Patient Preference and Adherence

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REVIEW

Understanding Patient Preferences Regarding the Important Determinants of Breast Cancer Treatment: A Narrative Scoping Review

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Objective: Conventionally, optimal treatment strategies for breast cancer have been largely determined by physicians, with a scant understanding of patients' treatment values and preferences. Incorporating patient preferences in the decision-making process for breast cancer treatment is gaining recognition and can potentially improve treatment outcomes and compliance. This scoping review aims to synthesize evidence on the key determinants that are most valued by breast cancer patients when deciding on their treatment options.

Methods: We searched three electronic databases (PubMed/MEDLINE, SCOPUS, and CINAHL Plus) utilizing a systematic scoping review method. Two reviewers independently screened, applied inclusion criteria, reviewed, and synthesized findings. A mixed-method narrative approach combining the inductive thematic analysis and content analysis methodologies was used to synthesize and summarize the findings.

Results: The review included 22 studies, leading to the conceptualization of 5 overarching themes and 17 sub-themes. Among these, the most frequently cited theme was treatment benefits, followed by treatment-related process, treatment-related risk, quality of life, and cost of treatment. Women with breast cancer highly value treatments that offer good effectiveness, prolong survival, prevent recurrence, and maintain quality of life. Patient concerns include treatment-related side effects, safety, the risk of secondary cancer, and direct or indirect out-of-pocket costs. Additionally, patients also consider treatment duration, mode of administration, physician recommendation, and treatment availability and accessibility when deciding on their preferred treatment.

Conclusion: The evidence synthesized in this review offers insights into refining breast cancer treatment strategies to align more closely with patient values. Recognizing and integrating patient perspectives in breast cancer care could potentially lead to improved treatment outcomes, enhanced patient compliance, and more personalized care. Healthcare professionals are encouraged to incorporate these key determinants in their treatment decision-making processes, aiming to deliver a patient-centered care that aligns with the unique preferences and values of each patient.

Plain Language Summary: Breast cancer is a significant health concern, and treatment decisions have traditionally driven by physicians, often without due consideration for patients' preferences in their treatment choices. This scoping review aimed to explore and summarize what matters most to breast cancer patients when deciding on their treatment options. We found five main themes that were important to patients:

(1) Effectiveness: Patients highly value treatments that are effective in fighting cancer, prolonging survival, and preventing recurrence.
(2) Treatment-related process: The length of treatment and availability of different therapies influenced patients' choices. Patients trust their doctors' expertise but also value being involved in the decision-making process to have their preferences considered.
(3) Side Effects and Safety: Concerns about treatment-related side effects and the risk of secondary cancer were critical factors in decision-making.
(4) Quality of Life: Maintaining a good quality of life during treatment is crucial for patients.
(5) Financial Burden: The additional direct and indirect out-of-pocket costs of treatment were important considerations for patients.

Understanding patients' preferences is vital in developing personalized treatments that align with their values. Healthcare professionals need to communicate effectively with patients and involve them in the decision-making process. Patient decision aids and

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tailored financial assistance programs could also be helpful. Further research is needed to identify effective strategies to tailor treatments to meet patients' preferences. Overall, this review sheds light on what matters most to breast cancer patients, empowering them to be more active participants in their treatment decisions and potentially improving treatment outcomes and overall well-being.

Keywords: breast cancer, patient preference, treatment decision making, narrative scoping review

Introduction

Breast cancer (BC) is the most common cancer in women and the fifth leading cause of cancer-related deaths worldwide.[1] According to projections, the incidence of BC is expected to increase significantly in the future, with estimates suggesting that by the year 2070, the annual number of diagnosed cases will surpass four million worldwide, representing a doubling of current rates.[2]

The prognosis for women with early-stage BC (eBC) is generally positive, whereas those with advanced or metastatic BC (mBC) have a low 5-year survival rate of approximately 20%.[3] The primary treatment objectives for eBC involve the surgical removal of the tumour from the breast and regional lymph nodes, preventing locoregional recurrence, and improving survival.[4] In addition, systemic therapy may be administered before surgery (neoadjuvant), after surgery (adjuvant), or both, depending on the subtype of BC and the extent of local disease at diagnosis. On the other hand, the primary aims of therapy for mBC are to control the growth of the tumour thereby extending life expectancy and alleviating symptoms for a better quality of life, as mBC is incurable. The current systemic therapy landscape for mBC includes chemotherapy, endocrine therapy, immunotherapy, and targeted therapy.[5] Different treatments pose different benefits and drawbacks. Whilst the majority of treatments contribute to an increase in survival rates, they may also bring unwanted adverse effects for patients, which potentially diminish their overall quality of life. Acute adverse effects may manifest in the form of fatigue, alopecia, cytopenia, myalgia and arthralgia, and chemotherapy-induced peripheral neuropathy. Long-term complications may include heart disease, premature menopause, and psychological effects.[6]

Traditionally, the decision-making process for BC treatment has been predominantly driven by physicians, guided by the treatment guidelines, such as the European Society for Medical Oncology (ESMO) BC Guidelines[7] and National Comprehensive Cancer Network (NCCN) Guidelines in Breast Cancer,[8] and little is known about patient's preference for treatment. The preference for characteristics of different therapy choices is subjective and dependent on a variety of cultural and individual factors, and the preferences of patients and healthcare providers regarding the treatment of various diseases, including cancer, have been shown to vary.[9] Given the significant variation in the prognosis of distinct stages of BC, there is substantial potential for patient preferences to be incorporated into the decision-making process. Over recent years, the role of patient preference and value has gained growing recognition in individual clinical decision-making and the shaping of public health policy. Patient preference, which reflects their perceptions of risk and general comfort with the various approaches, is an important determinant of treatment selection.[10] There has been increasing interest in the integration of patient values and perspectives in the development of treatment recommendations and patient decision aid in clinical practice. For instance, the ESMO guidelines strongly recommend that healthcare providers actively involve patients in all treatment decision-making,[11,12] while patient decision aids have demonstrated their value in facilitating shared decision-making between healthcare providers and patients when deciding on treatment options.[13,14]

Prior systematic review studies in the context of BC treatment from the patient's perspective have placed a greater emphasis on the type of care, the satisfaction of the healthcare system, post-cancer treatment care, patient-reported outcome measures, and management of treatment-related side effects rather than on values and perceptions of the attributes that may influence treatment preferences.[15–19] Therefore, the primary objective of this scoping review is to explore and synthesize evidence regarding the important determinants in BC treatment that are most valued and preferred by patients.

Materials and Methods

We conducted a scoping review to assess and consolidate the evidence concerning important determinants in the treatment of BC that matter to patients, guided by the six-step theoretical frameworks developed by Arksey and O'Malley[20] along with the refinements proposed by Levac et al.[21] Due to the considerable heterogeneity in the existing literature on this subject, conventional data synthesis methods like systematic reviews or meta-analyses would not have been suitable approaches. Scoping reviews, on the other hand, facilitate the mapping and synthesis of evidence across a wide range of related literature, which aids in addressing broad research questions and enhancing a deeper understanding of the subject.[22,23]

A research team of five members collaboratively established a research protocol and agreed upon the scope of the review, including the research questions, search strategy, and methodology to be used to conduct the review. The PIOS (population, intervention, outcome, and study type) format was employed to define the research question and the inclusion and exclusion criteria (Table 1). Studies were eligible for inclusion, regardless of methodology, if they empirically determined the attributes or factors associated with the treatment preference of BC patients. To ensure our review encompassed the most up-to-date evidence on significant determinants that matter to patients in the current rapid evolving landscape of BC treatment, we restricted the search period to span from January 2010 to June 2023. The full search strategy in this study was documented according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[24]

Search Strategy

In line with rapid review recommendations,[25] we limited our searches to three databases: PubMed/MEDLINE, SCOPUS, and CINAHL Plus. A broad search of keywords (titles, abstracts, and subject headings) was conducted to identify relevant studies that combined terms for "breast cancer", "treatment", and "patient preference", adapted to each interface and database. The Medical Subject Headings (MeSH) terms and explosions were applied across the terms where applicable. The detailed search strategy is described in Supplementary Table 1: Search Strategy.

Article Screening and Data Extraction

All search tasks were completed by a single researcher (HYY) in July 2023 and all returned articles were entered into EndNote^{TM} X9 for screening and data extraction, and duplicates were removed. Two reviewers independently screened the titles and abstracts according to the inclusion and exclusion criteria (HYY and SJC), and full-text articles were retrieved if all inclusion criterion was met. The full-text articles were then independently reviewed and synthesized by two reviewers (HYY and ACL). One reviewer (ACL) extracted the data from the included articles into a pre-defined and piloted data extraction table, while a second reviewer (HYY) cross-checked them for consistency and reliability. Disagreements in data extraction and interpretation were resolved through team discussion with a third reviewer (CM). The information included in the data extraction tables (Microsoft Excel spreadsheet, Microsoft Corporation, Redmond, Washington) were the following: first author; year of publication; country(s); study objective (s); method/ design; sample size; cancer stage; treatment type; outcomes; plausible attributes/levels; and strength/limitation.

