Shared Decision-Making about Treatments for Early Breast Cancer: Preferences of Older Patients and Clinicians

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COLOPHON

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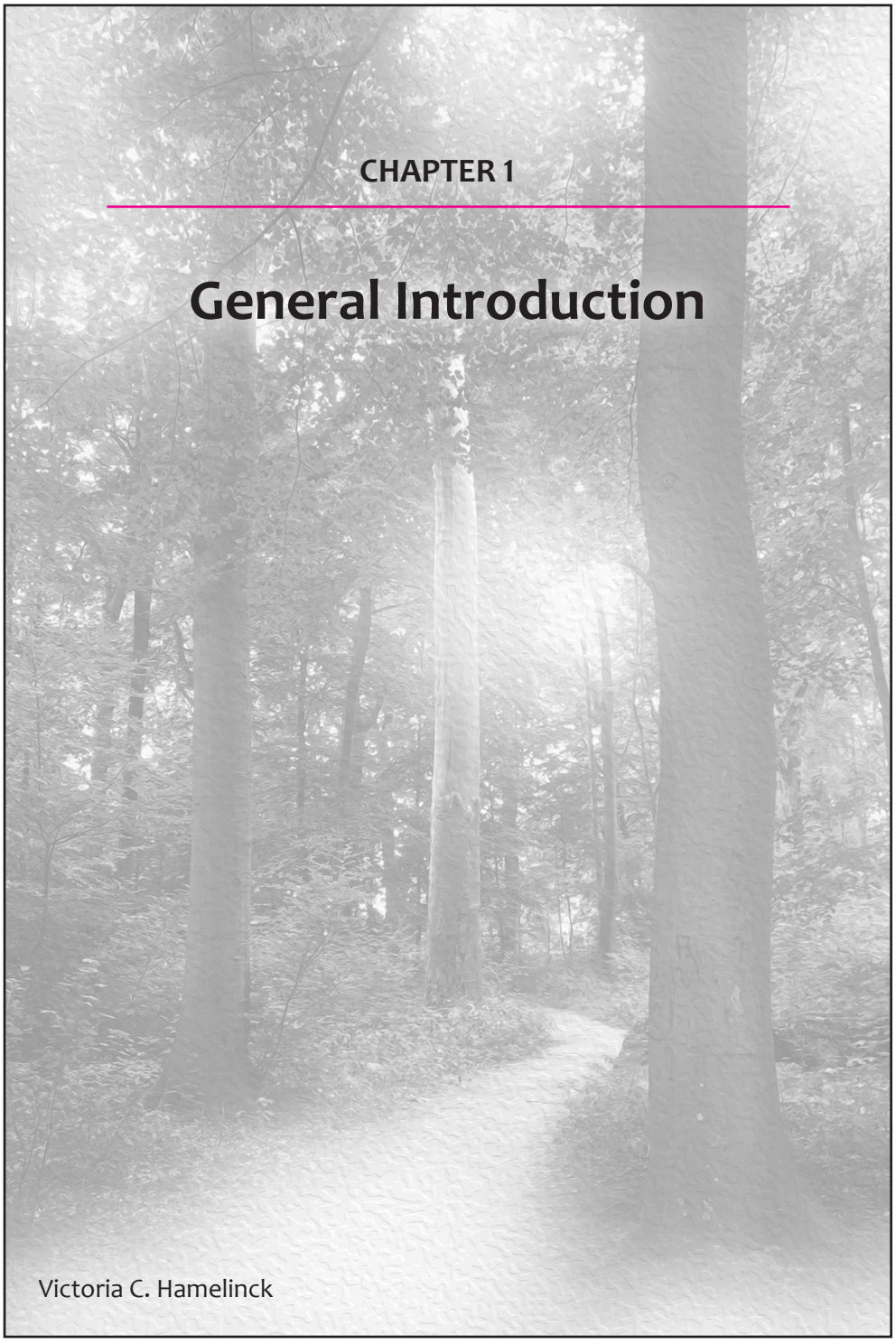

CHAPTER 1

General Introduction

Victoria C. Hamelinck

Background

Breast cancer is the most common cancer in women in Western countries.[1] In the Netherlands, nearly 17,000 new breast cancer cases were diagnosed in 2016.[2] Although the disease affects women of all ages, it is more common among older women. Currently, about 40% of all cases are in women aged ≥65 years[3] and this percentage is expected to increase as the population ages.[4] Older patients also have a greater breast cancer mortality than younger patients.[2,5-7] Consequently, there has been much concern about how to optimize cancer care for this patient population.[8]

Despite this significant and growing patient population, little evidence is available to guide the management of breast cancer in older patients.[9,10] Randomized clinical trials have frequently excluded older women based on their age or comorbid conditions.[9-11] Consequently, the benefits and risks of treatment are often uncertain for older patients and results from trials conducted in younger patients can possibly not be extrapolated to the geriatric population. In addition, the few older patients that have been included in trials may not reflect the older patients in daily clinical practice, as they are generally healthier and might have more favourable tumour characteristics.[12]

An important aspect in cancer treatment decision-making for older patients, is the patient's preference. Currently, decision-making of breast cancer treatment is often done without the input of patients.[13,14] Lack of shared decision-making between the clinician and the patient could potentially entail a decrease in satisfaction and treatment adherence of the patients.[15,16] Therefore, it is stipulated that shared decision-making should be made a priority in breast cancer treatment in older patients,[9,10] especially as it is often not clear which treatment option is most appropriate.[17] Given this background, this thesis is directed towards exploring treatment decision-making between clinicians and older patients, with a focus on the preferences of the latter.

Tailoring treatment to the older patient's context

Treatment decision-making for older patients is generally complex. Older patients frequently suffer from other medical conditions besides breast cancer and may take multiple medications, which may place them at increased risk of adverse outcomes.[18-20] Further, the older patient population is highly heterogeneous,[21] with patients of the same chronological age having large differences in physiological reserves, life expectancies, physical and cognitive functioning, geriatric health conditions, and possibly in preferences. These aspects make it difficult to determine the best individual treatment decision.

Due to a lack of treatment evidence, current (inter)national practice guidelines for breast

cancer are not able to recommend treatment options in older breast cancer patients.[22] This means that with the absence of age-specific guidelines, clinicians are left with general treatment recommendations. However, for many older patients with breast cancer, the general treatment recommendations are difficult to apply to. Since 2007, an international group of experts of the European Society of Breast Cancer Specialists and the International Society of Geriatric Oncology have put efforts in releasing a set of recommendations for the management of breast cancer in older patients.[9,10] Their recommendations state that treatment plans should not be based solely on the patient's chronological age alone, but be tailored to the individual older patient's context (e.g., general health status, comorbid conditions, and estimated life expectancy). In addition, it is recommended that as evidence about the best treatment option is often inconclusive, a shared decision-making approach between the clinician and the older patient should be an essential part of this process.

Shared decision-making

In recent years, it has become increasingly accepted that it is important to involve patients in medical decision-making and to elicit their preferences to make good individualized health care decisions.[23] Shared decision-making is a process in which clinicians inform patients about all possible treatment options and encourage them to consider the potential benefits and risks, so that patients can form their preferences. The patient's preferences are then combined with the best available medical evidence to decide which option best suits the patient.[24] Assessment and prioritization of the patient's preferences is particularly essential in decisions when there is more than one reasonable treatment option from a medical standpoint[25] or when trade-offs between potential benefits and risks have to be made for which patient preferences vary.[26] This is the case in the treatment of early-stage breast cancer as will be illustrated in following subparagraphs.

Treatment of early stage breast cancer

The majority of patients with breast cancer are diagnosed with stage 0-II ('early stage') disease,[27,28] which typically refers to small tumours (i.e., a clinical lesion size ≤ 5.0 cm) that have not spread beyond the breast or lymph nodes close to the breast.[22] Depending on the type and extension of the early BC, its treatment often involves a combination of different modalities (i.e., primary surgery potentially followed by adjuvant systemic therapies). Generally, patients with this diagnosis and their clinicians face a difficult decision-making process, which revolves around whether to perform a mastectomy or a breast-conserving surgery, potentially followed by adjuvant systemic therapies (hormonal or chemotherapies). Each of the abovementioned modalities involves risks and benefits, which clinicians clearly need to discuss with the patients, so that they can develop informed treatment preferences.[24] Moreover, as this is a high impact decision-making process, it is preferable to elicit their

preferences in the early stages of this process.

