the carriers of pathogenic variants of highly penetrant predisposition genes, prophylactic mastectomy does reduce the risk of breast cancer [4–6]. Simultaneously, breast reconstruction preserves body integrity, maintaining HRQoL [7] – therefore, subjective data gathered from patients are essential in the evaluation of the outcomes.

A large body of literature has been published on PROs in women, who have undergone mastectomy for breast cancer followed by breast reconstruction [8–12]. Furthermore, there is a considerable number of PRO studies in women, who had undergone prophylactic mastectomy to reduce the risk of the cancer. However, many of these studies include both women with bilateral and those with contralateral prophylactic mastectomy (reviewed in Ref. [13]), although research suggests that PROs in women with bilateral versus contralateral prophylactic mastectomy differ [14]. Other studies focus on bilateral procedure, but they include both women with and without reconstruction following the mastectomy [15,16]. Nevertheless, it has been shown that satisfaction

and HRQoL differ in women with mastectomy only versus in those who had undergone mastectomy with reconstruction [17].

Yet, the number of BPMs performed has increased enormously in recent years [18], being preferably performed together with breast reconstruction [19]. Therefore, we focus on and review PROs solely in those women, who had undergone bilateral prophylactic procedure followed by reconstruction.

1.1. Hereditary breast cancer

Hereditary breast cancer is often associated with a positive family history of this disease. In patients with hereditary breast cancer, bilateral cancer is more common than in sporadic cases and the risk of other types of cancer may also be increased. Furthermore, the patients tend to develop cancer at a younger age [20–22].

The highest proportion of hereditary breast cancers are caused by germline mutations in BRCA1 and BRCA2 genes [23,24]. The BRCA1 and BRCA2 genes are involved in the repair of DNA damage and thus they are important regulators of genomic integrity [25,26]. BRCA1 or BRCA2 mutations, in turn, are significantly increasing risk of cancer [27,28], including breast cancer, ovarian cancer, and based on the current

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Nomenclature

BPM	bilateral prophylactic mastectomy
HRQoL	health-related quality of life
PROs	patient-reported outcomes
PROMs	patient-reported outcome measures

evidence also pancreatic cancer [29]. BRCA genes are inherited in an autosomal dominant pattern – therefore, any offspring of a carrier of BRCA mutation have a 50 % chance of inheriting the pathogenic or likely pathogenic variant [30,31]. The cumulative risk for breast cancer at age 80 years is 72 % for BRCA1 mutation carriers and 69 % for BRCA2 mutation carriers [32]. Nevertheless, the probability of cancer development is variable, even within affected individuals of the same family [33]. Besides BRCA1 and BRCA2, several other breast cancer susceptibility genes contributing to the hereditary breast cancer spectrum have been described [34], including TP53 (Li-Fraumeni Syndrome; 50 %–90 % lifetime risk of breast cancer), PALB2 (33 %–58 %), PTEN (PTEN hamartoma tumor syndrome; 25 %–50 %), STK11 (32 %–54 %), CDH1 (30 %–50 %), CHEK2 (20 %–40 %), NBN (20 %–30 %), or ATM (20 %). [35–37].

1.2. Risk management in hereditary breast cancer

In order to reduce the risk of developing a cancer in the women at high risk, multiple strategies have been employed, including surveillance, chemoprevention, and BPM [38]. BPM has been shown to significantly reduce the breast cancer risk in high-risk women with family history of breast cancer [5,39,40]. However, studies analyzing the role of BPM in reducing mortality are still forthcoming. Additionally, in women carrying mutations in moderate penetrance genes, outcomes of BPM are not available, and prophylactic surgery is generally not encouraged [41].

First, it should be considered that prophylactic mastectomy with reconstruction might be associated with significant physical morbidities; those include implant failure, partial or total autologous flap loss, tissue ischemia, hematomas, infections, loss of sensitivity, or possible oncological failure [42,43]. Second, the female breast is perceived as a symbol of femininity [44]; thus, a disturbance of its integrity might lead to psychological morbidity in some women [45].