Table 1 The PIOS and Inclusion and Exclusion Criteria of the Review

Elements	Inclusion Criteria	Exclusion Criteria
Population (P)	The population of the studies was people with a primary diagnosis of breast cancer. The gender, age, and clinical stage are not restricted.	Studies not reporting exclusively from the patient's perspectives (eg, the perspective of physicians or caregivers).
Intervention (I)	Treatment for breast cancer (eg, surgery, radiotherapy, hormone therapy, chemotherapy, targeted therapy, immunotherapy, or neoadjuvant therapy).	Studies not reporting on non-pharmacologic breast cancer intervention (eg, breast reconstruction, cancer screening, biopsy for cancer diagnosis, physical exercise, complementary and alternative medicines, etc.).
Outcome (O)	Any preference for attributes/features of breast cancer treatment derived from the patient's perspective.	Studies not reporting patients' preferences on attributes of breast cancer treatment.
Study type (S)	Original research using any research methodology; published in peer-reviewed journals between January 2010 and June 2023; available in English full text only.	Abstracts, systematic reviews/scoping reviews/any review studies; protocols, editorials, commentaries, errata, and features; grey literature; studies published before January 2010 and after June 2023; not available in English full text.

Additionally, to provide more breadth to the analysis, findings from qualitative studies in the form of textual data were extracted, which included either a verbatim quote from patients or statements by the authors that were corroborated by patient-reported data.

Data Analysis

To provide a more comprehensive and nuanced understanding of the research questions, we utilized a mixed-method narrative approach to synthesize and summarize findings in this review, integrating the inductive thematic analysis and content analysis methodologies.[26–28] Our analysis followed an inductive approach, meaning that we did not predefine themes or codes to guide data extraction and analysis. Instead, themes were developed using a "constant comparison" method, wherein the data was broken down into discrete "events", and related events' were coded into descriptive themes. Key themes that emerged from the studies that correspond to our research objectives were systematically identified by two reviewers (HYY and ACL). First, HYY coded findings from both qualitative and quantitative studies, followed by analysing patterns in the textual data to generate a preliminary thematic layout. Then, ACL reviewed the preliminary thematic layout and refined the themes through a series of discussions with HYY until a consensus was reached. Disagreements in data analysis were resolved through team discussion with a third researcher (CM). A minimum of three papers' worth of pooled data had to be coded to the same theme for a distinct theme to emerge. The final thematic layout was collectively described as a team with a consensus reached. In addition, the frequency of themes and sub-themes mentioned in the included papers was counted and summarized in a table.

Results

A total of 1984 studies were retrieved electronically after removing duplicates. After titles and/or abstract screening, 1892 studies that did not meet the inclusion criteria were excluded. The full text of the remaining 92 studies was reviewed, and 70 studies that did not meet the inclusion criteria were excluded. Ultimately, 22 studies that met our eligibility criteria were included (Figure 1).

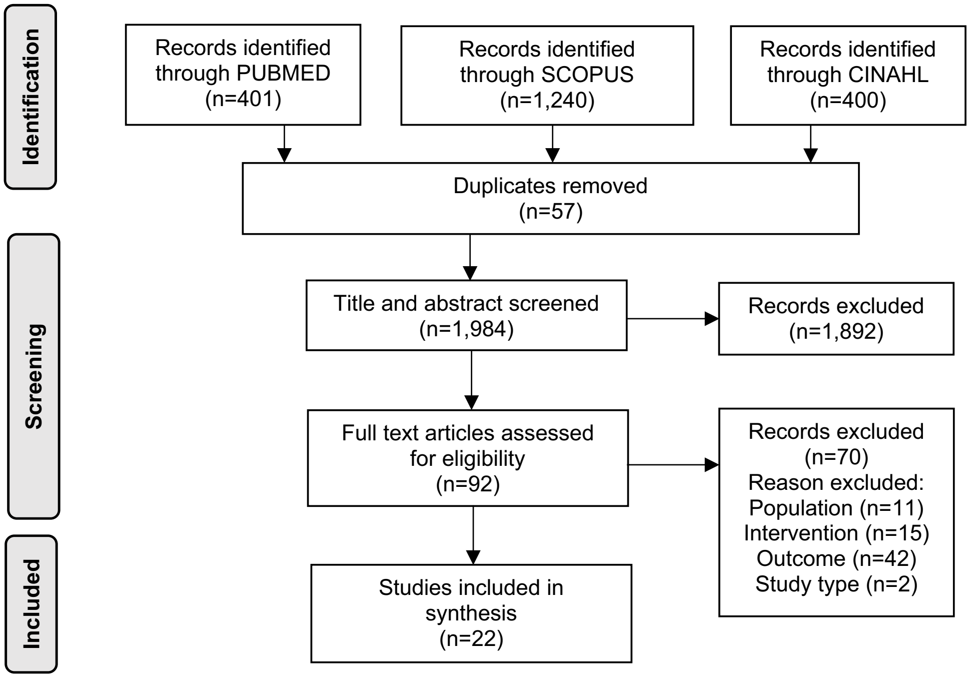

Figure 1 PRISMA study flow diagram.

Note: Adapted from Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group* t. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Annals of internal medicine. 2009;151(4):264-269.24.[24]

Characteristics of the Included Studies

A total of 7 studies with a qualitative methodology[13,29–34] and 15 studies with a quantitative methodology[35–49] were included. The total number of participants in these studies was 3817. The published studies included articles from the United States of America (USA) (n=4,), the Netherlands (n=4), Canada (n=4), United Kingdom (UK) (n=2), Spain (n=2), European countries (n=2), France (n=1), Japan (n=1), Korea (n=1), Germany (n=1), and Australia (n=1). A total of 9 studies reported on population with eBC, 7 studies on mBC, 2 studies on BC of all stages, and 4 studies did not specifically report on the cancer status. Out of the seven qualitative studies conducted, five of them employed individual interviews as the primary method to gather data. One of the studies opted for a focus group discussion, while the remaining study utilized a combination of both individual interviews and focus group discussions. For the quantitative studies included in this review, ten of them relied on surveys as the primary method for data collection, which were conducted either through paper-based, online, or phone-based approaches. Additionally, two studies utilized the conjoint analysis survey method, one employed the discrete choice experiment method, another used the time trade-off method, and one more used the contingent valuation method. The included studies are summarised in Table 2.

Important Determinants in Breast Cancer Treatment That Patient Values

Five broad themes were conceptualized from the important determinants in BC treatment, characterized by 17 sub-themes (Table 3). A narrative summary of themes and sub-themes is illustrated below.

Treatment Benefits

Prolong Survival or Life Expectancy

The vast majority of patients diagnosed with BC, regardless of the stage of the disease, expressed a strong preference for survival benefits compared to other benefits in treatment decision-making.[30,31,39–44,47,48] Women with eBC tend to opt for mastectomy over breast-conserving surgery (BCS) as a means to increase their chance of survival so that they could spend more time with their families, particularly those with young children.[30] Furthermore, the decision to undergo chemotherapy was often related to the patient's desire to be cancer-free, fear of cancer recurrence, and the desire to extend life expectancy.[31] Patients with eBC tend to judge small to moderate benefits, in terms of increase in survival rates, as sufficient to consider systemic therapy worthwhile. In contrast, Hamelinck et al reported that approximately one-fifth of women from the study would refuse hormonal therapy even with an absolute survival benefit of 25%.[40,41] The individual patient's attitudes towards the benefits and risks of treatment might vary considerably, with some patients willing to accept treatment for little or no benefit, while others would refuse treatment regardless of the potential benefit.[48] On the other hand, Harding et al documented that patients with mBC were more willing to trade off the treatment side effects for a longer life expectancy. Nevertheless, it is worth highlighting that while most patients in the study reported by Harding et al prefer a treatment that can prolong their survival, a minority expressed their desire to live out their time without any medical intervention.[42]

Treatment Efficacy

Patients with a cancer remission treatment goal prioritized treatment efficacy over other factors.[32] However, older women exhibited heightened concerns over the efficacy and likelihood of cures following surgical or hormonal therapy interventions.[35] Furthermore, the efficacy of different treatment options for mBC was a prominent concern for patients, with treatment efficacy being rated as the most important attribute, surpassing other attributes related to side effects by almost threefold. Women with mBC revealed a preference towards a treatment that can effectively control the growth of the tumour.[39] Similarly, two separate studies have reported a consistent patient preference for a treatment that would effectively reduce the growth of the tumour.[30,47] Patients expressed a strong desire to expedite the removal of the tumour, as evidenced by the quote "I just want to get this out of me as soon as possible."[30] Chemotherapy was preferred over hormonal therapy as patients perceived it to have superior efficacy.[41] This is supported by evidence from a conjoint analysis study which also identified treatment efficacy as the most important attribute.[49]