Type of surgery

Primary treatment for patients with ductal carcinoma in situ (the most common type of stage 0) and stage I-II breast cancer consists of surgery. In most cases, patients of all ages are eligible for two surgical treatment options, namely a mastectomy or a breast-conserving surgery. Mastectomy involves a surgical procedure in which the breast is removed, while breast-conserving surgery is a less invasive procedure, but is followed by radiotherapy. Trials comparing the outcomes of both options have shown similar overall survival rates.[29-31] However, the surgical options are different with respect to cosmetic outcome, local recurrence, and use of additional surgery or radiotherapy.[32] As there is no best surgical treatment option from a medical standpoint, the decision between breast-conserving surgery and mastectomy can be made according to the patient's individual preferences and values.-

Adjuvant systemic therapy

After surgery, the next step in the treatment of stages I and II breast cancer may be chemotherapy and/or hormonal therapy. Adjuvant systemic therapy is generally recommended for patients with unfavourable tumour characteristics and a 10-year disease recurrence risk of ≥25%, and when treatment would result in an absolute benefit of ≥10%.[22] Although these adjuvant systemic therapies have been shown to reduce breast cancer recurrence,[33] each of these therapies may cause side effects.[34]

In the Dutch treatment guidelines for BC treatment options, decision-making about adjuvant hormonal therapy is driven by the hormone receptor status and not by the patient's age. With regard to adjuvant chemotherapy, the benefits of this systemic therapy are less clear for patients aged ≥70 years. The guidelines currently recommend that adjuvant chemotherapy may be considered for patients aged ≥70 years who are in good general health.[22]

In general, older patients diagnosed with early breast cancer may benefit from adjuvant systemic therapy,[35,36] however the benefits in this patient group may only be marginal. This means that both accepting and declining the therapies are clinically possible options. As there is no best treatment option, the patient's informed treatment preference in which the benefits and risks are weighed should determine the treatment decision.

Differences in treatment by age

Population-based studies have reported that older patients less often receive standard treatment than younger patients. Despite the fact that the decision between breast-conserving surgery and mastectomy can be made independent of the patient's age,[22] lower rates of breast-conserving surgery in older patients have been observed.[37,38] Also,

radiotherapy is more likely to be omitted after breast-conserving surgery in older patients and they less frequently receive (guideline recommended) adjuvant chemotherapy than younger patients with similar disease severity.[35,39,40] After taking into account differences in patient and tumour characteristics (e.g., comorbid conditions, tumour size), there was still substantial variation between different age groups. This has directed the focus towards the preferences of patients and clinicians as potential important determinants of the decision-making process for older patients.[41]

Older patients' decision-making about breast cancer treatment

Extensive research to date has been performed on the factors that patients with breast cancer consider important when facing a decision between breast-conserving surgery with radiotherapy and mastectomy.[42] Various influencing factors have been found, including fear of cancer recurrence[43] and the impact of the surgery on body image.[44] Studies on the association between age and breast cancer treatment have implied that a patient's preference for a specific treatment option or willingness to undergo treatment is influenced by a patient's age.[45] For example, it is often believed that older patients may attach less importance to body image than younger patients and that they consider several weeks of radiotherapy to be a larger burden,[46,47] and therefore are more likely to prefer mastectomy over breast-conserving surgery. It is also often assumed that many older patients judge that the small possible survival benefits of adjuvant systemic therapy do not outweigh the possible side effects[48] and therefore they are more likely to refuse therapy. Also, it is often thought that older patients' preferences may be based on other aspects than prolongation of life only, for example, on maintaining mobility and independence and quality of life.[47]

Older patients' treatment preferences are however an understudied topic in the field of breast cancer,[47,49] in particular with regard to their preferences for adjuvant systemic therapy. A systematic review of studies on older cancer patients' preferences found that none of the studies focused on adjuvant treatment for breast cancer.[49] The few studies that have concentrated on older patients with breast cancer involved only patients aged ≥65 or ≥70 years,[50-56] making it hard to decide whether the decision-making process of older patients is actually different from that of younger patients. In addition, other studies including breast cancer patients of all ages have generally not aimed to determine age-differences in treatment preferences or in the reasons for choosing one treatment over the other.[57]

Clinicians' decision-making about breast cancer treatment

Clinician preference has also been proposed to strongly influence the treatments that older patients undergo.[58] Firstly, although the majority of patients want to be involved in treatment decision-making, it is often suggested that decision-making role preferences differ by patient

age. Older patients are thought to more often prefer to leave the decision to their clinician,[59-61] thereby indicating that the treatment decision mainly depends on the clinician's preference rather than on the patient's preference. Secondly, there are indications that for their older patient clinicians often make unilateral decisions with regard to which treatment options are relevant based on the patient's chronological age.[62-64] Making decisions without having complete information available about the patient (e.g., comorbid conditions, social situation, concerns and preferences), may not result in a decision that is right for that particular older patient.

Previous research on clinicians' preferences for treatment of older patients has mainly focused on oncologists of one specialty.[65] In the Netherlands, it is nowadays standard of care that treatment plans are discussed in multidisciplinary team meetings.[22] The team constitutes of at least a surgical, a radiation and a medical oncologist who collaborate together to come to a treatment advice that is in their patient's best interest. Each of these different specialties is expected to approach the same patient from their own perspective, which could result in different treatment recommendations.[66] This may be particularly present with regard to older patients, as clinicians can make different interpretations of the clinical evidence, since the benefits to older patients are not clearly defined and since the content of the treatment guidelines leaves room for alternative interpretations. Thus, opinions of the specialists involved in the treatment of older patients also require examination.

Aims of this thesis

FOCUS study

The research in this thesis is part of the FOCUS project (Female breast cancer in the elderly: Optimizing Clinical guidelines Using clinico-pathological and molecular data). This project was funded by a grant of the Dutch Cancer Society in 2007, and aimed to increase knowledge about tumour biology, treatment and survival outcomes of older patients with breast cancer.[67] Amongst others, this resulted in a data set with detailed treatment and patient-related information of more than 3,000 female breast cancer patients of ≥65 years and who were diagnosed in the South West region of the Netherlands between 1997 and 2004.[5-7,18,20,27,39,68-71] During data collection it became apparent that data about the preferences of older patients were largely absent. Consequently, older patients' preferences was added to the FOCUS project as a new research topic.

This thesis

It is often suggested that older patients may have different preferences and motivations than younger patients, because of different life circumstances, values, priorities and medical conditions. However, little attention has been paid to assessing possible differences in the

perspectives of younger and older patients. With the addition of data on older patients' treatment preferences and the factors that distinctively affect their preferences, clinicians will be able to better inform, support and guide older patients in decision-making. To better understand the process of treatment decision-making for older patients, it is also relevant to understand the opinions of their clinicians and which factors of the older patient they consider important when making treatment recommendations.

The overall aim of this thesis therefore is to gain a greater understanding of the preferences of both older patients with early breast cancer and clinicians with regard to treatment, with the first group being the central focus of this thesis.

Outline of this thesis

The first part of this thesis describes the perspectives of patients with early breast cancer on decision-making about surgical and adjuvant systemic therapy. **Chapter 2** presents the results of a systematic literature review which identified studies on patients' preferences for surgery and adjuvant systemic therapy in early breast cancer. PubMed and EMBASE databases were searched up to October 2012. The aim of this systematic review was to provide an overview of the factors that affect patients' preferences for type of surgery and the minimal survival benefit that patients require from adjuvant systemic therapy to consider the therapy worthwhile.

Chapter 3 to 5 report on a prospective study which was carried out among patients with early-stage breast cancer who were scheduled to undergo primary surgery and who were eligible for both breast-conserving surgery and mastectomy. This study had a unique design characteristic where preferences were measured before patients had seen a surgical or medical oncologist to decide upon a treatment plan. Based on a psychological mechanism (i.e., cognitive dissonance reduction or post-hoc justification), individuals may have a strong preference for the treatment they are recommended.[72] To minimize the impact of this phenomenon, we conducted this study in patients who had not yet been informed about their clinician's advice.

Chapter 3 describes the preferences for type of surgery of both younger and older patients, and the factors they consider important when making the decision between breast-conserving surgery with radiotherapy versus mastectomy. Secondarily, older patients' preferences for breast reconstruction following mastectomy are compared to those of younger patients. In **Chapter 4**, we assess whether there are differences in younger and older patients' willingness to undergo adjuvant systemic therapy (i.e., adjuvant chemotherapy and adjuvant hormonal therapy) and their motivations for or against undergoing therapy. **Chapter 5** presents a

comparison of both age groups' preferred and perceived roles in making the decision about surgery and adjuvant systemic therapy.

The final chapter of this thesis focuses on the perspectives of clinicians about treatment of older patients. **Chapter 6** describes the treatment recommendations of breast cancer specialists concerning older patients. Via an anonymous, online questionnaire, we presented hypothetical cases of older patients (aged ≥70 years) to surgical, radiation and medical oncologists to identify how different patient-related characteristics affect their treatment recommendations, and whether the specialties differ in their recommendations.

In **Chapter 7**, the main findings, the implications for clinical practice and health care policy, and the future perspectives for research in this field are discussed. A summary in Dutch of this thesis is given in **Chapter 8**.

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CHAPTER 2

Patients' Preferences for Surgical and Adjuvant Systemic Treatment in Early Breast Cancer: a Systematic Review

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ABSTRACT

Purpose | Treatment decisions in early breast cancer can revolve around type of surgery and whether or not to have adjuvant systemic therapy. This systematic review aims to give an overview of patient self-reported factors affecting preferences for breast-conserving surgery (BCS) versus mastectomy (MAST), the minimal benefit patients require from adjuvant chemotherapy (aCT) and/or adjuvant hormonal therapy (aHT) to consider it worthwhile, and factors influencing this minimally-required benefit.

Methods | PubMed and EMBASE were searched for relevant articles. Two reviewers independently selected articles and extracted data.