Nowadays, risk reduction strategies are under continuous development [46] and many questions remain [47]. Thus, the decision-making process should be personalized, based on the individual risk assessment and woman's personal preferences. [47,48] Besides traditional clinical measurements such as morbidity and mortality [49], patient-reported health data are in high demand, particularly for facilitation of the clinician and the patient healthcare decision-making process.

1.3. Patient-reported outcomes

Recently, PROs became an integral part in the evaluation of clinical outcomes, capturing the patient voice and allowing it to be incorporated in the assessment of risk and benefits of different types of treatment. Patient's subjective assessment can provide a completely new perspective and significantly change the approach to the choice and performance of surgery and subsequent postoperative care [50]. For example, St-Pierre et al. claim that women considering prophylactic breast surgery reported a desire to discuss the outcomes with women who had undergone such a procedure [51]. Some authors suggest that PROs seem to be of more importance in future than clinical, physiological, or caregiver-reported outcomes [52]. Others assume that they might help drive global patient-centered healthcare reform [53]. The aim of this narrative review is to outline and update current understanding of PROs

in different types of BPM and different reconstruction techniques, versus postoperative PROs, and PROs in women with BPM followed by reconstruction versus reference population.

1.4. Patient-reported outcome measures

To capture patient-reported health data, some authors conduct interviews with patients [54–56], whereas others use self-assessment scales or questionnaires developed to capture patients' subjective experience, i.e., PROMs [57]. The conceptual framework of PROMs should be created based on patient input [58]. Furthermore, they should be psychometrically validated and standardized [59]. The advantage of PROMs is that they can be easily administered to a large number of patients and, more importantly, yield quantitative data. That allows comparison across e.g., different patient groups, surgery settings, or healthcare providers [60]. The next aim of this review is to summarize knowledge about PROMs, which can be administered to women at high risk undergoing BPM with reconstruction.

2. Methods

The literature search was conducted between January 2023 and June 2023 using the databases Google Scholar, PubMed, and Web of Science. The search focus was patient-reported outcomes in bilateral prophylactic mastectomy with breast reconstruction. Following keywords were utilized: “bilateral prophylactic mastectomy”, “prophylactic surgery”, “risk-reducing mastectomy”, and “breast reconstruction”. The search was refined using the following keywords: “patient-reported outcomes”, “quality of life”, and “satisfaction”. The articles were included if they were in English, original, published in peer reviewed journals, and the full text was available. There was no limit on the date of publication.

Furthermore, the articles were excluded if they were unrelated to the search focus. Exclusion criteria were: focus exclusively on genetic testing or surgical treatment; evaluation of PROs on a combination of prophylactic mastectomy and oophorectomy or other risk-reducing procedures; inclusion of women with unilateral mastectomy; inclusion of women with contralateral prophylactic mastectomy; inclusion of both women with bilateral and those with contralateral prophylactic mastectomy; inclusion of women with prophylactic mastectomy without reconstruction; inclusion of both women with prophylactic mastectomy with reconstruction and those without reconstruction; evaluation of patient HRQoL or satisfaction based on patient interviews instead of using PRO instruments. In total, 12 studies met our criteria as mentioned above.

3. Results

Table 1 lists HRQoL instruments and breast surgery-specific PRO instrument which were used to evaluate PROs in women with BPM followed by reconstruction except for The Dutch Relationship Questionnaire [61]. The latter mentioned instrument used by Gopie et al. [62] is not available in English. The aim of assessment, number of items, instrument subscales, and reliability using Cronbach's alpha values is included. Alpha values of 0.70 or greater are generally considered to be acceptable, indicating good internal consistency of questionnaire or scale [63].