Table 2 Summary of Included Studies by Study Design

First Author (Year), Country	**Study Objective**	**Methods, Sample Size, Cancer Stage, Treatment Type**	**Key Outcomes, Plausible Attributes/Levels**	**Strength/Limitation**
Qualitative studies				
Ataseven (2020), Germany[29]	Evaluate the identification and severity of side effects perceived by ovarian cancer and BC patients undergoing contemporary anticancer therapy.	Prospective cohort interview. A structured on-site interview was performed 12±3 weeks after starting treatment. Patients were asked to select and rank, according to severity, 72 physical or nonphysical symptoms potentially related to their treatment. Sample: 98 chemo-naïve Caucasian female patients. Cancer stage: UICC stage I or II (90.8%); UICC stage III or IV (9.2%). Treatment(s): Chemotherapy (anthracyclines, taxanes, and carboplatin) and targeted therapy with antibodies (trastuzumab and pertuzumab). No endocrine therapy.	*We only report the subgroup analysis for the BC cohort.* Median age 53 (range: 23–80). Physical attributes for side effect overall ranking (Top 5): 1. Loss of hair 2. Difficulty sleeping 3. Lethargy 4. Shortness of breath 5. Hot flashes Non-physical attributes for side effect overall ranking (Top 4): 1. Affects my family or partner 2. Affects my social activities 3. Forgetfulness 4. Affects my work/home duties	Strength(s): - Sub-group analysis for BC patients was reported. - The participants were chemo-naïve BC patients without any other underlying diseases, thereby avoiding the effect of several underlying diseases and treatment options on the results as indicated for heterogeneous cohorts. Limitation(s): - Only the initial 9–15 weeks of anticancer treatment were considered and baseline levels of the 72 symptoms were not obtained.
Dicks (2019), Canada[30]	Explore factors influencing surgical treatment decisions.	Semi-structured interview guided by an interview guide. Individual interviews lasted about 40 minutes; FGD lasted about 60 minutes. Sample: 35 (29 FGD, 3 written responses through email, and 3 telephones) Cancer stage: Not mentioned. Treatment(s): Breast-conserving surgery or mastectomy.	Mean age 54 (range: 38–76). High interest in mastectomy and increasing requests for prophylactic contralateral mastectomy were evident. A host of factors influence women's surgical treatment preference, including the concern of body image, treatment duration, recurrence (second surgery), longer survival, cost (financial burden), and accessibility (distance to the clinic). Attributes (levels): 1. Survival 2. Treatment duration 3. Travel distance 4. Cost 5. Quality of life (body image/sexuality, fears/worries) 6. The risk of cancer recurrence 7. Avoidance additional surgery 8. Surgeon's recommendation	Strength(s): - Sub-group analysis for women with BC was reported. Limitation(s): - Selection bias: only a small number of participants had chosen breast-conserving surgery (26%). - Recollection and memory biases: most women had made their surgical decision at least 5 years before being interviewed

Harder (2013), United Kingdom[31]	Explore older patients' experiences, preferences, and putative barriers to chemotherapy.	A structured interview by using an interview guide with open-ended and closed, fixed-response questions. Sample: 58 women aged ≥70 years. Cancer stage: Newly diagnosed early-stage BC. Treatment(s): chemotherapy.	Median age 73 years (Range: 70–83). Half of the participants who decided to have chemotherapy reported that the fear of recurrence, trust in clinician recommendation, survival benefits, and motivation of family influenced decision making. Factors for declining chemotherapy include side effects, low survival benefits, treatment duration, trust in the clinical recommendation, and lack of social support. Attributes (levels): 1. Side effects 2. Cancer recurrence 3. Treatment duration 4. Survival benefits 5. Physician recommendation 6. Social and family support	Strength(s): - Explored the experiences of older women (>70) with early BC on chemotherapy. - Participants were interviewed shortly (within 3 weeks) after chemotherapy had been offered to reduce the time impact. Limitation(s): - Small sample size with predominantly white and well-educated participants. - Consisted largely of women who decided to receive chemotherapy, which may not be representative. - Decision-making preference was assessed retrospectively, and most participants had already made up their minds about further treatment at the time of the interview.
Lawhon (2020), USA[32]	Explore factors influencing treatment selection in older patients with early-stage BC.	Semi-structured individual interviews utilizing a phenomenological approach to understand the factors that influence treatment selection. Participants completed a short demographic questionnaire and the Control Preferences Scale (a validated 2-item tool, evaluating preferred and perceived roles in decision-making) before interviews. Sample: 33 women aged ≥65 years. Cancer stage: Early-stage BC. Treatment(s): Not mentioned.	52% of participants were of age ≥75 years. Interviews revealed three major selection domains (intrinsic and extrinsic influences, clinical characteristics, and patient values), presented as themes of varying importance to individual patients. Extrinsic influences attribute ranking: 1. Physician recommendations 2. Opinion of friends or family Patient values attributes ranking: 1. Physical side effects 2. Physical appearance 3. Efficacy 4. Treatment logistics 5. Impact on activities of daily living 6. Cost 7. Personal responsibility/recovery time 8. Emotional side effects 9. Eligibility for clinical trials or new drugs 10. Burden on caregivers	Strength(s): - Revealed the factors that influenced treatment decision preferences of older women with EBC. Limitation(s): - Participants were purposively recruited from one academic institution, which might not be representative of a population or other geographic regions. - Social desirability bias: the interview was conducted by a radiation oncologist. - Participants were recruited from the radiation clinic, thus women who ultimately decided against radiation therapy were not represented.

(Continued)

Table 2 (Continued).

First Author (Year), Country	Study Objective	Methods, Sample Size, Cancer Stage, Treatment Type	Key Outcomes, Plausible Attributes/Levels	Strength/Limitation
Pivot (2014), EU and Canada[33]	Examine patients' preferences for conventional IV or SC delivery for trastuzumab administration.	International, multi-center, open-label, randomized, two-cohort, two-arm, crossover study. Patients were randomized to receive 4 adjuvant cycles of SC trastuzumab every 3 weeks followed by 4 cycles of IV every 3 weeks or vice versa (the crossover period). Patients received SC trastuzumab via the SID in Cohort 1 and the hand-held syringe in Cohort 2. Following the crossover period, patients received IV trastuzumab in Cohort 1 (unless participating in SID self-administration) and SC trastuzumab via hand-held syringe in Cohort 2. Two telephone interviews were conducted: one before randomization and one after the crossover period. Sample: 467 (235 patients SC+IV and 232 IV+SC). Cancer stage: HER2-positive primary invasive breast adenocarcinoma. Treatment(s): Targeted therapy (trastuzumab).	The median age of 53 years (Range: 29–78). Overall, 88.9% of patients preferred SC, 9.6% preferred IV, and 1.5% had no preference. Results on the mode of administration preference were consistent in both study arms. The overall preference for SC was 'very strong' in 64.9% of patients, 'fairly strong' in 17.3%, and 'not very strong' in 6.6%. Reasons for SC preferences include timesaving, and less pain/ discomfort/ side effects. Overall, 60.4% of patients expressed a hypothetical preference to receive SC at home. Attributes (level): • Mode of treatment administration (IV, SC, ease of administration, convenience) • Treatment duration • Pain/ discomfort/ side effects (bruising, irritation at the injection site) • Psychological • Stress/ anxiety • Efficacy • Environment/ staff • Receive treatment at home • Ecological consideration	Strength(s): • A large multi-center, randomized study.

Raphael (2020), the Netherlands[13]	Explore patients' and health professionals' perspectives with regard to the most relevant attributes in decision making on radiotherapy for BC.	A qualitative semi-structured face-to-face individual interview guided by an interview guide. Sample:15 female BC patients. Cancer stage: Low or intermediate risk DCIS after BCS or mastectomy. Treatment(s): Radiotherapy.	*We only report the subgroup analysis for the BC cohort.* The mean age was 59 years (range 38–79 years). Eight patients received radiotherapy. Attributes (levels): ● Skin toxicity (skin open, skin burns, redness) ● Fatigue/tiredness ● Oedema ● Pain (sensitivity of the breast, permanent burning sensation) ● Change in breast shape/fibrosis (malformation, deformation, scarring) ● Consequences for reconstruction (side effects affecting the ribs) ● Heart toxicity ● Increased risk for lung cancer ● Reduced arm mobility ● Treatment burden (number of times to go to hospital, radiotherapy duration, travel time)	Limitation(s): ● Selection bias: No patients were included from remote areas. ● Recall bias.
Smith (2018), Australia[34]	Investigate the patient experience of madarosis caused by treatment for BC.	Five semi-structured FGDs were conducted (mean duration 57 mins) using open-ended questions and more specific probes to discuss the impact of chemotherapy-induced madarosis on physical function, emotional well-being, and social function. The transcribed data were subjected to thematic analysis using a constant comparative methodology. Sample: 25 women with varying degrees of madarosis past 6 months following completion of treatment. Cancer stage: Invasive early BC. Treatment(s): Chemotherapy (taxane-based).	The median age of 50 years (Range: 35–64). Mean 25 months prior (range 1–89). Each of the women involved in the focus group reported partial to complete madarosis. Attributes (levels): ● Side effect: madarosis (timing of loss, regrowth, and permanent changes, physiological side effects, management of madarosis)	Strength(s): ● The interviews facilitated patient interaction and discussion around common experiences. Limitation(s): ● Recruitment bias: women were elected to participate and therefore may reflect more proactive patients. In addition, patients were recruited from a single center in a predominantly white, high socio-economic area. ● Participants with permanent hypotrichosis were not identified, and separate analysis was not attempted on this group.

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Table 2 (Continued).