Results | We identified 15 studies on surgical and six on adjuvant systemic treatment decision-making. Factors affecting patient preference for BCS most frequently related to body image (44%), while factors influencing preference for MAST most often related to survival/recurrence (46%). To make adjuvant systemic therapy worthwhile, the median required absolute increase in survival rate was 0.1-10% and the median required additional life expectancy was 1 day to 5 years. The range of individual preferences was wide within studies. Participants in the aHT studies required larger median benefits than those in the aCT studies. Factors associated with judging smaller benefits sufficient most often (44%) related to quality of life (e.g., less treatment toxicity).

Conclusion | Decisive factors in patients' preferences for surgery type commonly relate to body image and survival/recurrence. Most participants judged small to moderate benefits sufficient to consider adjuvant systemic therapy worthwhile, but individual preferences varied widely. Clinicians should therefore consider the patient's preferences to tailor their treatment recommendations accordingly.

INTRODUCTION

Breast cancer is the most common cancer in women worldwide and the leading cause of female cancer death. In 2008, an estimated 1.4 million women were diagnosed with breast cancer and more than 450,000 women died from the disease.[1] The European age-adjusted five-year relative survival for all stages is estimated to be 81% (95% CI: 80.2-81.7).[2] The estimated overall ten-year relative survival is 71% (95% CI: 69.9-72.1).[2] A significant proportion of the patients are diagnosed with early-stage invasive breast cancer.[3]

Different treatment options are available for early-stage invasive breast cancer. The majority of newly-diagnosed patients are eligible for two surgical options: breast-conserving surgery (BCS) with radiotherapy, or mastectomy (MAST). Randomized clinical trials with long follow-up periods have demonstrated similar survival rates for women who underwent BCS followed by radiotherapy or MAST.[4,5] Given that both treatment options are equally effective with respect to survival, patient preferences play a decisive role in determining the best treatment decision.

Another treatment decision may relate to systemic therapy following surgery. Adjuvant systemic treatments include chemotherapy and/or hormonal therapy and have been shown to significantly improve disease-free and overall survival,[6] but are associated with several adverse effects. These can negatively impact quality of life. The decision regarding adjuvant systemic therapy therefore involves a marked trade-off between the expected benefits and the potential risks. How patients value the benefits and risks will thus affect their preference for one treatment over the other.

Over the past decade, patient preferences have become an increasingly important determinant of treatment choice due to a greater emphasis on shared decision-making and patient autonomy. Breast cancer patients' involvement in treatment decisions has been shown to improve their satisfaction[7] and short and long-term well-being[8] and to increase their level of comfort with the decision made.[9] More recently, integration of data on patients' preferences into clinical treatment guidelines has been emphasized.[10,11]

Given that BCS with radiotherapy and MAST are equivalent from a strictly medical point of view, insight into the factors that play a decisive role in patients' preferences for surgery type is valuable for making treatment recommendations. Similarly, insight into patients' strength of preference for adjuvant systemic therapy is important to understand patients' willingness to accept such treatment. The aim of this systematic review is therefore twofold. First, to identify which patient self-reported factors influence their preferences for BCS versus MAST. Second, to give an overview of the benefit patients minimally require from adjuvant

chemotherapy (aCT) and/or adjuvant hormonal therapy (aHT) to consider it worthwhile, as well as of determinants of preferences and patient self-reported factors affecting minimally-required benefit.

METHODS

Search strategy

We searched PubMed and EMBASE for articles published between January 1, 1990 and October 2, 2012. Appendix 1 lists the search strings. Also, the reference lists of included articles and relevant review articles[12-16] were hand-searched for additional articles.

Selection criteria

Articles were selected if they (1) were published in English, (2) in a peer-reviewed journal, (3) included early-stage breast cancer patients, and assessed (4) patient self-reported factors affecting preferences for BCS versus MAST, or (5) patients' preferences for aCT and/or aHT. Both quantitative and qualitative studies were eligible for inclusion.

We considered the disease as early-stage if it was stage I/II(A), T_{1-2},N_{0-1},M_0 or invasive T_{1-2}. If not specified, articles were included if the words 'early', 'early stage', or 'early-stage invasive breast cancer' appeared in the sample description and/or article title. Studies also involving other patient or non-patient populations were included if results had been reported specifically for the subgroup of early breast cancer.

Articles regarding surgical treatment decision-making were selected if they (1) reported at least one patient self-reported factor (different than the surgeon's role) that distinguished preferences for BCS (with or without radiotherapy) or MAST, and (2) included participants who had been surgically treated within two years prior to the study.

Articles regarding adjuvant systemic treatment decision-making were included if a probability trade-off method[17] or a similar method was used to determine the strength of patients' preference for aCT and/or aHT. In short, the probability trade-off method requires respondents to consider potential benefits and risks of various treatment options, and the probabilities of obtaining those outcomes.[17] Minimally-required benefit is then determined by systematically increasing or reducing benefit of treatment until participants judge the benefit sufficient to outweigh the risks.

Data selection

Two reviewers (VCH, EB) independently selected articles that met the inclusion criteria based

on titles and abstracts. Next, they screened the full-texts of potentially relevant articles. When multiple articles reported on the same study, the article with the largest sample was included. Agreement about eligibility was achieved during consensus meetings.

Data extraction and analysis

The reviewers independently extracted data on study design (retrospective or prospective), participants, data collection method, time from treatment to study and response rates. If no subgroup details were reported, details regarding the total sample were extracted. Disagreements in data extraction and interpretation were resolved in consensus meetings.

From articles on surgical treatment decision-making, we extracted patient self-reported factors that were significantly ($p<0.05$, in univariable or multivariable analyses) associated with preferences for BCS or MAST, and information about whether these factors were measured through open or closed-ended questions. When articles did not report outcomes quantitatively, or test for statistical significance, all factors that patients reported to influence their preferences for BCS or MAST were extracted, in order to provide a complete as possible overview. The reviewers defined six categories based on the patient self-reported factors retrieved: (1) body image (e.g., wanting to keep one's breast, wanting to minimize scar size), (2) survival/recurrence (e.g., no difference in survival, concern about recurrence), (3) surgeon's opinion (e.g., surgeon's recommendation or preference for a particular type of surgery), (4) psychosocial (e.g., relevance of the breast to feelings of femininity, 'to get it over with'), (5) treatment (e.g., avoiding radiotherapy, recovery), and (6) costs (e.g., concern about costs). Two other reviewers (GJL, AMS) independently assigned the extracted factors to one of the six categories. If they disagreed, a third party (EB) resolved the disagreement. Next, for both BCS and MAST, factors within each category were counted and reported as a percentage of all retrieved factors. Percentages were also reported by study design.

From articles on adjuvant systemic treatment decision-making, details were extracted on the method for eliciting preferences, including how benefits and risks of adjuvant systemic therapy and their probabilities were presented; the minimally-required benefit; and the percentage of participants who would refuse treatment irrespective of treatment benefit. If not reported in the text, data were extracted based on figures or tables. If preferences had been examined at several time points, only the first measurement was extracted. We further extracted factors that patients reported to influence their preferences and determinants that were significantly ($p<0.05$, in univariable or multivariable analyses) related to patient preferences. VCH and EB defined four categories of determinants based on those retrieved: (1) treatment (e.g., having or not having received a particular treatment), (2) socio-demographic characteristics (e.g., age), (3) cognitive/affective factors (e.g., anxiety), and (4) quality of life (e.g., treatment toxicity). GJL and AMS independently assigned determinants to one of the four categories.

Again, EB resolved disagreements about categorization if necessary. Determinants within each category were counted and reported as a percentage of all retrieved determinants.

The quality of the studies examining patients' preferences for adjuvant systemic therapy was assessed using the PREFS checklist.[18] This checklist consists of five criteria: (1) Purpose of the study; (2) Respondent sampling; (3) Explanation of the preference assessment methods; (4) Findings reported for the total sample; and (5) Significance testing (Appendix 2). Studies were assessed against each of the five criteria. An item was scored as 'yes' if the information was present, as 'no' if the information was absent, or as 'unclear' if the information was not adequately reported. The total quality score for each study was calculated by adding the number of positive responses, resulting in a possible score from 0 to 5. In cases of discrepancy, two researchers (VCH and EB) discussed the study until consensus was achieved. As only three out of five criteria were applicable to the factors that influence patients' surgical preferences, we did not use the checklist to assess the quality of those studies.

RESULTS

Our search strategy yielded 3266 unique citations, of which 84 were selected for further review (Figure 1). Of these, 18 articles met the inclusion criteria. Another three articles were included after review of the reference lists of included articles. A total of 21 articles were included: 15 studies examined patient self-reported factors affecting preferences for surgery type and six studies examined patients' preferences for adjuvant systemic treatment.

Surgical treatment decision-making

Characteristics of the studies included

Retrospective studies

Ten studies with a retrospective design were included (Table 1).[19-28] Mean age of the participants ranged from 54 to 61 years[19,20,22,23,28] and their median age ranged from 47 to 58 years.[24-27] Timing of data collection relative to diagnosis or surgery varied widely between the studies. In studies that reported this information, mean time between diagnosis or surgery and the study ranged from one week to five months[21-23,27,28] and median time from diagnosis to study was 19 months.[24] Other studies only reported that factors were assessed after surgery,[26] during adjuvant radiotherapy or after completion of treatment[25] or within two years after surgery.[19]

Prospective studies

Five prospective studies were identified (Table 1).[29-33] Mean age of the participants ranged from 52 to 58 years[29,32] and their median age from 54 to 57 years.[30,33] Four studies[29-31,33] assessed

factors before surgery. The remaining study[32] collected their data before and after surgical treatment, but did not specify at what point in time factors were assessed.