Prophylactic breast surgery is linked to a variety of psychological aspects: women undergoing such procedures might experience cancer-related distress as well as concerns about their appearance and its potential changes. Thus, to evaluate subjective outcomes, multiple PROM questionnaires addressing different aspects might be administered. In the majority of the reviewed studies, authors used more than one questionnaire to address their questions. Table 2 lists PRO instruments used in the analyzed studies. Furthermore, a short summary about the outcomes of the analyzed studies is included.

Table 1

List of PRO instruments measuring PROs in BPM with reconstruction, including the aim of assessment, number of items, instrument subscales, and reliability values.

PROM	Aim of assessment	Number of items	Subscales	Cronbach's alpha
HRQoL instruments				
BODY-Q	Patient perceptions of weight loss or body contouring surgery, with focus on his/her appearance, HRQoL, and experience of healthcare	148	Body, Abdomen, Arms, Back, Buttocks, Hips and outer thighs, Inner thighs, Skin, Scars, Body image, Physical, Psychological, Sexual, Social, Doctor, Information, Medical team, Office staff	0.96, 0.98, 0.95, 0.96, 0.95, 0.97, 0.96, 0.95, 0.95, 0.96, 0.95, 0.95, 0.90, 0.95, 0.95, 0.92, 0.97, 0.97 [64]
The Body Image Scale (BIS)	Self-consciousness, physical and sexual attractiveness, femininity, satisfaction with body and scars, body integrity, and avoidance behavior after the cancer treatment, i.e., disfiguring surgery or radiotherapy	10	N/A	0.95 [65]
The Decision Regret Scale	Satisfaction with the treatment decision	5	N/A	0.81–0.92 [66]
The General Anxiety Disorder 7-Item scale (GAD-7)	Severity of general anxiety disorder - feeling anxious, worrying, trouble relaxing, or becoming irritable [67,68]	7	NA	0.83–0.93 [69]
The Hospital Anxiety and Depression scale (HAD)	Feeling tense, feeling restless, getting sudden feelings of panic, ability to laugh, feeling cheerful, or looking forward to things [70]	14	Anxiety, Depression	0.80, 0.76 [71]
The Impact of Event Scale (IES)	Subjective distress related to traumatic events [72–74]	15	Intrusion, Avoidance	0.87, 0.76 [75]
The Patient Health Questionnaire (PHQ-9) - depression module	Screening, diagnosing, monitoring and measuring the severity of depression [76]	9	N/A	0.851 [77]
The Patient-Reported Outcome Measurement Information System–29 (PROMIS-29)	Disease non-specific instrument [78,79]	29	Physical function, Anxiety, Depression, Fatigue, Sleep disturbance, Ability to participate in social roles and activities, Pain interference	0.82, 0.88, 0.90, 0.93, 0.71, 0.90, 0.95 [80]
The Satisfaction with Decision Scale (SWD)	Patient satisfaction with his/her decision about the healthcare	6	N/A	0.86 [81]
The Sexual Activity Questionnaire (SAQ)	Sexual functioning i.e., pleasure from sexual intercourse, discomfort during sexual intercourse, and habit [82]	7	Sexual pleasure, Sexual discomfort, Sexual habit	0.732, 0.839, 0.739 [83]
The short-form McGill Pain Questionnaire (SF-MPQ)	Type and intensity of pain using descriptors from sensory and affective categories [84,85]	15	N/A	0.72 [86]
36-item Short-Form Health Survey (SF-36)	Patient-reported health data related to disease and treatment [87,88]	36	Physical functioning, Role limitations due to physical problems, Role limitations due to emotional problems, Vitality, Emotional well-being, Social functioning, Pain, General health	0.924, 0.873, 0.862, 0.728, 0.766, 0.527, 0.836, 0.693 [89]
Breast surgery-specific PRO instrument				
BREAST-Q – reconstruction module	Satisfaction and HRQoL in women undergoing breast reconstruction [90–92]	38	Satisfaction with breasts, Satisfaction with outcome, Psychosocial well-being, Sexual well-being, Physical well-being: chest and upper body, Satisfaction with information	0.96, 0.88, 0.95, 0.93, 0.91, 0.94 [58]