First Author (Year), Country	**Study Objective**	**Methods, Sample Size, Cancer Stage, Treatment Type**	**Key Outcomes, Plausible Attributes/Levels**	**Strength/Limitation**
First Author (Year), Country **Quantitative studies**	Study Objective	Methods, Sample Size, Cancer Stage, Treatment Type	Outcomes, Plausible Attributes/Levels	Strength/Limitation
Burton (2017), United Kingdom[35]	Establish older women's information needs and decision-making preferences regarding surgery plus adjuvant endocrine therapy or primary endocrine therapy.	A retrospective, cross-sectional, survey of women aged ≥75 years. Sample: 101 women aged ≥75 years who were diagnosed with BC within the previous 5 years and had been offered a choice between primary endocrine therapy and surgery at diagnosis. Cancer stage: Early BC. Treatment(s): Primary endocrine therapy or surgery plus adjuvant endocrine therapy.	The median age was 82 years (Range: 75–99), with 58 having had surgery plus adjuvant endocrine therapy and 37 having primary endocrine therapy. Practical details about the impact, safety, and efficacy of treatment were of most interest to participants. Of least interest were cosmetic outcomes after surgery. Attributes (level) for surgery + adjuvant endocrine therapy ranking: 1. Length of hospital stay 2. Whole breast or only lump being removed 3. Safety 4. Side effects/ complications 5. Support/ care after surgery 6. Likelihood of cure 7. Level of independence after surgery Attributes (level) for primary endocrine therapy ranking: 1. Length of treatment 2. The need for further treatment 3. Side effects 4. Chance of cancer recurrence 5. Ways to take the tablets 6. Efficacy 7. Likelihood of cure	Strength(s): ● Synthesized the factors that influenced treatment decision preferences of older women with EBC. Limitation(s): ● Recall bias: the declining cognitive ability and memory function of older people may impact the reliability of findings. ● Convenience sampling with a small sample size and low completion rate impacted the validity of the results.

Byng (2021), The Netherlands[36]	Measure participants' preference for treatment, and the impact of clinical characteristics on treatment preference.	Cross-sectional, self-administered discrete choice experiment (DCE) survey. For each DCE question/ "choice task", respondents would choose between 2 hypothetical treatment strategy alternatives ("Option 1" and "Option 2") that consist of a unique combination of different attribute levels. Sample: 172 women aged ≥55 years diagnosed with primary low or intermediate grade DCIS detected on screening mammography, residing in the Netherlands. Cancer stage: DCIS. Treatment(s): Hypothetical treatment strategy of either no surgery, BCS, BCS + radiotherapy, or mastectomy.	*We only report the subgroup analysis for the BC cohort.* Median age 59 (range: 45–77). The preferred treatment option was no surgery, followed by BCS, BCS and radiotherapy. The least preferred option was mastectomy. The treatment option was the most important attribute dictating preference, followed by follow-up interval. Participants had very strong preferences for an active surveillance strategy with no surgery, irrespective of the 10-year risk of ipsilateral invasive BC. Attributes (levels) in the order of relative importance: 1. Locoregional treatment strategy (no surgery, BCS, BCS + radiotherapy, mastectomy) 2. 10-year risk of ipsilateral invasive BC (5%, 10%, 15%) 3. Surveillance mammography follow-up (6 months, 1 year, 2 years)	Strength(s): ● First published study evaluating treatment preferences in women with a recent diagnosis of DCIS. ● Large sample size of women with DCIS. Limitation(s): ● Hypothetical DCE scenarios measure 'stated preference, which can be contrasted with the concept of 'revealed preference'. ● The results cannot be compared directly across different preference studies due to differences in analytical methods and attributes.
Ciruelos (2019), Spain[37]	Estimate patient preferences and compare treatment characteristics for oral or IV chemotherapy.	Cross-sectional, self-administered survey (16-item questionnaire with single-choice questions scored on a 5-point Likert scale). Sample: 251 Cancer stage: Metastatic Treatment(s): Oral chemotherapy, and one prior IV chemotherapy (including adjuvant or neoadjuvant regimens)	The majority of participants preferred to take capsules at home instead of IV in the clinic (76%). Most patients were concerned about IV therapy-related issues, such as pain, nausea, and hospital waiting. Attributes (levels): 1. Route of administration (oral or IV) 2. Treatment location (home or clinic) 3. Quality of life (ability to maintain daily activities) 4. Side effects (pain, nausea, etc) 5. Waiting time during treatment (short for oral or long for IV)	Strength(s): ● Included a large sample of experienced patients. ● Both pooled and sub-group analyses were reported for breast and lung cancer. ● Used a validated questionnaire (the Spanish version was not validated). Limitation(s): ● The patient's demographic information was not collected. ● The time elapsed between completing IV therapy and starting oral treatment was not captured, which may influence the patient's objectiveness.

(*Continued*)

Table 2 (Continued).

First Author (Year), Country	Study Objective	Methods, Sample Size, Cancer Stage, Treatment Type	Key Outcomes, Plausible Attributes/Levels	Strength/Limitation
Ciruelos (2020), Spain[38]	Compare patients' preferences for IV versus SC administration of trastuzumab.	Phase III, randomized, open-label, multicentre study. Before the first SC dose, patients completed the first questionnaire. After cycles 2 and 4 (or at a time of earlier discontinuation), patients completed questionnaires 2 and 3, respectively. Patients were randomized to receive an initial 1 cycle of IV infusion followed by 4 cycles of SC injection, where 2 of the 4 SC cycles were administered as a single injection (SC-vial) and another 2 cycles were administered using the single injection device (SC-SID). Sample: 166 patients (81 to arm A [1 cycle of IV to 2 cycles of SC-vial) followed by 2 cycles of SC-SID] and 85 to arm B [1 cycle of IV to 2 cycles of SC-SID followed by 2 cycles of SC-vial]). Cancer stage: Metastatic (HER2-positive). Treatment(s): Targeted therapy (trastuzumab).	The median age was 60 years (Range: 35–93). Overall, 75% of patients preferred SC, 6.9% preferred IV, and 6.9% had no preference. On the other hand, 59.2% of patients preferred SID, 26.3% preferred vials, and 11.2% had no preference. Results were consistent across study arms. Attributes (levels): ● Mode of administration (IV plus SC (SC-vial or SC-SID)) ● Number of resources required for treatment preparation ● Time savings ● Convenience ● Pain during injection	Strength(s): ● The first study explored HER2-positive metastatic BC patients' preference for IV vs SC and either vial or SID delivery method. Limitation(s): ● Potential bias due to the low number of patient preferences for IV or no preference.

daCosta DiBonaventura (2014), USA[39]	Evaluate how patients trade off medication side effects with improved effectiveness and/or quality of life.	A cross-sectional, online choice-based conjoint survey. Participants rated the importance of various attributes and completed a choice-based conjoint task consisting of 7 choice scenarios, each containing 2 profiles of hypothetical treatments, with 11 different attributes. Sample: 181 women recruited from cancer-specific online panels. Cancer stage: Metastatic. Treatment(s): Hypothetical treatment for metastatic BC.	The mean age was 52.2 years (SD 9.1). When asked directly, the most important treatment attributes were related to effectiveness, followed by QoL, ability to perform daily activities, and side effects/ safety. Cost-related attributes were the least important. Results from the conjoint model indicated that effectiveness (overall survival) was of primary importance to patients, followed by side effects and finally, the dosing regimen. The total monthly OOP costs per patient were approximately \$303 (SD \$785) for treatments related to BC and approximately \$107 (SD \$200) for physician visits related to BC. Stated importance of treatment attributes: 1. Effectiveness: Slow down cancer progression 2. Effectiveness: Prolong the life expectancy 3. Effectiveness: Efficacy 4. QoL: overall, ability to perform daily activities 5. Side effects/ safety 6. Dosing regimen: Mode of administration, treatment duration 7. Mental/emotional health 8. Cost of treatment 9. Patient support program Attributes (level) ranking from the conjoint model: 1. Overall survival (0, +1 month, +3 months) 2. Side effect: Alopecia (0%, 48%, 94%) 3. Side effect: Fatigue (0%, 8%, 24%) 4. Side effect: Neutropenia (0%, 9%, 23%) 5. QoL (difficulty performing work or other activities) 6. Side effect: Motor neuropathy (0%, 4%, 10%) 7. Side effect: Nausea/vomiting (0%, 4%, 15%) 8. Side effect: Diarrhoea (0%, 5%, 15%) 9. Side effect: Myalgia/arthralgia (0%, 4%, 15%) 10. Side effect: Mucositis/stomatitis (0%, 5%, 10%) 11. Dosing regimen: Treatment duration, mode of administration (tablet, IV)	Strength(s): ● The only study examined patient preferences using a conjoint method in women with metastatic BC. Limitation(s): ● Recall bias: all data were self-reported and may be subjected to other self-presentation effects. ● Hypothetical conjoint tasks: the true benefit or risks cannot be known with certainty. ● The results cannot be compared directly across different preference studies due to differences in analytical methods and attributes. ● Patient selection bias: convenience sampling of women from high socioeconomic status; participants might be more engaged and/or knowledgeable which may influence their preference.

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Table 2 (Continued).