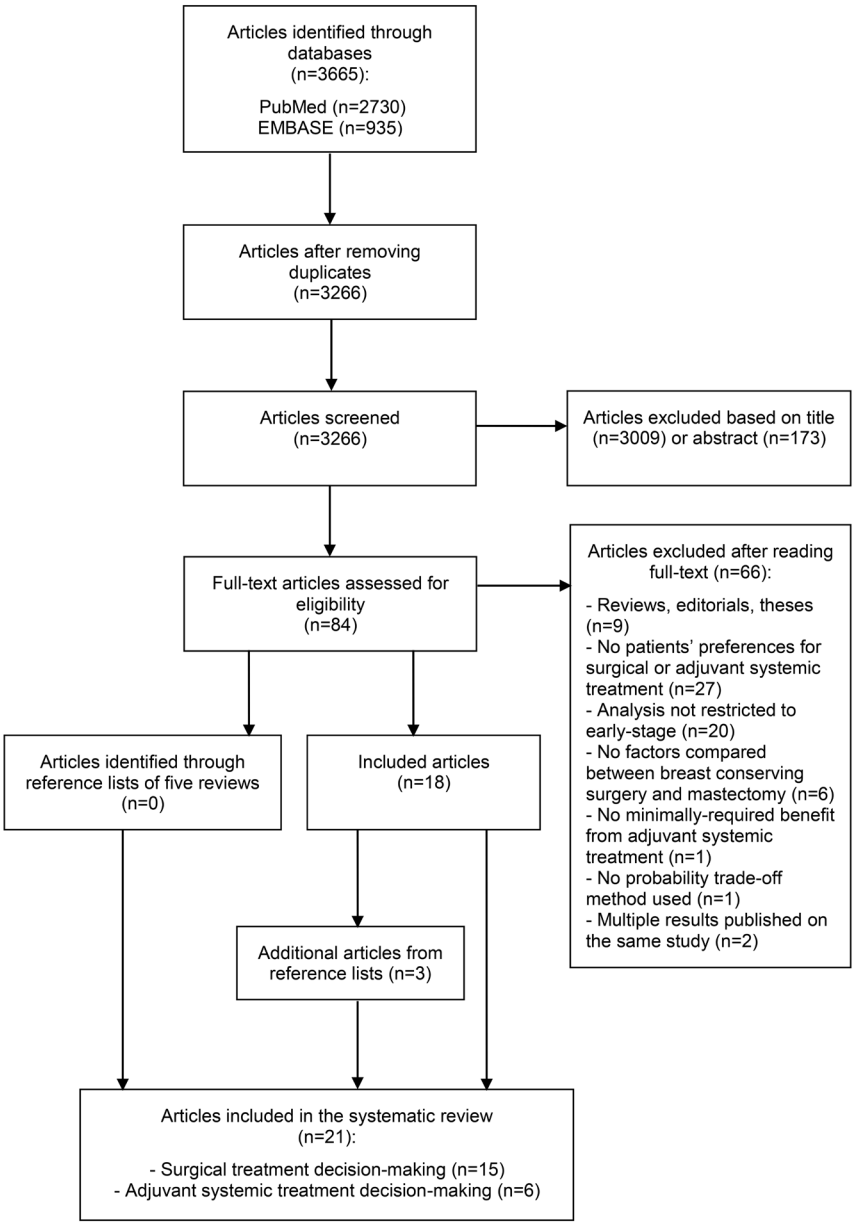

Figure 1. Flow diagram of the literature search and inclusion of articles

Table 1. Description of the studies (N=15) comparing patient self-reported factors affecting their preference for surgery type

First author (year)	Study design	Country (Setting)	Participants	N	Mean age in years (range/ sd)[a]	Data collection method	Time from diagnosis or surgery to study	Response rate
Retrospective (n=10)								
Guadagnoli (1998)[21]	Cohort	USA (Multicenter)	- Early-stage - Diagnosed between 1993-95 in Massachusetts and Minnesota - Identified from hospital pathology offices/ hospital tumor registries - Results described for women who reported that both BCS and MAST were mentioned	Unclear[b]	NR	(telephone) Interview	An average of 3 to 5 months after diagnosis	Massachusetts: 61%[c] Minnesota: 84%[c]
Benedict (2001)[20]	Cohort	USA	- Patients treated between 1995-98 - Selected from mailing lists of community-based cancer groups in two states - Results described for patients who recalled being asked to choose either BCS or MAST without surgeon making a recommendation	54	BCS: 54.2 (35-70) at diagnosis MAST: 57.4 (30-86) at diagnosis	Questionnaire	NR	58% (421/730)
Katz (2001)[22]	Cohort	USA	- All primary DCIS and a 15% random sample of non-metastatic invasive breast cancer - Diagnosed in 1998 - Identified from a SEER registry - Analyses stratified for patients who perceived a choice between BCS and MAST	122	61.4 (30-92)	Questionnaire	Average time between diagnosis and completion of survey was approximately 13 weeks	71% (183/257)[d] 85% (183/215)[e]
Mastaglia (2001)[23]	Population-based	Australia	- Early-stage - Diagnosed between 1 Oct 1996-31 March 1997 - Identified through Cancer Registry	175	57.9 (31-89) BCT: 56.1 (13.88) MAST: 59.3 (13.11)	Questionnaire	Mean time since surgery was 4.3 months (range, 0-8)	49% (175/350)
Schou (2002)[28]	Cohort	Norway (Single center)	- Primary breast cancer, clinically T_{1-2} (<5 cm) - Surgery between Sept 1999-Aug 2001 - Invited by nurse after consultation with surgeon	194	56.7 (21-83) BCS: 54.9 (8.9) MAST: 58.9 (11.7)	Questionnaire	Completed within 1 week after surgery (thus before histology report was available)	79% (194/245)

Sepucha (2007)[24]	Cohort	USA (Multicenter)	- Early-stage - A sample of newly-diagnosed patients and a sample of survivors - Identified through participating physicians of two hospital cancer centers - A pilot study to assess a decision quality measure	35	52.5[a] (32-80)	Questionnaire	Median time since diagnosis was 19 months (range, 2-100)	68% (42/62)
Ballinger (2008)[19]	Cohort	UK (Single center)	- Patients who said being offered a choice between BCS and MAST - Surgery between 2005-06 - Identified using hospital records	97	59.9 (NR) BCS: 56.2 (NR) MAST: 63.5 (NR)	Questionnaire	Within 2 years of surgery	69% (131/189)
Caldon (2011)[27]	Cohort	UK (Multicenter)	- Patients who were eligible for both BCT and MAST - Invited by members of the breast team, as soon as possible after surgery	65	58[a] (33-73)	(face to face) Interview	Mean time since surgery was 6 weeks (range, 1.9-20.6)	Unclear
Agrawal (2012)[25]	Cohort	India (Single center)	- Early-stage - Recruited at a tertiary hospital, after definitive surgical treatment	47	47[a] (NR)	(face to face) Interview	During adjuvant radiotherapy or follow up	NR
Zhang (2012)[26]	Cohort	China (Multicenter)	- Preoperative assessment showing stage I or II - Recruited at five oncology departments of tertiary hospitals - 20.5% (326/1590) did not undergo surgery	1590	48.8[a] (22-77)	Questionnaire	After surgery	88% (1590/1800)
Prospective (n=5)								
Cotton (1991)[30]	Cohort	UK (Single center)	- Primary operable breast cancer - Diagnosed in 1988 - Invited by nurse after diagnosis and outline of surgical options - Results described for patients who were eligible for both BCS and MAST	91	57.4[a] (29-69)	(face to face) Interview	The day before their surgery	Unclear

Kraus (1999)[32]	Cohort	USA (Single center)	- Early-stage - Through breast health center - Contacted by investigator by telephone and at the pre-admission screening site - The primary goal was to describe women's satisfaction with body image before and after BCS or MAST, compared to women without breast cancer	31	52 (29-82)	Questionnaire	Unclear (either 1 week before or 8 weeks after surgery[f])	100%
Molenaar (2004)[33]	Cohort; a quasi-experimental design	The Netherlands (Multicenter)	- Early-stage - Treated between 1996-99 - Were eligible for both BCT and MAST - Invited after diagnosis and treatment options was discussed - All patients received standard information, or a decision aid as a supplement, depending on the period of inclusion	180 Standard: 88 Decision aid: 92	54[a] (29-85)	Questionnaire	Completed before the treatment decision was made or before provision of the decision aid (and before treatment decision was made)	95% (180/189)
Collins (2008)[29]	Cohort	USA (Single center)	- Early-stage - Were eligible for both BCS and MAST - Who had not yet met with a surgeon to discuss surgical options - Diagnosed between Feb 2005-Aug 2007 - Standard practice includes a video decision aid before surgical consultation	125	58 (11.8) BCS: 60 (11.0) MAST: 55 (12.8)	Two questionnaires (one administered by telephone)	At two points in time: (1) after viewing a decision aid, but before surgical consultation, and (2) after surgical consultation	50% (125/249)
Gollop (2009)[31]	Cohort	New Zealand (Multicenter)	- Breast cancer patients - Diagnosed between May 2004-Dec 2006 - Invited after diagnosis and information on surgical options from their surgeon - Analyses stratified for patients who were eligible for both BCT and MAST	135	NR	Questionnaire	Completed preoperatively	Unclear