3.1. Cancer-related distress, anxiety, depression, and feelings of regret

Research assumes that carriers of breast cancer predisposition genes commonly experience anxiety prior to a BPM. This anxiety is related to cancer worry. PRO studies on prophylactic breast surgery show that the anxiety levels significantly decreased after BPM with reconstruction compared to preoperative levels [93,94]. Besides that, feelings of regret regarding the decision about the surgery were almost non-existent [95]. When it comes to women's depression pre- versus postoperatively, no differences were reported [94]. Metcalfe et al. [96] collected PROs from 137 women who had undergone nipple-sparing or skin-sparing prophylactic mastectomy to investigate whether the type of mastectomy has influence on cancer-related distress, anxiety, or depression. (Nipple-sparing mastectomy is the procedure to remove the breast tissue, while most of the breast skin and the nipple areolar complex are left intact. During the skin-sparing mastectomy, most of the skin is also preserved, but the nipple areolar complex is removed along with the breast.) 50 months after the surgery, no statistically significant differences were observed between the two groups. Of note, women with lower cancer distress reported better body image [62] and higher satisfaction with a reconstruction [97].

3.2. Satisfaction and health-related quality of life

It is suggested that all aspects of HRQoL might be negatively impacted by chronic pain [98]. Several studies show that in breast cancer patients who had undergone mastectomy with reconstruction, persistent pain commonly occurs following the procedures [99–102]. However, when it comes to pain following prophylactic breast surgery, little is known. Spindler et al. [103] analyzed PROs in women who had undergone BPM with immediate reconstruction using breast implant (i.e., silicone shell filled with saline or silicone gel). The outcomes were compared to reference values of the general female population; 2 years after the surgery, women with BPM and reconstruction reported significantly higher body pain compared to values of the reference population. Accordingly, Gahm et al. [95] analyzed PROs in a cohort of 55 women, who also opted for BPM and immediate implant reconstruction. 2 years after the surgery, 87 % of the women reported pain or discomfort in the breasts. Conversely, no significant differences were identified in physical functioning, physical role functioning, general health perception, vitality, social role functioning, emotional role functioning, and mental health between women with BPM followed by reconstruction and the reference population [95,103].

Postoperative satisfaction depends on the healthcare conditions as well as on patient's personal situation and expectations [104]. Metcalfe et al. [97] analyzed a cohort of 37 women who opted for BPM and

Table 2
List of PRO instruments used in the analyzed studies and summary about the outcomes of the studies.