First Author (Year), Country	Study Objective	Methods, Sample Size, Cancer Stage, Treatment Type	Key Outcomes, Plausible Attributes/Levels	Strength/Limitation
Gandhi (2011), Canada[40]	Determine the minimum additional survival benefit and decrease in disease recurrence acceptable to continue aromatase inhibitors (AI) therapy for an additional 5 years.	A cross-sectional, self-administered paper survey. Data gathered including demographic, treatment received, side effects, and the minimum benefit deemed worthwhile in continuing the AI for another 5 years (denoted as a percentage decrease in cancer recurrence, and a percentage increase in survival at 5 years, ranging from <1% to > 20%). Sample: 153 women who were undergoing adjuvant AI therapy for at least 1 year. A total of 44.4% of women were on anastrozole, 22.9% on exemestane, and 36% on letrozole. Cancer stage: Early and locally advanced BC (stage I–III). Treatment(s): Endocrine therapy (AI).	*We only report the subgroup analysis for the BC cohort.* The median age was 60 years (Range: 38–87). The mean duration of AI therapy use was 31 months. A total of 30.1% of women required an absolute 5-year survival benefit of <1% and 27.5% needed a decrease in recurrence risk of <1% to continue an AI beyond the initial 5 years of therapy. Another 14.4% of patients required an absolute survival benefit and reduction of recurrence risk of 1–2%. Therefore, almost 45% of patients required an absolute survival and recurrence benefit of <2% to continue on an AI beyond 5 years. In contrast, 17% of women required an absolute 5-year survival benefit of >20%, and 14.4% needed an absolute decrease in recurrence risk of >20% to continue an AI beyond 5 years. Patient preference to continue on AIs correlated to the severity of AI-related side effects. Attributes (level): ● Survival benefit (OS, DFS) ● Risk of cancer recurrence ● Side effects	Strength(s): ● Inclusion of women who were already on treatment and were thus able to integrate actual treatment experience into the survey. Limitation(s): ● Recruitment bias: women who were already on AI therapy may be more willing to continue AI therapy than women who had chosen not to have endocrine therapy at all. ● A small sample size may hinder the generalisability of the results or find trends in treatment expectations and other patient variables. ● Patients might underestimate the actual recurrence risk and overestimate the actual treatment benefit.

Hamelinck (2016), Netherlands[41]	Examine patients' preferences for chemotherapy and adjuvant hormonal therapy, the factors related to minimally required benefits, and patients' self-reported motivations.	Prospective mixed-method study. Telephone interview held before post-surgical consultation, using the probability trade-off method to elicit the minimal required benefit from chemotherapy and hormonal therapy (in terms of additional 10-year DFS). The hypothetical scenarios with varying recurrence risk and absolute benefit were read aloud, and participants were to choose their preferred scenarios. At the end of each scenario, participants were prompted to answer their motivations for preference. Sample: 81 women aged ≥ 40 years. Cancer stage: First primary invasive tumour (clinical T1-2) scheduled to undergo surgery with curative intent. Treatment(s): chemotherapy and hormonal therapy.	Median age 61 years (range: 42–86). Minimal-required benefit in 10-Year DFS for hormonal therapy: The participants considered it worthwhile at a median of 8–10% absolute benefit. As many as 17% of the older participants would refuse hormonal therapy at an absolute benefit of 25%. Minimal-required benefit in 10-Year DFS for chemotherapy: The participants considered it worthwhile at an absolute median benefit of 4–5%. One-quarter of the older participants would refuse chemotherapy at the maximum absolute benefit of 25%. The most often reported concerns against chemotherapy were the potential side effects, wish to maintain current QoL, negative treatment experience of others, and the benefits not outweighing side effects. For hormonal therapy, the participants reported that side effects and the long duration of treatment were arguments against the therapy. Attributes (levels): 1. 10-year disease-free survival (0–25%) 2. Side effects 3. Quality of life (independence, continuing working) 4. The risk of cancer recurrence 5. Treatment effectiveness 6. Treatment duration 7. Flexibility to stop treatment in case of side effects 8. Treatment location (hospital) 9. Mode of treatment administration 10. Clinician's recommendation	Strength(s): ● Explored the older patients' preferences for chemotherapy and hormonal therapy. ● Sub-group analysis for both younger and older patients. ● Explored patient benefit-risk trade-offs. ● Interviews conducted before the physician's consultation ruled out recommendations influencing participants' preferences. Limitation(s): ● Preference may be different after participants had received a recommendation from a physician. ● Small sample size with only 29 older participants (≥ 65 years).

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Table 2 (Continued).

First Author (Year), Country	Study Objective	Methods, Sample Size, Cancer Stage, Treatment Type	Key Outcomes, Plausible Attributes/Levels	Strength/Limitation
Harding (2013), EU countries[42]	Explore the treatment information needs and treatment priority for women with locally advanced and metastatic BC.	Multiple-choice, anonymous online survey in the local language explored topics on patients' experiences of diagnosis and treatment, the information provided and made available, and patients' views on improving the future care offered. Sample: 216 women aged ≥20 years recruited through local patient groups. Cancer stage: Locally advanced or metastatic BC. Treatment(s): Not mentioned.	The majority of the participants were between 40–69 years. Patients expressed a strong willingness to trading-off side effects to prolong life expectancy and have more time to spend with family/friends. Attributes (levels): ● Survival ● Risks versus benefits of treatment ● Participation in clinical trials ● Complementary therapies ● Non-medical treatment (counselling) ● Choice of specialist ● Continuity of care ● Waiting time to access diagnosis and/or treatment ● Good physician-patient communication ● Hands-on or regular support (out-of-hours support, monetary support)	Strength(s): ● Provided insight into the unmet needs of women living with locally advanced and metastatic BC in the EU. ● Multilanguage surveys decreased the bias for English speakers. Limitation(s): ● Recruitment bias: online methodology restricts participation to those with internet access and who were actively seeking information.
Irwin (2014), USA[43]	Explore experience and preferences concerning discussions of cost and views on cost control.	Cross-sectional, pilot-tested, self-administered, anonymous, paper survey. The validated In Charge Financial Distress/Financial Well-Being Scale (IFDFW) was used to assess financial distress. Sample: 134 participants within 5 years of initial diagnosis. Cancer stage: Not explicitly specified. Treatment(s): Not specified.	The median age was 61 years (Range: 29–88). Most participants (88%) were concerned about the costs of cancer care. A total of 13% of respondents reported changing their medical decisions as a result of the costs, and 12% avoided treatment of non-cancer-related health issues because of costs. Most respondents (58%) agreed with generic substitution, while others endorsed other cost-controlling measures such as preferential selection of drugs that prolong survival, using more physician assistants and nurses, paying doctors less, greater means testing, or greater cost sharing. Attributes (level): ● Cost ● Original/ generic drugs ● Treatment that prolongs survival	Strength(s): ● Provided insight into the importance of discussing the costs of care with patients. ● Assessed patients' views on methods of cost control in cancer care. Limitation(s): ● Recruitment bias: small sample size in a single center. The majority of the participants were insured and of the high-income group. ● The actual out-of-pocket cost was not captured.

Mandelblatt (2010), USA[44]	Explore patient preference for chemotherapy in older women and examine relationships between preferences and chemotherapy use.	The telephone interview lasted 45 mins. Patient preference was measured by a modified time trade-off approach to evaluate the amount of benefit women would require choosing chemotherapy in a hypothetical situation. Choosing chemotherapy for the shortest period of gain (ie, 1 week) indicates the highest preference for chemotherapy, whereas not choosing chemotherapy for even a 5-year gain represents the lowest preference. Sample: 801 women aged ≥65 years. Cancer stage: Newly diagnosed with invasive non-metastatic BC (tumours more than or equal to 1 cm). Treatment(s): Chemotherapy.	The mean age of 73 years (Range: 65–100). Women who would choose chemotherapy for an increase in survival of ≤12 months (high preference) were 4 times more likely to receive chemotherapy than women who would only choose chemotherapy if it added >12 months (low preference). Attributes (levels): ● Survival (≤12 months, >12 months) ● Patient-physician communication	Strength(s): ● One of the largest primary observational data sets of older women to examine determinants of chemotherapy use in the USA. Limitation(s): ● Referral bias: the sample had a greater proportion of poor prognosis tumours than older women in the general population. ● Not all preferences were measured before oncology consultations, which might affect the preference rating due to the effect of the actual treatment. ● Almost all participants reported seeing an oncologist, which is a strong predictor of treatment, and that limits the external generalizability of the results.
Oh (2012), Korea[45]	Evaluate the WTP to return from the current health state (metastatic BC) to the pre-cancer health state.	Cross-sectional, multi-center structured individual interview contingent valuation to elicit WTP. Patients' WTP for BC treatment was assessed using an open-ended question following three rounds of bidding, starting with one of three randomly assigned start bids. WTP amounts were elicited using a consumption-based approach with the assumption that the treatment would not be covered by insurance and that therefore the full cost would be borne by the patient. Sample: 188 patients who had received or were currently receiving chemotherapy or radiotherapy. Cancer stage: Metastatic. Treatment(s): Palliative chemotherapy.	The mean age of 49.8 years (Range: 30–77). The average WTP per month for a hypothetical treatment to return the current state to its pre-cancer state was KRW 8,696,329 (US$7555) per month. Attributes (levels): ● WTP	Strength(s): ● The first WTP study in Korea on metastatic BC patients. Limitation(s): ● Recall bias: the use of the patients' pre-cancer health state. ● The contingent valuation exercise was difficult to understand for some respondents. ● Starting bid bias.
Pivot (2017), France[46]	Assess the preference towards SC or IV infusion of trastuzumab.	An open label, randomized, cross-sectional, multicentre Phase III study. Sample: 92 (47 in the SC to IV arm and 45 in the IV to SC arm). Cancer stage: Metastatic (HER2-positive). Treatment(s): Targeted therapy (trastuzumab).	The median age was 59 (Range: 35–85). Overall, SC is the most preferred administration method by the patients (84–87%). Attributes (level): ● Mode of treatment administration (IV, SC)	Strength(s): ● The 2nd clinical trial assessed the preference between SC and IV administration and the 1st in the metastatic setting. Limitation(s): ● Recruitment bias: selection of patients with previous long exposure to trastuzumab.