NR: not reported; BCS: Breast-conserving surgery; MAST: Mastectomy; BCT: Breast-conserving therapy (breast-conserving surgery with radiotherapy); DCIS: Ductal carcinoma in situ

[a] Median

[b] A total of 1570 participants were interviewed, but the number of participants in the subgroup analysis was unclear

[c] Response rate after exclusion of women who missed the informed consent procedure, women who had language difficulties or were not located

[d] Response rate among women who were eligible for the study

[e] Response rate among women who received a questionnaire

[f] Unclear at which of the two points in time factors were assessed

Assessment of patient self-reported factors

Retrospective studies

Three studies[20,25,26] did not clearly report if they assessed patient self-reported factors through open or closed-ended questions. Two studies[21,27] used open-ended questions to assess factors and five studies[19,22-24,28] asked participants to rate the importance of predefined factors, varying from four to 17 items, on a Likert-type scale. These studies derived factors from the literature only,[22,23,28] or also from reports on focus groups and interviews with patients and providers,[24] or from consultations with a breast cancer self-help group.[19]

Prospective studies

Two studies[30,32] examined factors using open-ended questions. In the other three studies,[29,31,33] participants had to rate the importance of predefined factors on a Likert-type scale. The number of items varied from five to eight and they were based on a decision aid,[29,33] or were self-designed.[31]

Patient self-reported factors affecting their preference for BCS or MAST

Overall, 77 factors that affected patients' preferences for BCS (36 factors, Table 2) or MAST (41 factors, Table 3) were identified. The reviewers assigned 58 (75%) factors to the same category. They disagreed with the categorization of 19 factors (25%). Thus, the third party resolved the categorization of these factors.

Overall, 44% of the factors relating to preferring BCS involved body image (Table 2). The remaining factors related to survival/recurrence (17%), treatment (17%), psychosocial factors (11%) and surgeon's opinion (11%). In retrospective studies, body image-related factors were most frequently (40%) reported to affect patients' preferences. In the prospective studies, this predominance was even more pronounced (67%).

Overall, factors influencing preference for MAST most often related to survival/recurrence (46%) and treatment (39%) (Table 3). Specifically, most treatment-related factors revolved around radiotherapy. The remaining factors involved psychosocial factors (7%), surgeon's opinion (5%) and costs (2%). Body image was not reported to affect preference for MAST. Factors relating to survival/recurrence and treatment most strongly affected preferences, both in studies using a retrospective (43% versus 39%) and prospective (54% versus 38%) design.

Table 2. Number of factors reported (N=36) to affect patients' preferences for breast-conserving surgery (BCS)

First author	Body Image	Survival/ Recurrence	Surgeon's opinion	Psycho-social	Treatment	Costs
Retrospective (n=30 factors)						
Guadagnoli[21 a]			1			
Benedict[20 a]	1	1			1	
Katz[22 b,e]	1			1		
Mastaglia[23 d]		1	1			
Schou[28 d]	1			1		
Sepucha[24 d]	1					
Ballinger[19 d]	3				1	
Caldon[27 a]	3	1			1	
Agrawal[25 a]	1	1	1			
Zhang[26 a]	1	1		2	3	
Total, n (%):	12 (40)	5 (17)	3 (10)	4 (13)	6 (20)	0 (0)
Prospective (n=6 factors)						
Cotton[30 a]	1					
Kraus[32 a]	1	1				
Molenaar[33 c,d]	1					
Collins[29 e]	1					
Gollop[31 e]			1			
Total, n (%):	4 (67)	1 (17)	1 (17)	0 (0)	0 (0)	0 (0)
Overall, N (%):	**16 (44)**	**6 (17)**	**4 (11)**	**4 (11)**	**6 (17)**	**0 (0)**

[a] The study did not statistically test for significant differences
[b] No significant differences in factors between participants with ductal carcinoma in situ and invasive breast cancer
[c] No significant differences in factors between participants who received the decision aid and those who did not
[d] All factors were tested in univariable analysis only
[e] All factors were tested in multivariable analysis only

Table 3. Number of factors reported (N=41) to affect patients' preferences for mastectomy (MAST)

First author	Body Image	Survival/ Recurrence	Surgeon's opinion	Psycho-social	Treatment	Costs
Retrospective (n=28 factors)						
Guadagnoli et al.[21 a]		1	1			
Benedict et al.[20 a]		2			2	
Katz et al.[22 b,e]		2			2	
Schou et al.[28 d]		1				
Sepucha et al.[24 d]					1	
Ballinger et al[19 d]		1			2	
Caldon et al.[27 a]		2			2	
Agrawal et al.[25 a]		1	1			
Zhang et al.[26 a]		2		2	2	1
Total, n (%):	0 (0)	12 (43)	2 (7)	2 (7)	11 (39)	1 (4)
Prospective (n=13 factors)						
Cotton et al.[30 a]		2		1	1	
Kraus et al.[32 a]		2			1	
Molenaar et al.[33 c,d]		1			1	
Collins et al.[29 e]		1			1	
Gollop et al.[31 e]		1			1	
Total, n (%):	0 (0)	7 (54)	0 (0)	1 (8)	5 (38)	0 (0)
Overall, N (%):	**0 (0)**	**19 (46)**	**2 (5)**	**3 (7)**	**16 (39)**	**1 (2)**

[a] The study did not statistically test for significant differences
[b] No significant differences in factors between participants with ductal carcinoma in situ and invasive breast cancer
[c] No significant differences in factors between participants who received the decision aid and those who did not
[d] All factors were tested in univariable analysis only
[e] All factors were tested in multivariable analysis only

Adjuvant systemic treatment decision-making

Characteristics of the studies investigating patient preferences for adjuvant chemotherapy

Three retrospective studies[34-36] and one prospective study[37] were included (Table 4). Mean age of the patients ranged from 42 to 54 years[35,37] and the median age from 49 to 55 years.[34,36] Two studies[34,36] reported they included patients who had been treated with aCT, but in one[36] it was unclear whether a proportion (<1%) of the participants did receive aCT. The remaining retrospective study included patients with and without aCT experience.[35] The prospective study specifically aimed to compare preferences between patients who were about to start aCT (50%) versus those who would not undergo aCT (50%).[37] The quality assessment of the studies is presented in Table 4. Three studies were considered to be of high quality[34,35,37] (scoring four out of five criteria) and one study[36] was judged to be of low quality (two out of five).

Table 4. Description of the studies (N=6) examining patients' preferences for adjuvant systemic treatment

First author (year)	Study design	Country (Setting)	Participants	N	Mean age in years (range/sd)[a]	Data collection method	Time from aT to study	Response rate	Quality score (0-5)[b]	P	R	E	F	S
aCT (n=4)														
Lindley (1998)[35]	Retrospective, cohort study	USA	- Early-stage - Completed aT between 1988-91 and were disease-free - Review of records of a breast cancer program - 36% (31/86) did not undergo aCT	86	54 (29-86)	Questionnaire and (telephone) Interview	>2 years from completion of aT	72% (86/120)	4	√		√	√	√
Simes (2001)[36]	Retrospective, cohort study	Australia (Single center)	- Early-stage - Recruited in participating clinic between Nov 1986-Dec 1987 - Unclear whether <1% had received aCT	104	49[a] (25-67) at time of interview	(face to face) Interview	≥3 months after completion of aCT	81% (104/129)	2			√		√
Duric (2005)[34]	Retrospective, cohort study	Australia (Multicenter)	- Early-stage - Recruited in participating clinics	97	55[a] (25-69) at time of interview	(face to face) Interview	Average time between finishing aCT and interview was 17 months (range, 3-34)	86% (131/152)	4	√		√	√	√
Jansen (2001)[37]	Prospective, cohort study	The Netherlands (Multicenter)	- Early-stage - Recruited in hospitals between June 1996-Nov 1999 - Two patient groups: patients scheduled for aCT and patients not scheduled for aCT	76 aCT: 38 no-aCT: 38	aCT: 42 (29-50) no-aCT: 55 (38-77)	(face to face) Interview	Before start of aCT and at a similar point in time in the no-aCT group	54% (38/71)	4	√		√	√	√

aHT (n=2)													
Duric (2005)[38]	Retrospective, cohort study	UK (Multicenter)	- Early-stage - Premenopausal - Had been treated with tamoxifen, goserelin, or both, in a randomized trial (goal was to evaluate 2 years of aHTs in women ≤50 years) - 8% (7/85) did not undergo aHT	85	45[a] (31-54) at time of interview	(face to face) Interview	6-30 months after finishing aHT	71% (85/120)	4	√	√	√	√
Thewes (2005)[39]	Retrospective, cohort study	Australia	- Early-stage - Premenopausal - Had been treated with tamoxifen, goserelin, or both (with or without oophorectomy) for ≥3 months - Majority still treated at the time of the study - Review of databases of clinics	102	36 (sd, 3) at time of diagnosis	(face to face) Interview	Mean time since diagnosis was 27 months (sd, 5)	75% (102/137)	3	√	√		√

aT: Adjuvant systemic therapy; aCT: Adjuvant chemotherapy; aHT: Adjuvant hormonal therapy; [a] Median; [b] Quality assessment according to the PREFS checklist; P: Purpose; R: Respondents; E: Explanation; F: Findings; S: Significance; √: the criterion was met