Authors	Title	Instruments	Summary
Gahm J, Wickman M, Brandberg Y	Bilateral prophylactic mastectomy in women with inherited risk of breast cancer - prevalence of pain and discomfort, impact on sexuality, quality of life, and feelings of regret two years after surgery	SF-36 + study-specific	BPM and immediate implant reconstruction was associated with pain, discomfort, and decrease in sexual well-being. General HRQoL was not affected and feelings of regret were almost non-existent.
Gopie JP, Mureau MAM, Seynaeve C, Ter Kuile MM, Menke-Pluymers MBE, Timman R, Tibben A	Body image issues after bilateral prophylactic mastectomy with breast reconstruction in healthy women at risk for hereditary breast cancer	The Dutch Relationship Questionnaire + SF-36 + IES + study-specific	In women with BPM and immediate implant reconstruction, body image decreased, whereas cancer-related distress was improved postoperatively.
McCarthy CM, Hamill JB, Kim HM, Qi J, Wilkins E, Pusic AL	Impact of Bilateral Prophylactic Mastectomy and Immediate Reconstruction on Health-Related Quality of Life in Women at High Risk for Breast Carcinoma: Results of the Mastectomy Reconstruction Consortium Study	Numerical Pain Rating Scale (NPRS) + SF-MPQ + GAD-7 + PHQ-9 + PROMIS-29 + BREAST-Q	In women with BPM and immediate implant reconstruction, satisfaction with breasts and psychosocial well-being improved and anxiety was reduced postoperatively.
Metcalf KA, Cil TD, Semple JL, Li LDX, Bagher S, Zhong T, Virani S, Narod S, Pal T	Long-Term Psychosocial Functioning in Women with Bilateral Prophylactic Mastectomy: Does Preservation of the Nipple-Areolar Complex Make a Difference?	IES + HAD + The Decision Regret Scale + SWD + BREAST-Q + study specific	Nipple-sparing mastectomy provided better body image and sexual well-being than skin-sparing mastectomy whereas it didn't increase cancer-related distress.
Gahm J, Edsander-Nord Å, Jurell G, Wickman M	No Differences in Aesthetic Outcome or Patient Satisfaction between Anatomically Shaped and Round Expandable Implants in Bilateral Breast Reconstructions: A Randomized Study	study-specific	No difference in satisfaction was observed between women with BPM and reconstruction with anatomical versus round implants.
Miseré RML, Joosen MEM, Claassens EL, de Grzymala AAP, Heuts EM, van der Hulst RRRWJ	Patient-reported outcomes following bilateral prophylactic mastectomy and immediate breast reconstruction: comparing implant-based with autologous breast reconstruction	SF-36 + BODY-Q + BREAST-Q + study specific	Women with BPM and autologous reconstruction reported higher satisfaction with breasts and better physical well-being than women with BPM and implant reconstruction.
Maruccia M, Elia R, Tedeschi P,	Prepectoral breast reconstruction: an	BREAST-Q	BPM with implant reconstruction and

Table 2 (continued)

Authors	Title	Instruments	Summary
Gurrado A, Moschetta M, Testini M, Giudice G	ideal approach to bilateral risk-reducing mastectomy		ADM was associated with postoperative increase in satisfaction with breasts, psychosocial well-being, physical well-being, and sexual well-being.
Salibian AA, Bekisz JM, Frey JD, Miller B, Choi M, Karp NS	Prophylactic nipple-sparing mastectomy in young previvors: Examining decision-making, reconstructive outcomes, and patient satisfaction in BRCA + patients under 30	BREAST-Q + study-specific	BPM with immediate implant or autologous reconstruction was associated with high patient satisfaction and well-being.
Brandberg Y, Sandelin K, Erikson S, Jurell Gr, Liljegren A, Lindblom A, Lindén A, Wachenfeldt A, Wickman M, Arver B	Psychological Reactions, Quality of Life, and Body Image After Bilateral Prophylactic Mastectomy in Women At High Risk for Breast Cancer: A Prospective 1-Year Follow-Up Study	SAQ + BIS + HAD + SF-36 + study-specific	BPM with implant reconstruction had no negative effect on depression and HRQoL. Anxiety improved. Contrary, sexual well-being and body image decreased.
Spindler N, Ebel F, Briest S, Wallochny S, Langer S	Quality of Life After Bilateral Risk-Reducing Mastectomy and Simultaneous Reconstruction Using Pre-Pectoral Silicone Implants	SF-36 + BREAST-Q	BMP with implant reconstruction was associated with postoperative decrease in physical well-being of the chest and improvement in satisfaction with breasts.
Metcalf KA, Semple JL, Narod SA	Satisfaction with breast reconstruction in women with bilateral prophylactic mastectomy: a descriptive study.	study-specific	Majority of women with BPM and immediate implant or autologous reconstruction were satisfied with outcomes. Complications were associated with lower satisfaction.
O'Connell RL, Tasoulis MK, Hristova E, Teoh V, Agusti A, Ward A, Montgomery C, Mohammed K, Self J, Rusby JE, Gui G	Satisfaction with Long-Term Aesthetic and 10 Years Oncologic Outcome following Risk-Reducing Mastectomy and Implant-Based Breast Reconstruction with or without Nipple Preservation	study-specific	Women with nipple-sparing mastectomy reported higher satisfaction with the nipples, whereas women with skin-sparing mastectomy were more satisfied with nipple position.