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Table 2 (Continued).

First Author (Year), Country	**Study Objective**	**Methods, Sample Size, Cancer Stage, Treatment Type**	**Key Outcomes, Plausible Attributes/Levels**	**Strength/Limitation**
Sakai (2020), Japan[47]	Clarify the priority of the unmet medical information needs of BC patients and detect discrepancies in perceptions between patients and physicians or nurses.	Cross-sectional, internet survey. The information collected included priorities for treatment selection, side effects to avoid, and the most necessary information on BC treatment. Sample: 207 patients aged 20–69 years recruited from a consumer panel. Cancer stage: Not explicitly specified. Treatment(s): Chemotherapy, hormonal therapy, and targeted therapy.	*We only report the subgroup analysis for the BC cohort.* The median age was 50.8 years (range 26–69 years). The most distressing side effects were hair loss, followed by skin and nail problems, weariness/fatigue, taste disorders, peripheral neuropathy, and oedema. Nausea/vomiting and hair loss were highly ranked as side effects most desirable to avoid when selecting treatment. Side effects attribute ranking (top 10): 1. Hair loss 2. Skin/nail problem 3. Fatigue/Weariness 4. Taste disorder 5. Numbness in hands and legs (peripheral neuropathy) 6. Oedema 7. Constipation 8. Loss of appetite 9. Nausea/vomiting 10. Drowsiness/sleep disorder Psychological attribute ranking (top 10): 1. Changes in appearance and mood 2. Fear of metastases and recurrence 3. Uncertainty about the future 4. Vague anxiety and depressed mood 5. Anxiety about dying 6. Anxiety about failure to achieve expected treatment responses 7. Work-related and social rehabilitation 8. Difficulty taking care of oneself 9. Relationship with partner 10. Relationship with friends Desirable attributes for future treatment: ● Maintaining QoL ● Longer survival ● Cancer reduction ● Mild side effects ● Inexpensive treatment cost ● Can be treated as an outpatient	Strength(s): ● Large sample size with sub-group analysis conducted for BC cohort. Limitation(s): ● Recruitment bias: selection of patients from a consumer panel that excluded patients not on the list. Participants might be those who were highly conscious of BC treatment.

Savard (2021), Canada[48]	Assess older patients' experiences and perceptions regarding radiotherapy and hormonal therapy, and participation interest in de-escalation trials.	Cross-sectional, self-administered 40-item questionnaire. Sample: 102 patients aged 71–76 years (mean age 74). Cancer stage: Early-stage BC treated with BCS. Treatment(s): Radiotherapy or hormonal therapy.	A total of 71% patients were receiving or had received both radiotherapy and hormonal therapy, 12% were receiving or had received radiotherapy only and 9% hormonal therapy only. Patients shared their varied concerns and expectations of radiotherapy and hormonal therapy benefits. Attributes (levels): ● Risk of ipsilateral tumour recurrence at 5 years (a reduction of risk ranging from 1%-50%) ● Risk of occurrence of a contralateral BC ● Risk of metastatic recurrence at 5 years (a reduction of risk ranging from 1%-50%) ● Survival benefit at 5 years (an increase of survival ranging from 1%-50%) ● Improvement in QoL ● Risk of side effects without additional benefit ● Possible side effects ● Impact on carrying daily activities ● Treatment duration ● Commuting for treatment	Strength(s): ● First survey on the perceptions of older adults towards radiotherapy and hormonal therapy and de-escalation trials. ● Sample size has a good representation of the elderly population. Limitation(s): ● Sample selection bias due to the Covid-19 pandemic.
Wouters (2013), Netherlands[49]	Examine BC patients' trade-offs between the benefits and drawbacks of endocrine therapy.	An adaptive conjoint analysis study, where 15 choice tasks of hypothetical treatment options 'Endocrine therapy A' and 'Endocrine therapy B' with different attributes and levels. Women rated their preference on a 9-point scale (1, strong preference for 'Endocrine therapy A'; 9, strong preference for 'Endocrine therapy B'). Respondents participated by answering the online questionnaire or through a face-to-face interview. Sample: 241 women recruited from hospitals, community pharmacies, and patient organizations. Cancer stage: Not mentioned. Treatment(s): Two hypothetical endocrine therapies.	Efficacy was the most important attribute. However, the benefit/drawback ratio showed that 16% of women considered the efficacy to be less important than or equally important than the other attributes (ratio ≤ 1). Attributes (level) relative importance ranking: 1. Efficacy in the prevention of recurrence (in 3/10, in 5/10) 2. Side effects: osteoporosis (lessens risk, aggravates risk) 3. Side effects: risk of endometrial cancer (in 1/1000, in 5/1000) 4. Side effect: joint and muscle pain (abit, moderate to severe) 5. Side effect: fluid retention (abit, moderate to severe) 6. Side effect: libido decrease (abit, moderate to severe) 7. Side effect: host flashes (some per month, some per week) 8. Regimen duration (2 years, 5 years)	Strength(s): ● Adaptive conjoint analysis choice task better mimics the real-world trade-off between the benefits and drawbacks of BC treatment. Limitation(s): ● Sub-groups were too small for further analysis. ● The benefit outweighs the drawbacks could have been underestimated. ● The choice task might be difficult to understand for certain patients.

Abbreviations: AI, aromatase inhibitor; BC, breast cancer; BCS, breast-conserving surgery; DCIS, ductal carcinoma in situ; DFS, disease free survival; ESBC, early stage breast cancer; EU, Europe; FGD, focus group discussion; OOP, out of pocket cost; OS, overall survival; SC, subcutaneous; SC-SID, single-use injection device; SC-vial, subcutaneous single injection; SD, standard deviation; UICC, Union International Contre le Cancer; USA, United States of America; WTP, willingness to pay.

Table 3 Conceptual Framework of Important Determinants in Breast Cancer Treatment from Patient's Perspective, and Percentage of Studies Under Each Sub-Theme

Theme (% of Total Studies)	Sub-Theme	% of Total Studies, N=22
Treatment benefits (68.2%)	Prolong survival or life expectancy	45.5%[30,31,39–44,47,48]
	Treatment efficacy	36.4%[30,32,33,35,39,41,47,49]
	Cancer recurrence risk reduction	31.8%[13,31,35,40,41,47,48]
Treatment-related process (68.2%)	Treatment duration/waiting time/recovery time	54.5%[13,30–33,35,37–39,41,48,49]
	Mode of treatment administration	31.8%[33,35,37–39,41,46]
	Social support, counselling, and continuity of care	22.7%[31,32,35,39,42]
	Treatment location	22.7%[13,33,37,41,47]
	Accessibility and availability of treatment	22.7%[13,30,32,42,48]
	Physician's recommendation	18.2%[30–32,41]
Treatment-related risks (63.6%)	Side effects and safety	50.0%[13,31,32,35,37–42,48]
	Treatment-related secondary cancer and/or the need for additional therapy	27.3%[13,30,35,36,48,49]
	Alopecia	18.2%[29,34,39,47]
	Lethargy/fatigue and sleep disturbances	18.2%[13,29,39,47]
Quality of Life (54.5%)	Ability to maintain daily activities	50.0%[13,29,31,32,35,37,39,41,47,48]
	Emotional/mental health	27.3%[29,30,32,33,39,47]
	The burden to family/partner/caregiver	13.4%[29,32,47]
Cost of treatment (31.8%)	Out-of-pocket cost, willingness to pay, and monetary support	31.8%[30,32,39,42,43,45,47]

Cancer Recurrence Risk Reduction

BC patients, particularly older patients, often opt for chemotherapy to reduce the risk of cancer recurrence.[31] This desire to evade recurrence was also observed in both younger and older patients as a key motivation for undergoing chemotherapy and hormonal therapy.[41] In fact, older patients indicated that they wanted to ascertain the likelihood of the treatment they were receiving in preventing cancer recurrence.[35] Furthermore, Gandhi et al found that a decrease in recurrence risk of less than 5% was considered worthwhile for continuing hormonal therapy beyond the initial 5 years by women with eBC.[40] It is worth noting that the psychological impact of cancer recurrence was a significant concern for BC patients undergoing treatment. Patients undergoing chemotherapy in particular experienced high levels of anxiety and fear, with "fear for metastases and recurrence" being quoted as a major concern.[47]