Assessment of patient preferences for adjuvant chemotherapy

All four studies presented participants with two treatment strategies: treatment with aCT versus treatment without aCT. Descriptions of potential risks of aCT varied between the studies. In two studies,[34,36] patients were asked to state their preference based on their own experiences with aCT. The other studies[35,37] gave patients information about the risks of aCT regardless of the patient's experience or treatment plan. The studies differed in how much detail they gave about aCT schedules, e.g., describing aCT as a six-month therapy,[34,36] or as an outpatient administration of one cycle of therapy per month for six months.[35,37] In the studies, the benefit of aCT was expressed as an increased probability of cure[35] or (disease-free[37]) survival,[34,36] or in terms of additional life expectancy.[34-36] In all studies, the survival probabilities or life expectancies for both treatment options was made explicit. Three studies used probability of survival without aCT as starting point, and then asked participants what additional benefit of aCT they would require to make it worthwhile.[34,36,37] In contrast, in Lindley et al.[35] the starting point was probability of survival with aCT and likelihood of survival without aCT was systematically decreased.

Median required increase in survival rate from adjuvant chemotherapy

Table 5 summarizes the minimum absolute increase in survival rate that participants considered sufficient to make aCT worthwhile. The median required benefit ranged from 0.1% to 7%. Required benefit seemed to be independent of baseline survival probabilities.[34-36] Although most participants judged small benefits sufficient to make aCT worthwhile, individual preferences varied widely within each study. Additionally, 2-19% of the participants would refuse aCT irrespective of benefit. Jansen et al.[37] observed that most patients who were scheduled for aCT would accept it for significantly less benefit than patients who were not scheduled for aCT (median required benefits: 1% versus 12%). Moreover, a higher proportion of patients would accept aCT for no (0%) benefit in those who were scheduled for aCT than in those who would not undergo aCT (39% versus 8%). Similarly, Lindley et al.[35] showed that for each scenario, patients who had been treated with aCT were significantly more willing to accept aCT than patients who had not been treated with aCT.

Median required additional life expectancy from adjuvant chemotherapy

Three studies assessed patients' preferences in terms of additional life expectancy (Table 5).[34-36] Most participants considered small increases, ranging from 1 additional day to 0.8 additional years, sufficient to make aCT worthwhile. Simes et al.[36] reported that participants required larger benefits on the longer (15 years) versus shorter (5 years) term. Variation in individual preferences was large within the studies and 1-10% would refuse aCT irrespective of benefit. Again, Lindley et al.[35] observed that the proportion of patients who would accept aCT was higher in those treated with aCT than those without such treatment experience.

Table 5. Minimum increase in survival rate and life expectancy that participants considered worthwhile

First author	Minimum increase in survival rate				Minimum increase in life time				Significant determinants of preferences[f]
	5-year survival rate without aT (%)	Median desired increase (%)	Range (%)	Participants unwilling to accept aT(%)	Life expectancy without aT (yrs)	Median desired increase	Range	Participants unwilling to accept aT(%)	
aCT (n=4)									
Retrospective studies									
Lindley[35 g]	95[a] 75[a] 50[a]	5 5 5	5-25[b] 5-25[b] 5-25[b]	11 12 13	5[c]	6 m	1-24 m[d]	10	- Less life disruption during aCT (Q) - Having had previous aCT (T)
Simes[36 h]	65 85	2 2	>0-25 >0-15	2 3	5 15	0.6 yrs 0.8 yrs	>0-15 yrs >0-5 yrs	1 9	- Less treatment toxicity (Q) - Received a full dose of aCT(T) - Not received radiotherapy (T) - Had better social support (S) - Had others at home dependent on their support (S)
Duric[34 h]	65 85	0.1 0.1	0.1-35 0.1-15	0 3	5 15	1 d 1 d	1 d-20 yrs 1 d-20 yrs	2 4	- Recalled being less troubled by nausea[i] (Q), fatigue[i] (Q), altered sense of taste[i] (Q), or hair loss[i] (Q), - Recalled a better appetite[i] (Q), emotional[i] (Q), physical (Q) and overall well-being (Q) during aCT - Recalled being less troubled by problems with needles or injections[i] (T) - Recalled being less troubled by anxiety[i] (C), problems concentrating[i] (C), thought of actually having aCT[i] (C), or problems coping with aCT[i] (C) - Had a friend or relative who died from cancer (C) - Had dependents (S) - Had support available at all times during aCT[i] (S)
Prospective studies									
Jansen[37 g]	80[e]	7	0-20	19	NS	NS	NS	NS	- Scheduled for aCT (T)
aCT no-aCT		1 12	0-20 0-20	3 34					

aHT (n=2)									
Retrospective studies									
Duric[38 h]	60	10	1-40	0	5	3 yrs	1 d-20 yrs	0	- Less treatment toxicity (Q)
	80	10	1-20	0	15	5 yrs	1 d-30 yrs	0	- Had tamoxifen (with or without goserelin) (T)
Thewes[39 h]	65	2	0-35	2	5	3 m	0-15 yrs	0	- Less treatment toxicity (Q)
	85	2	0-15	7	15	6 m	0-15 yrs	1	

aT: Adjuvant systemic therapy; aCT: Adjuvant chemotherapy; aHT: Adjuvant hormonal therapy; NS: not studied; d: days; m: months; yrs: years; Q): factor related to quality of life; (T) treatment-related factor; (C) cognitive/ affective-related factor; (S) factor related to socio-demographic characteristics

As an example, in Simes and Coates[36] approximately half of the participants considered aCT to be worthwhile for an absolute increase in survival of 2%, in addition to a 5-year survival rate of 65% without aCT. Thus, most participants would accept aCT if the 5-year survival rate with aCT was 67% (65+2%). In this scenario, the required benefit ranged from more than 0 to 25%. Two per cent of the respondents indicated that they would refuse aCT irrespective of benefit. In the other scenario, a 5-year survival rate of 85% without aCT, the median required benefit was also 2% and the required benefits ranged from >0-15%. Three per cent of the respondents would refuse aCT. In the same study, most participants required an absolute gain of 0.6 years, if the life expectancy was 5 years without aCT. The required benefit ranged from >0-15 years. One per cent of the respondents indicated that they would refuse aCT, irrespective of a maximum benefit of 15 years in that scenario. In another scenario, if the life expectancy was 15 years without aCT, the median required benefit was 0.8 years in this study. In that scenario, the minimally-required benefit ranged from >0-5 years. Nine per cent would refuse aCT irrespective of benefit.

[a] Starting point was a survival rate with aCT, survival time was not reported
[b] The minimum benefit was set at a gain of 5% and the maximum benefit at 25%
[c] Starting point was a 5-year life expectancy with aCT
[d] The minimum benefit was set at a gain of three months and the maximum benefit at a gain of 24 months
[e] 5-year disease-free survival rate without aCT
[f] Factors significantly associated with judging smaller benefits sufficient to consider adjuvant systemic therapy worthwhile
[g] All factors were tested in univariable analysis only
[h] All factors were tested in univariable and multivariable analyses
[i] The factor was significant in univariable analysis only

Characteristics of studies investigating patient preferences for adjuvant hormonal therapy

Table 4 describes the characteristics of two retrospective aHT studies.[38,39] Both studies included only premenopausal patients. In Thewes et al.[39], most participants were undergoing aHT during the study. In Duric et al.[38] 7% of the participants had not been treated with aHT, but were included in the analyses. The studies were considered to be of medium[39] (scoring three out of five criteria) and high[38] (four out of five) quality, respectively (Table 4).

Assessment of patient preferences for adjuvant hormonal therapy

The aHT studies used similar methods as those used in two aCT studies.[34,36] In short, participants were asked to choose between treatment with aHT versus treatment without aHT based on their personal experience. In Duric et al.[38], those participants without aHT experience received information about the potential side effects of aHT. The studies explored patients' preferences for both survival rate and life expectancies scenarios (5 versus 15 years).

Median required increase in survival rate from adjuvant hormonal therapy

In Thewes et al.[39], most participants judged small (2%) benefits sufficient to make aHT worthwhile, while in Duric et al.[38], the majority required moderate (10%) benefits (Table 5). In both studies, the range in individual preferences was wide. In Thewes et al.[39], 5% of the participants would consider the treatment worthwhile for a benefit of 0%, while 2-7% would refuse aHT irrespective of benefit.

Median required additional life expectancy from adjuvant hormonal therapy

Table 5 also shows the minimum absolute increase in life expectancy judged sufficient to consider aHT worthwhile. While Thewes et al.[39] reported that most participants required an additional 3-6 months to consider aHT worthwhile, Duric et al.[38] observed larger (an additional 3-5 years) median required benefits. Both studies reported larger median required benefits in the 15-year versus the 5-year life expectancy scenario. Individual preferences varied greatly within the studies. Thewes et al.[39] reported that few participants (4-5%) would accept aHT at no benefit, while 1% would refuse aHT irrespective of benefit.