immediate implant or autologous reconstruction (i.e., using patient's own skin, fat, and sometimes muscle tissues from other parts of the body to restore breast form and shape). Within this cohort, women had undergone autologous reconstruction using transverse rectus abdominis musculocutaneous flap. Questionnaire focusing on satisfaction with reconstruction cosmetic outcome was administered at a mean time of 54 months after the surgery; the majority of women reported being satisfied or extremely satisfied. Expectably, women who reported an improved

body image after reconstruction were significantly more likely to report higher levels of satisfaction than those who reported diminished body image.

3.3. Preoperative versus postoperative outcomes

When comparing preoperative expectations with postoperative reactions in women who had undergone BPM with reconstruction, no differences in proportions of positive/negative expectations versus positive/negative reactions were found. Moreover, no significant difference in general HRQoL pre- versus postoperatively was reported [94].

Studies investigating differences in satisfaction with the breast and psychological well-being pre- versus postoperatively have shown ambiguous results; Spindler et al. didn't show any significant difference pre- versus postoperatively [103], whereas McCarthy et al. claimed that satisfaction with the breast and psychological well-being improved significantly after the surgery [93]. Nevertheless, none of the studies demonstrated a decrease in the latter characteristics.

With regards to physical feeling, decrease in physical well-being of the chest was observed: McCarthy et al. analyzed PROs in a cohort of 204 women who had undergone BPM with immediate implant or autologous reconstruction, showing significant decrease in well-being of the chest 1 and 2 years postoperatively [93]. Gopie et al. [62] analyzed a cohort of 48 women undergoing BPM with immediate breast reconstruction; 39 women opted for implant reconstruction and 9 women opted for autologous reconstruction using deep inferior epigastric artery perforator flap. 21 months after the surgery, more than one third of the women claimed their breasts felt unpleasantly. Additionally, women reported significant decrease in body image in terms of satisfaction with their breast appearance and feeling embarrassed for their naked body.

Overall partner relationship satisfaction did not change over time [62]. Besides that, Brandberg et al. collected PROs from 90 women undergoing BPM with implant reconstruction before, 6 months after, and 12 months after the surgery; no significant differences for the three assessment points were reported in frequencies of sexual activity pre- versus postoperatively [94]. Accordingly, other authors demonstrated there were no differences in sexual well-being postoperatively compared to preoperative state [93,103].

Furthermore, Brandberg et al. suggest there is no difference in sexual discomfort postoperatively compared to preoperative state; contrarily, women reported significant decrease in pleasure 1 year after the surgery [94]. Besides that, sexual relationship satisfaction decreased 21 months after the reconstruction compared to baseline [62]. Gahm et al. [95] suggest that in the women who had undergone BPM with immediate implant reconstruction, lost or much reduced sexual sensations were reported by 85 % of women and enjoyment of sex was negatively impacted for 75 % of women 2 years after the surgery.

3.4. Skin-sparing versus nipple-sparing mastectomy

Nipple-sparing mastectomy provides cosmetic results superior to skin-sparing mastectomy [42]. In prophylactic breast surgery, conservation of the nipple areolar complex is generally considered to be safe and oncologically effective [105]. However, long term follow-up data are required to confirm oncological safety in the long-term [106,107]. Taken together, decision-making about the type of prophylactic breast surgery should involve a tradeoff between potential oncological benefit and resulting HRQoL [42]. That said, knowledge of PROs after skin-sparing mastectomy versus nipple-sparing mastectomy is particularly important [108].