Treatment-Related Process

Treatment Duration, Waiting Time, and Recovery Time

For many patients, the long waiting time during treatment was a source of concern, as it can have a profound impact on their daily lives.[37] Patients with young children or family members requiring care, in particular, were anxious about the length of time they will be unable to fulfill their familial duties.[30,31] On the other hand, the total treatment duration of hormonal therapy was frequently a deterrent, with some patients commending chemotherapy due to its shorter total treatment duration in comparison to hormonal therapy.[41,49] Furthermore, it is interesting to note that a conjoint model revealed that the treatment duration was rated as one of the least significant attributes of treatment preference by patients compared to survival, side effects, and QoL.[39] Recovery time was also a pertinent deciding factor for patients who have work or personal responsibilities. Patients with significant work or personal responsibilities were more likely to choose BSC and radiation over mastectomy as their preferred surgical treatment, as it allows them to resume their daily activities more quickly.[32] Time savings and convenience were reported as the main rationales for preference towards SC administration compared to IV.[33,38]

Mode of Treatment Administration

BC patients' preferences for the mode of administration of their cancer treatment vary widely. A multi-center randomized clinical trial revealed a strong patient preference for SC treatment compared to the conventional IV delivery method, particularly for patients with high personal, familial, and occupational commitments.[33] The preferences for SC were corroborated by two other studies, citing similar reasons.[38,46] Furthermore, in another study, a majority of patients with mBC preferred oral over IV chemotherapy, due to the ease of administration.[37] Patients' opinions on the mode of administration varied, with some preferring oral delivery due to their aversion to needles, while others preferred IV delivery due to their perception that taking a pill every day was burdensome.[41]

Social Support, Counselling, and Continuity of Care

The lack of social support was identified as a significant factor that can affect patients' decisions regarding their treatment.[31] Specifically, women who lacked social support or were the primary caregiver for their families were more likely to refuse treatments that require them to be away from home.[30] Additionally, older women expressed concerns about the availability of support following surgery.[35] While not the top priority for some patients, those with mBC expressed a desire for patient support programs offered by drug manufacturers or financial assistance from charities or research organizations.[39] Interestingly, patients with mBC expressed a desire for complementary medicines, counselling, out-of-hours support, continuity of care with the same healthcare providers, and involvement in clinical trials in addition to their existing cancer treatment.[42]

Treatment Location

In general, BC patients preferred a treatment that could be administered as an outpatient, whereas patients with eBC were less likely to prefer chemotherapy due to the burden of frequent hospital visits.[41,47] In one study, a significant number of patients expressed a preference for receiving SC chemotherapy in the comfort of their homes, while patients who preferred having treatment at the hospital or clinic enjoyed being in the company of other women and exchanging experiences.[33] In another study, however, women with mBC preferred the convenience and privacy of home administration of oral treatment to IV infusion in a clinic setting.[37]

Accessibility and Availability of Treatment

Research has highlighted the role of travel distance in predicting surgical choice. Women living in rural and remote areas may opt for mastectomy over BSC to avoid subsequent radiation therapy due to the greater distances travelled for radiation treatment.[30] Moreover, logistical issues, such as distance to care and transportation, had been identified as significant barriers to treatment access and uptake, particularly for patients residing in rural areas or reliant on others for transportation. Such patients tend to refuse treatment, citing difficulties in accessing care.[32] Notably, patients expressed a desire for reduced waiting times for treatment and an improved gap in the delay between diagnosis and treatment commencement. Additionally, they emphasized the importance of having a choice of their preferred physicians, reflecting their desire for greater autonomy in treatment decision-making.[42]

Physician's Recommendation

Physicians' recommendations have been found to play a vital role in shaping patients' treatment decision-making and preferences. Patients have expressed that a clear and definitive recommendation from their healthcare provider would significantly impact their decision to accept or reject a particular treatment.[31,41] Nevertheless, shared decision-making between patients and physicians was also found to be the preferred approach by most patients, where they valued the expertise of physicians and would collaboratively work with their physicians in selecting the treatment that aligns with patient care goals.[30–32] This trust is reflected in statements such as, "They're the experts and I'm not, so their training and everything should be what would lead me to go in a certain direction".[32]

Treatment-Related Risks

Treatment-Related Side Effects and Safety

A central theme that emerged from the literature is the paramount importance of considering the treatment-related side effects and safety of the available treatment options. For instance, patients may refuse chemotherapy due to the side effect and its adverse impact on health.[31] Patients, irrespective of whether they were in the early or advanced stages of BC, expressed significant concerns about the potential toxicity and long-term safety of a treatment or surgery as major considerations.[32,35,39] Notably, younger and older patients had distinct concerns regarding the potential side effects of chemotherapy, highlighting the need for a nuanced approach to treatment decision-making that accounts for the diverse needs and preferences of the patient population.[41] Besides, patients' preference for continuing hormonal therapy appeared to be closely linked to the severity of associated side effects and the flexibility to stop treatment in case of severe side effects.[40,41]

Treatment-Related Secondary Cancer and/or the Need for Additional Therapy

Among those who underwent radiation therapy, the fear of developing treatment-related secondary cancer was a pervasive concern, compounded by the anxiety associated with the radiation itself. Women who had young children or acted as caregivers to their partners declined radiation or further therapy due to the need to be concomitantly away from home to receive treatment.[30] Patients on different anticancer therapy were constantly troubled by the fear and uncertainties of cancer metastases or treatment-related secondary cancer that would expose them to the need for additional therapy.[35] Notably, women tend to consider the small risk of developing endometrial cancer (5 out of 1000) to be almost as significant as the substantially higher benefit of hormonal therapy's efficacy (5 out of 10).[49] In contrast, women in the Netherlands assigned less importance on the future risk of a secondary BC compared to the risk of surgery.[36]

Alopecia

BC patients undergoing chemotherapy often reported alopecia as the most distressing and most desired to be avoided side effects.[29,47] Among those receiving taxane-based chemotherapy, madarosis had been shown to significantly impact their daily lives. Interestingly, the severity and timing of regrowth for both eyebrows and eyelashes appeared to vary widely among patients, with several women also experiencing dry and irritated eyes leading to increased tearing as a physiological side effect of madarosis.[34] A conjoint analysis revealed that the relative importance of alopecia was ranked second just behind the survival benefit when considering treatment preference.[39]

Lethargy/Fatigue and Sleep Disturbances

Fatigue and sleep disturbances are common side effects of BC treatment that can significantly impact a patient's daily life and overall well-being. In fact, lethargy and difficulty sleeping were ranked among the most troublesome concerns reported by women undergoing chemotherapy.[29,47] In hypothetical treatment preference analysis, it was observed that women tend to avoid treatments that have the potential to induce fatigue as a side effect.[39] Additionally, while sleep disturbances were ranked lower in terms of distress compared to fatigue or weariness, they remained an important consideration among Japanese patients.[47]

Quality of Life

Ability to Maintain Daily Activities, Work, and Home Duties

BC patients faced a complex decision-making process when considering their treatment options, as their preferences were often influenced by a range of factors related to their quality of life (QoL), ability to maintain daily activities, and fulfil their work and home duties.[29,40,47,48] These concerns were often rooted in a desire to maintain independence and continue living life as fully as possible, despite the challenges posed by their illness. For some patients, chemotherapy could be a source of significant anxiety, as they worried about the impact it might have on their QoL and ability to perform activities of daily living, such as grocery shopping and household tasks.[31] Others expressed concerns about the impact of treatment on their ability to pursue hobbies, spend time with loved ones, attend life events, social rehabilitation, and travel, all of which were deemed important for maintaining a sense of normalcy and emotional well-being.[32,47] Older women with eBC, who may be more vulnerable to the physical and emotional toll of BC and its treatment, may be particularly concerned about the impact of surgery on maintaining their QoL, independence, and ability to perform daily activities.[35,41]

Emotional/Mental Health

BC patients' emotional and mental health can be severely impacted by anticancer treatment, causing a range of emotional struggles such as fear, worry, stress, and anxiety.[39] Some of these emotions might be related to specific aspects of treatment, such as fear of radiation or surgery, while others described an overall depressed moods and anxiety related to the uncertainty of treatment responses and future outcomes.[30,47] It was evident that patients who experienced better well-being during adjuvant systemic therapy were more inclined to accept that particular treatment.[33] The effects of BC treatment, such as madarosis, could cause a profound sense of emotional distress, disconnection from one's appearance, and discomfort in social situations. Patients reported withdrawing from public places and refrain social interactions to avoid being judged by others.[34] Patients receiving IV chemotherapy had reported anxiety related to the pain, side effects, and complications associated with the IV line.[37,38]

Burden to Family/Partner/Caregiver

BC not only takes a toll on the physical health of patients but also exerts a significant psychosocial impact on their relationships with family members, partners, and caregivers.[29] The extent of this impact and its influence on treatment preferences has been found to vary among studies. In some cases, patients may opt out of treatment altogether as they do not want to burden their loved ones with the added stress of caring for them.[32] Furthermore, BC patients may experience anxieties about the potential ramifications of their illness on their relationships with partners and friends, adding to their already substantial emotional burden.[47]