Factors affecting patient preferences for adjuvant systemic treatment

Determinants of patient preferences

All six studies examined associations between patient characteristics and treatment preference. The number of determinants examined varied from nine to 37. Altogether, the studies reported 27 significant determinants of patient preferences (24 for aCT and three for aHT, Table 5). The reviewers assigned 78% (21/27) of the determinants to the same category. The third party resolved the categorization of the other six determinants (22%).

Most significant determinants related to quality of life (12/27, 44%). The remaining determinants related to treatment (6/27, 22%), cognitive/affective factors (5/27, 19%) and socio-demographic characteristics (4/27, 15%). As shown in Table 5, significant determinants of preference varied between the studies. Additionally, some determinants were not consistently associated with treatment preference. For example, two[34,36] out of five studies[34,36-39] found that having dependents was significantly associated with judging smaller benefits worthwhile. Another socio-demographic factor with no consistent significant association included having (better[36]) social support.[34] As described earlier, the prospective study[37] ascertained a significant association between being versus not being scheduled for aCT and preferences for the therapy. This study found no other significant associations.

Patient self-reported factors influencing their preferences

Thewes et al.[39] qualitatively explored factors that patients reported had influenced their treatment preferences and found three main factors: (1) altruism (e.g., the belief that accepting treatment would increase knowledge and therefore benefit future patients), (2) a sense of control, or the idea of doing something to deal with the disease, and (3) the belief that accepting treatment could offer benefits that are not yet fully known.

DISCUSSION

Our systematic review of patient preferences for breast-conserving surgery (BCS) versus mastectomy (MAST) and the benefit patients minimally require from adjuvant chemotherapy (aCT) and/or adjuvant hormonal therapy (aHT) to consider it worthwhile, show that patients who prefer one or the other type of surgery are driven by different motives and that patients' preferences for adjuvant systemic therapy widely vary.

Surgical treatment decision-making

Patients who prefer BCS are predominantly driven by body image, while for patients who prefer MAST survival and/or recurrence is the most prominent factor. It is disturbing that survival was a driving factor in preferring MAST over BCS, because survival probabilities are the same, regardless of surgery type, in early breast cancer. Possible explanations are that women were not informed about the equivalent survival rates or that the information was unconvincing.

As one may expect, factors determining preferences varied according to whether they were assessed prospectively or retrospectively. Prospective assessment of factors revealed that body image and survival/recurrence determined patient preferences for, respectively, BCS or MAST. Retrospectively, other factors, and mainly those related to treatment, were influential

as well. In those who have undergone treatment, this experience may well outrank factors that determined preferences when the decision was made.

Adjuvant systemic treatment decision-making

Most patients judged small to moderate benefits sufficient to consider adjuvant systemic therapy worthwhile. However, studies reported that some patients would accept treatment for little or no benefit, while others would refuse treatment no matter the benefit. Determinants most consistently associated with patient preferences, once patients had experienced the treatment, related to quality of life. Patients were more willing to accept therapy if they had experienced better well-being during the particular adjuvant systemic therapy.

Our review revealed that clinical characteristics (e.g., nodal status) did not predict patients' preferences, nor did socio-demographic factors. These findings imply that it is difficult to predict individual preferences based on disease or socio-demographic characteristics. One retrospective study[39] qualitatively explored patients' motives and found other factors (e.g., doing something to deal with their disease). It is possible that such motives better explain patients' treatment preferences. Hence, future research should examine potential determinants beyond socio-demographic or disease characteristics, and preferably in a prospective manner in order to be able to generalize findings to new patients.

Interestingly, one aHT study found higher median required benefits than those reported by the aCT studies. At first sight this is surprising, as it is commonly assumed that patients perceive the side effects of aHT to be milder compared to aCT. Yet, the results cannot be easily compared because the aHT studies involved premenopausal patients who were significantly younger than patients in the aCT studies. At the same time, the results are in line with recent studies showing that some breast cancer patients who had received aHT did not consider its efficacy to outweigh its side effects.[40,41] Clearly, clinicians should not underestimate how impactful patients can perceive side effects of aHT. To examine how differently patients value the risks and benefits of these therapies, further research could examine preferences for aCT and aHT within the same patient population.

Limitations and future research

Some limitations of the included studies should be noted. Most studies were retrospective or carried out after a treatment decision had been made. As a result, findings most probably were influenced by patients' need for so-called 'cognitive dissonance reduction'. According to this theory, individuals have a tendency to reduce inconsistencies between previous decisions, in this case the treatment decision, and current beliefs or treatment preferences.[42] Thus, patients are expected to have adjusted their current beliefs about treatments in favor

of the treatment they received or would undergo. Therefore, generalization of the findings to patients who are facing a treatment decision should be done with caution. We recommend that future studies are carried out before the treatment decision is made to exclude this cognitive dissonance reduction and to be better able to generalize the findings to new patients.

Regarding surgical treatment decision-making, it is important to note that in most studies, patients were asked to rate the importance of a predetermined list of items. A possible drawback of this method is that it does not invite participants to identify other factors. Nevertheless, studies that used open-ended questions to elicit factors reported factors that were very much comparable to those from the predetermined lists.

Remarkably, none of the aHT studies included postmenopausal patients. Future research should focus on this patient group, as a majority have hormone receptor-positive disease and are eligible for aHT. Furthermore, it has been shown that aHTs in older patients have increased over time.[43]

Furthermore, only one study[28] addressed preferences of patients aged 65 years and older; it found that fear of recurrence and the need for additional treatment (e.g., radiotherapy) most frequently affected older (≥70 years) patients' preference for MAST. We identified a few studies[44-49] that examined treatment decision-making in older breast cancer patients, but they did not meet our inclusion criteria. These studies showed that fear of recurrence,[45] the surgeon's recommendation,[45] and wanting no additional therapy beyond surgery[47] influenced older patients' preference for MAST. Body image[45,47] and equivalence of survival rates[45] affected preference for BCS. Others examined whether factors affecting surgical decision-making differed by age[44,48] and showed that older patients were less concerned about body image,[44,48] recurrence,[44,48] or work-related issues[48] than younger patients. Interestingly, one study[48] found that older versus younger patients were more concerned about transportation, while others[44] reported that frequent trips for radiotherapy were of greater concern to younger patients. Considering the increasing number of older breast cancer patients,[50] preferences in this population should be further explored, especially since current disease management in older patients can involve aCT. To date, the evidence is inconclusive as to whether older patients would require greater survival gains from aCT than younger patients, to consider it worthwhile.[46,49,51-53]

Clinical implications

The large variation in patients' preferences and factors influencing their preferences suggests that individual patient views and preferences should be sought and incorporated in treatment decisions. Clinicians should inform patients about all available treatment options

and discuss the benefits and risks with each patient. Body image and survival/recurrence are important issues that should be addressed during consultations between patients and their surgeon. Additionally, clinicians should explicitly ask the patient which potential benefits and risks she considers important, and correct possible misconceptions about breast cancer and treatment. By identifying patient preferences, clinicians will be better able to tailor treatment recommendations to the needs, values and priorities of individual patients.

Conclusion

Breast cancer patients' preferences for surgery type most frequently relate to body image and survival/recurrence. Most patients considered small to moderate benefits sufficient to make adjuvant systemic therapy worthwhile, however patient's preferences varied widely and some patients would accept adjuvant systemic therapy for no benefit. Additional studies are needed that focus on older and postmenopausal patients and that assess determinants and preferences before the treatment decision is made.