Women who had undergone nipple-sparing mastectomy reported similar satisfaction with decision and decision regret regarding mastectomy compared to women who had undergone skin-sparing mastectomy [96]. Furthermore, O'Connell et al. [109] studied a group of 93 women who had undergone skin-sparing or nipple-sparing mastectomy, demonstrating there was no difference in terms of satisfaction with the

decision regarding nipple preservation in a long-term follow-up (median 98.4 months). Besides that, overall satisfaction with nipples was same in both groups [109]. Predictably, women with nipple-sparing mastectomy were generally less satisfied with a position of the nipple than women with skin-sparing mastectomy [109,110].

Nevertheless, with regards to satisfaction with breasts and satisfaction with outcome, Metcalfe et al. [96] showed significantly higher scores in women who had undergone nipple-sparing mastectomy compared to those with skin-sparing mastectomy. In accordance with that, Salibian et al. studied a cohort of 22 women who had undergone nipple-sparing mastectomy followed by reconstruction; 6 months after reconstruction, women reported high levels of satisfaction with breasts and well-being [111]. Women with nipple-sparing mastectomy also reported significantly higher mean scores for sexual well-being compared to those with skin-sparing mastectomy [96]. In contrast, Van Verschuer [110] compared patient-reported health data in 45 women who opted for either skin sparing mastectomy or nipple sparing mastectomy with immediate implant reconstruction, showing no differences in post-operative body image, satisfaction with breasts, satisfaction with outcome, or sexual well-being. It should be noted, however, that the median follow-up in the skin-sparing mastectomy group was more than twice longer compared to nipple-sparing mastectomy group in this study.

3.5. Type of reconstruction

In patients who had undergone breast reconstruction following mastectomy for breast cancer, autologous reconstruction is linked to significantly better overall satisfaction with outcome as well as satisfaction with the breast than implant reconstruction [112]. In the context of prophylactic breast surgery, Miseré et al. [113] compared PROs in women who had undergone immediate implant reconstruction versus autologous reconstruction following BPM. The study showed similar trend: women with autologous reconstruction reported significantly higher satisfaction with breasts and physical well-being compared to women with implant reconstruction. With regards to implant shape, Gahm et al. [114] analyzed a cohort of 36 women who had undergone BPM and immediate reconstruction with anatomically shaped versus round permanent expander implants. 30 months after the surgery, no differences were found between the two groups in the satisfaction with outcome, satisfaction with appearance in clothes, underwear, nudity, and difficulty finding a well-fitting bra. Maruccia et al. [115] investigated satisfaction and HRQoL in women who had undergone BPM followed by prepectoral reconstruction with implant completely covered by acellular dermal matrix. Overall satisfaction with breasts, psychosocial, physical, and sexual well-being all significantly increased 1 year postoperatively compared to preoperative state. Generally, women experiencing complications following BPM were significantly less satisfied with reconstruction outcomes than those who didn't experience any complications [97].

3.6. Summary of current knowledge

So far, only a few studies have focused on PROs in women with BPM followed by reconstruction. In sum, the studies demonstrated that BPM was linked with significant decrease of women's cancer-related anxiety levels; furthermore, the anxiety decrease was reported by both women with skin-sparing mastectomy as well as women with nipple-sparing mastectomy. Besides that, satisfaction with the breast and psychological well-being increased postoperatively. Conversely, although women with bilateral prophylactic surgery reported similar levels of physical functioning or general health perception to the reference population, they experienced higher pain in a long-term follow-up. Also, when it comes to comparison of pre- versus postoperative outcomes, they reported a decrease in physical well-being of the chest and decrease in pleasure, sensations, and sexual relationship satisfaction. When it comes

to the type of surgery, women with nipple-sparing mastectomy and skin-sparing mastectomy reported the same overall satisfaction with nipples. However, preservation of nipples resulted in higher satisfaction with breasts, satisfaction with outcome, and sexual well-being. Women with autologous reconstruction reported higher satisfaction and HRQoL compared to women with implant reconstruction. Generally, an important factor influencing satisfaction with a reconstruction was a level of cancer distress.