Cost of Treatment

BC patients face a significant financial burden associated with the cost of cancer treatment. This burden is particularly pronounced in the context of radiation therapy, which entails a prolonged stay away from home, the hiring of caregivers to tend to family needs and additional transportation costs for those residing in remote areas.[30] According to the study conducted by Lawhon et al, older women with eBC exhibited differing levels of concern regarding the cost of treatment, with over a quarter of women stated that cost was not their primary consideration when making decisions about their treatment.[32] Willingness to pay (WTP) for treatment varies significantly across patients, with higher household income being associated with greater WTP and patients with higher financial burden elicited a lower WTP, respectively, for a treatment that would restore them to their pre-cancer health status. Notably, patients with brain metastases were willing to pay substantially more for treatment than those with bone metastases.[45] However, patients prioritized treatment effectiveness over cost when making treatment decisions, indicating that out-of-pocket costs may not be the sole factor affecting their treatment decisions. The majority of patients, especially those with mBC, voiced a desire for financial support options and less expensive treatments.[39,42,47] The financial burdens arising from BC treatment had led to alterations in treatment decisions and even the postponement of treatment for non-cancer-related health issues, mainly due to the high out-of-pocket expenses involved. Nevertheless, despite the high financial burden experienced by some patients, Irwin et al found that the majority of patients did not perceive non-out-of-pocket costs, such as costs to insurance companies or society, as significantly impacting their medical decisions. Most patients indicated a willingness to accept generic drug substitutions in order to mitigate costs.[43]

Discussion

BC remains a major public health concern, and treatment modalities have evolved considerably in recent years. However, patients' preferences for BC treatments are not always fully considered in the development and implementation of these treatment advancements. The evidence pooled across studies in this review highlights the important determinants of cancer treatment that matter to BC patients, as well as the existence of significant unmet needs among them.

BC treatment involves a delicate balance between achieving optimal outcomes while minimizing the risks, side effects, and safety concerns that patients may have. In this study, alopecia and madarosis have emerged as profoundly distressing adverse effects of BC treatment. These adverse effects have consistently ranked high on the lists of most challenging concerns from the patient's perspective for the past four decades.[50–52] Considerably varying preferences towards the benefits and risks of treatment were observed among individual patients. Interestingly, our review revealed that some patients demonstrated a willingness to undergo treatments that conferred relatively small survival benefits, but with significant risk or toxicity.[39–41] Several factors could account for these inconsistent results. Firstly, inadequate patient awareness regarding the treatment's benefit-to-risk ratio could be a plausible explanation. Secondly, patients might encounter difficulty comprehending the statistical data presented to them. Lastly, the fear of developing secondary cancer due to the treatment could have influenced their capacity to make well-informed and rational decisions. Even with the observed intra-patient variation, it was evident that patients' perspectives on BC treatment for all stages of cancer differed significantly from those of healthy individuals or their healthcare providers.[30,40,44,47] For instance, patients who were treated with aromatase inhibitors therapy demonstrated a willingness to continue the treatment even for marginal treatment benefits, a threshold lower than what physicians typically prefer for prescribing beyond the 5-year mark.[40] In addition, Sakai et al reported that patients, nurses, and physicians exhibited distinct priorities when it came to the severity of treatment-related side effects.[47]

The QoL of BC patients, especially older women, is notably affected by the treatment they receive. Such treatment has a profound impact on their ability to perform daily activities, fulfil work and home duties, maintain their emotional and mental well-being, and manage their relationships with loved ones and caregivers. The emotional distress stemming from BC treatment may lead to withdrawal from public places and social interactions, particularly in cases where treatment side effects lead to changes in appearance. Likewise, a recent survey of Australian women with BC diagnosis highlighted the significance of body image or sexuality in association with a patient's emotional and psychosocial well-being.[53] BC can also take a toll on patients' relationships with family members, partners, and caregivers, affecting their psychosocial well-being. The extent of this impact and its influence on treatment preferences varies among studies, with some patients even opting out of treatment entirely to avoid burdening their loved ones. In recent years, there has been a growing awareness of the importance of addressing the mental, emotional, and psychosocial well-being associated with BC treatment, particularly as advancements have made the physical side effects more manageable.[54,55] Incorporating a focus on these non-physical mental and emotional health issues into clinical practice is crucial in enhancing the overall QoL of BC patients. By doing so, patients may be more inclined to adhere with their treatment, leading to improved treatment outcomes and an overall health related QoL.

The findings in this review suggest that prolonged treatment duration, especially for chemotherapy or radiotherapy, can have a considerable impact on patient's daily lives. Nevertheless, it is noteworthy that both conjoint analysis studies in the review identified treatment duration as the least significant factor influencing patients' treatment preferences.[39,49] This implies that while treatment duration and other attributes are relevant, they have a less significant impact on patients' treatment decisions compared to other treatment attributes. Some patients discussed facing challenges in accessing and availing treatment due to a range of factors, including travel distance, local clinic availability, transportation, and long waiting times for diagnosis and treatment, all of which can significantly impact treatment decision-making. Addressing these challenges may help reduce disparities in BC outcomes, particularly for patients living in rural and remote areas. Moreover, targeted interventions aimed at enhancing the patient experience and reducing waiting times can contribute to improved treatment uptake and better clinical outcomes.[56,57]

Physicians' recommendations play a crucial role in shaping patients' treatment decision-making and preferences, and their guidance and recommendations can have a profound impact on treatment outcomes, as patients value the expertise of physicians and trust that their training and knowledge will guide them toward the right treatment option. However, participants also expressed a desire to be more involved in decision-making, where they collaboratively work with their physicians in selecting the treatment that aligns with their treatment goals. The shared decision-making approach acknowledges patients' autonomy and their entitlement to participate in the treatment decision-making process.[32,58] Although patients prioritize treatment effectiveness over cost when making treatment decisions, the financial toxicity associated with BC treatment remains a substantial concern for many patients.[59] A significant proportion of patients reported experiencing financial toxicities as a direct result of their BC treatment, with these financial burdens often causing them to alter their treatment decisions or forgo treatment for non-cancer-related health issues due to the high out-of-pocket expenses. BC was found to impose a greater financial burden than other cancers, as evidenced by substantially higher out-of-pocket costs compared to the combined out-of-pocket costs for colorectal, lung, and prostate cancers.[60] Healthcare policy makers shall ensure that necessary measures are taken to implement policies aimed at alleviating the financial burden of both medical and non-medical expenses, thus enhancing the financial well-being of vulnerable patients with BC.

While we came across three systematic review studies[61–63] that examined treatment decision-making in patients with BC, they did not meet our inclusion criteria. These studies, however, revealed that patients' treatment preferences were influenced by various factors, including treatment benefits (such as survival, life expectancy, and probability of cure), treatment risks (including side effects, toxicity, risk of recurrence, and progression), QoL, treatment availability and accessibility, social support, surgeon's recommendation, treatment cost, and the desire for no additional therapy beyond surgery. Interestingly, these findings align with the results of our own review. In contrast to the systematic review studies mentioned, our review introduces a novel perspective and demonstrates increased comprehensiveness. Our analysis encompasses all stages of BC and the broader landscape of BC treatment, distinguishing it from existing studies that exclusively concentrate on patient preferences in eBC[61,62] or on the treatment decision-making of patients with ductal carcinoma in situ.[63]

This paper employed a narrative review method to examine the important determinants in BC treatment that matter to patients. Narrative reviews have been frequently criticized for their lack of systematicity and explicitness compared to other review methods. However, they offer great flexibility as they can accommodate a vast array of evidence, such as qualitative and quantitative data, research, and non-research sources, without merging findings or creating new theories. Despite the limitations, narrative reviews continue to be useful in policy and management, particularly when time is scarce. Since narrative reviews do not require complex data transformation, they can provide a comprehensive and inclusive analysis.[26] Nevertheless, there are several limitations of our review that should be noted. We did not conduct a quality appraisal, which might limit the uptake and relevance of the scoping study.[21] However, Arksey and O'Malley[20] state that quality assessment is not a standard component of a scoping review. Some articles included in this review had limited details, leaving the review team to exercise their own reflexivity in content extraction, which may lead to incorrect interpretation of the results. Since the purpose of this review was to identify the important determinants of BC treatment from patient's perspective, formal statistical meta-analysis would have been inappropriate.[22,23] Nevertheless, this review provides an overview of the patient's values and preferences concerning BC treatment, which allows for a detailed exploration of patients' experiences and perspectives, whilst also providing a rich data source to inform future studies and interventions focused on patient-centered care.

Conclusion

In conclusion, BC patients reported a wide array of preferences regarding the important determinants of cancer treatment. Among 5 overarching themes identified, treatment benefits emerged as the most frequently cited theme, with treatment-related process, treatment-related risk, quality of life, and cost of treatment following in sequence. This literature review emphasizes the importance of considering these key determinants when making treatment decisions for BC patients. Our findings serve as an initial contribution towards developing conceptual frameworks that underpin the important determinants of BC treatment. There is an urgent need for healthcare professionals to engage in effective communication with their patients and involve them in the treatment decision-making process to ensure that their preferences and values are considered. Moreover, the findings highlight the need for personalized medicine, patient decision aids, and tailored financial assistance programs to mitigate the financial toxicity of cancer treatment. To optimize patient outcomes, future research should focus on identifying effective strategies to tailor treatments that align with patients' preferences.

Data Sharing Statement

The data supporting the findings of this literature review was obtained from the literature. It is available within the article and its Supplementary Information files.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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