3.7. Patient samples - breast cancer history

That said, it should be emphasized that PROs in women, who were never diagnosed with cancer, are assumed to differ from PROs in those, who in the past experienced breast cancer diagnosis and oncological treatment [116,117]. It implies that within bilateral prophylactic breast surgery, PROs might differ between high-risk women without breast cancer history and women, who in the past experienced breast cancer with oncologic treatment such as lumpectomy and radiation. Nevertheless, not all of the reviewed studies employed history of breast cancer as an exclusion criterion; some authors indicated in the Methods parts, that included women had no history of breast cancer [62,94–96,109,114,115], whereas others not [93,97,103,113]. Van Verschuer included high-risk women without breast cancer experience as well as women with a history or current diagnosis of breast cancer [110]. Salibian et al. [111] indicate in the title that the study was conducted in previvors, whereby *previvor* is defined as someone, who is not yet sick, but who has a genetic predisposition to disease [118]. Although the title suggests that the women with a history of breast cancer were excluded from the study, Methods part doesn't indicate so.

3.8. Patient samples – histopathological examination

Besides that, Gandhi et al. [119] analyzed PROs in a large cohort of women who had undergone BPM followed by reconstruction and related them to results of histopathological examinations of the prophylactic mastectomy specimens. They demonstrated that women with benign findings reported e.g., higher satisfaction with breasts and higher scores for sexual well-being compared to the women whose histopathological examination revealed breast cancer. That implies that PROs differ between women at high risk who underwent purely prophylactic surgery and those who had a therapeutic component in their BPM. For example, O'Connell et al. excluded the women whose postoperative histopathology incidentally revealed breast cancer [109]. Similarly, Maruccia et al. [115] didn't include the women who were found to have cancer at the time of the surgery. However, it is commonly unclear if the PRO studies on prophylactic breast surgery consider breast cancer status of the women. For example, Spindler et al. [103] didn't include "patients with current cancer and/or on cancer therapy". That leaves it up to the reader to interpret, whether the women whose postoperative histopathology revealed breast cancer were additionally excluded or not. Gahm et al. [114] excluded patients who had undergone implant exchange during the follow-up period; nevertheless, histopathological examination revealing breast cancer was not an exclusion criterion from the study.

4. Limitations of this study

Summarized, some of the studies on PROs in women with BPM and reconstruction analyze heterogeneous patient samples with regards to the breast cancer history or histopathological status of prophylactic mastectomy specimens. That might preclude drawing unequivocal conclusions from those studies. Accordingly, it might also be a limitation of this review.

5. Conclusions

Hereditary breast cancer and its prevention strategies have recently

gained remarkable attention. BPM significantly reduces the risk of developing the cancer, whereas the reconstruction maintains HRQoL. However, surgeries are not without complications; women considering prophylactic breast surgery should be informed about the risk of complications as well as about possible changes in HRQoL resulting from the procedures [19]. Given the recent increase in the number of performed bilateral prophylactic surgeries, there is a strong need for appropriate patient-reported health data.

Whereas multiple studies have analyzed PROs in prophylactic breast surgery, there are limitations when it comes to study design; study cohorts often consist of both women with bilateral as well as contralateral mastectomy, or women with and without reconstruction, although PROs among these groups differ. Furthermore, the studies which focus solely on women with BPM followed by reconstruction often don't consider breast cancer status of the women, which might also impact patient-reported health data.

To organize and deepen understanding of PROs in prophylactic breast surgery, it would be of paramount importance to determine laterality of mastectomy and whether the reconstruction followed. Besides that, future studies should consider the oncological history of the women undergoing the surgery, and if the surgery is purely prophylactic or if it has a therapeutic component. Taken together, we believe that findings of this review provide useful recommendations and justification for further research in this field.

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Ethical approval

Approval was not required.

Declaration of competing interest

None.

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