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APPENDIX 1. Search strategy per database	
Database	**Search strategy**
PubMed	("Patient Preference"[MeSH] OR "patient preference"[ti] OR (Patients'[ti] AND preferences[ti]) OR "patient preferences"[ti] OR (Patients'[ti] AND preference[ti]) OR "prefer"[ti] OR "preferred"[ti] OR "preference"[ti] OR "preferences"[ti] OR "Choice"[ti] OR "choices"[ti] OR "choose"[ti] OR "decision"[ti] OR "decide"[ti] OR "Choice Behavior"[MeSH:NoExp] OR "Patient Education as Topic"[Majr] OR "Decision Making"[Mesh] OR "Patient Satisfaction"[Majr]) AND ("Breast Neoplasms"[Mesh] OR ((breast*[tiab] OR mammary[tiab]) AND (neoplasm*[tiab] OR tumor[tiab] OR tumors[tiab] OR tumour*[tiab] OR cancer*[tiab] OR carcinoma*[tiab]))) AND ("therapy"[Subheading] OR "therapy"[All Fields] OR "therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapeutic"[All Fields] OR "treatment"[All Fields] OR "mastectomy, simple"[MeSH Terms] OR "mastectomy"[All Fields] OR "mastectomy"[MeSH Terms] OR "surgery"[Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR "surgical"[All Fields] OR "general surgery"[MeSH Terms] OR "breast conserving"[All Fields] OR "lumpectomy"[All Fields] OR "drug therapy"[Subheading] OR "chemotherapy"[All Fields] OR "drug therapy"[MeSH Terms] OR "radiotherapy"[Subheading] OR "radiotherapy"[All Fields] OR "radiotherapy"[MeSH Terms] OR "adjuvants, pharmaceutic"[MeSH Terms] OR "adjuvants"[All Fields] OR "adjuvant"[All Fields] OR "adjuvants, immunologic"[Pharmacological Action] OR "hormonal"[All Fields] OR "hormones"[MeSH Terms] OR "hormones"[All Fields] OR "hormone"[All Fields] OR "hormones"[Pharmacological Action] OR "reconstructive surgical procedures"[MeSH Terms] OR "reconstructive surgical procedures"[All Fields] OR "reconstruction"[All Fields])
EMBASE	(patient* preference*.mp. OR exp patient preference/ OR ((patient*.ti.) AND ("prefer".ti. OR "preferred".ti. OR preference*.ti. OR Choice*.ti. OR "choose".ti. OR "decision*".ti. OR "decide".ti.)) OR exp *Decision Making/ OR exp *Patient Satisfaction/) AND (exp breast tumor/ OR ((breast*.ti,ab. OR mammary.ti,ab.) AND (neoplasm*.ti,ab. OR tumor*.ti,ab. OR tumour*.ti,ab. OR cancer*.ti,ab. OR carcinoma*.ti,ab.))) AND (exp "therapy"/ or therapy.mp. OR "therapeutic*".mp. or "treatment".mp. or exp mastectomy/ or "mastectomy".mp. or exp surgery/ or "surgery".mp. or exp surgical technique/ or "surgical".mp. or "breast conserving".mp. or "lumpectomy".mp. or exp chemotherapy/ or "chemotherapy".mp. or exp drug therapy/ or "drug therapy".mp. or exp radiotherapy/ or "radiotherapy".mp. OR adjuvant*.mp. or exp cancer adjuvant therapy/ or exp adjuvant therapy/ or exp adjuvant chemotherapy/ OR hormon*.mp. or exp hormone/ OR exp breast reconstruction/ or reconstructi*.mp.)

APPENDIX 2. PREFS checklist for assessing quality[18]		
Question	**No/not clear**	**Yes**
(1) Purpose: Is the purpose of the study in relation to preferences clearly stated?	The purpose/research question/ objectives/aim doesnot mention preference, but may mention satisfaction, quality of life, ratings, acceptance	Any reference in the research question/ objectives/aim to preference, utility/disutility, willingness to pay, importance, priorities, goals, revealed preference (e.g., choice to continue)
(2) Respondents: Are the responders similar to the non-responders?	Evidence of significant differences OR No assessment of the difference between responders and non-responders OR Responders are compared only to a target population rather than non-responders	Any evidence that the responders do not differ significantly from the non-responders
(3) Explanation: Are methods of assessing preferences clearly explained?	The question(s) or response options are not clear	The actual preference question is reported in the text or an appendix, or if it is referenced and available elsewhere, and if it is clear what response options were available to respondents, even if the mode of the question (e.g., written, oral, online) is not clear OR For studies with multiple questions relating to preferences such as conjoint/discrete choice studies, it is clear what was presented to respondents and what responses were available
(4) Findings: Were all respondents included in the reported findings and analysis of preference results?	Some responses are excluded from the analysis and the possibility of this introducing systematic bias has not been ruled out OR It is not clear whether all respondents were included in the analysis	All respondents who completed the preference question were included in the analysis OR For studies with multiple questions relating to preferences such as conjoint/discrete choice studies, all respondents who at least partially completed the preference questions were included in the analysis OR If some respondents who at least partially completed the preference questions were excluded from the analysis (e.g., non-traders, lexicographic preferences, failed test question, irrational preferences, did not complete) AND there is any evidence that those excluded do not differ significantly from those included
(5) Significance: Were significance tests used to assess the preference results?	The study reports only proportions, counts, graphs, etc.	The study reports p values, p value ranges (e.g., $p<0.05$), confidence intervals, means with standard deviations or standard errors in relation to the preference results (e.g., testing the preference hypotheses or study objectives)

CHAPTER 3

A Prospective Comparison of Younger and Older Patients' Preferences for Breast-Conserving Surgery versus Mastectomy in Early Breast Cancer

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To the Editor,

Older women with breast cancer (BC) currently comprise about 40% of all new cases, and this percentage will increase in coming decades.[1] Most early BC patients are eligible for either mastectomy (MAST) or breast conserving-surgery (BCS). These treatments are equivalent in terms of survival rates,[2] but differ in cosmetic outcome, use of additional surgery or radiotherapy, and local recurrence. Patient age is not a contraindication for BCS,[3] but older patients less frequently undergo BCS than younger patients.[4] This variation by age remains after accounting for clinical and nonclinical factors (e.g., tumour stage, comorbidities).[4] An explanation may be different patient preferences. Given older patients' higher occurrence of medical and nonmedical challenges (e.g., limited transportation access),[3] their preferences may differ from those of younger patients. They may also value the impact of treatment (on e.g., body image) differently.

Older patients also less often undergo breast reconstruction following MAST.[5] Although the procedure is suggested to be safe for older patients with comparable complication rates and quality of life improvements as in younger patients,[5] older patients are thought to more often decline reconstruction.[5] However, little is known about their preferences.

Age-differences in treatment decision-making have received little attention.[6] Most studies identified which factors influenced patients' choice for type of surgery. Other studies were restricted to older patients, thereby making it difficult to determine whether the decisive factors count only in older patients. A shortcoming of most studies is that they assessed preferences after surgery, or after the treatment decision had been made.[6] Consequently, cognitive justification may account for patients' strong preference in these studies for the treatment they received or were recommended.[7] The findings may therefore not reflect the preferences of patients facing the decision.

We prospectively compared younger versus older patients' surgical treatment preferences, influencing factors and preferences for breast reconstruction.

METHODS

Participants

Eligible patients had a first primary ductal carcinoma in situ or T_{1-2} invasive disease and were candidates for both BCS with radiotherapy and MAST. Exclusion criteria were bilateral tumour, *BRCA 1/2* mutation, malignancy within the past five years, poor proficiency in Dutch, mental/cognitive problems, neo-adjuvant therapy, and metastatic disease. Participants were

recruited in three (academic and non-academic) hospitals from January 2012-December 2013. The Medical Ethical Committee of the Leiden University Medical Center and the review boards of the participating hospitals approved the study. All patients provided informed consent.

Patients were approached after having been informed about their diagnosis in the first surgical consultation. The surgeons were instructed to discuss the benefits and risks of each option in their usual fashion, but were asked to explicitly mention that the patient had a choice between BCS and MAST, and to not direct the patient towards one or the other option. At the end of the consultation, the surgeon handed out a questionnaire and asked the patient to complete it shortly after the consultation. During the second surgical consultation, the surgeon discusses the options again and gives a recommendation for either surgical option. To prevent the surgeon's recommendation from influencing the participant's preference, participants were asked to complete the questionnaire before the second consultation.

Measures and analyses

The questionnaire included a one-page overview of the differences in the main features of BCS and MAST (Appendix A.1). Except that both options have equivalent survival rates, similarities were not presented (e.g., indication for systemic therapy), to limit the amount of information and because we expected that this information would not influence the participant's choice. Participants were then asked: *'Imagine that both BCS (with radiotherapy) and MAST were available options, which type of surgery would you prefer?'* The response scale ranged from (1) *definitely prefer BCS with radiotherapy*, to (3) *no preference for either option*, to (5) *definitely prefer MAST*. Subsequently, they rated a list of factors (e.g., the surgeon's recommendation) based on literature.[8]

After a short description of breast reconstruction (Appendix A.2), all participants were also asked: *'Imagine that you would undergo a MAST, which option would you prefer (probably would choose reconstruction/probably would not choose reconstruction/do not know)?'.*

Participants were categorized into 'younger' (40-64 years) and 'older' (≥65 years) patients. Response categories were recoded into preference for BCS with radiotherapy; preference for MAST; and no/unknown preference ('no preference for either option' and the participants not answering the question). Mean scores were calculated for each factor and compared between the younger and older participants indicating a preference for either BCS or MAST.

RESULTS

One hundred and seventeen patients agreed to participate (72%). Participants were excluded

if they completed the questionnaire after the second consultation (n=20) or if, for logistic reasons, the decision had been made in the first consultation (n=18). The median age of the remaining 79 participants was 61 years (range, 42-80); 34% (n=27) were aged ≥65 years (Table 1).

Table 1. Characteristics of the study population overall and by age category

	Total (n=79)		**40-64 years** (n=52, 66%)		**≥65 years** (n=27, 34%)		
Variables	n	%	n	%	n	%	*p*
Patient characteristics							
Median age in years (range)	61 (42-80)		56 (42-64)		70 (65-80)		-
Marital status							
married/living together	54	68	37	71	17	63	0.46
single/divorced/widowed	25	32	15	29	10	37	
Educational level[a]							
low	24	30	15	29	9	33	0.50
intermediate	34	43	21	40	13	48	
high	21	27	16	31	5	19	
Employment status							
full/part-time	39	49	37	71	2	7	**<0.001**
housekeeper	10	13	3	6	7	26	
unemployed/long-term sick leave	5	6	5	10	0	0	
retired	25	32	7	13	18	67	
Having children							
no children	16	20	9	17	7	26	0.05
yes, children not living at home	45	57	27	52	18	67	
yes, children living at home	18	23	16	31	2	7	
Number of comorbid conditions							
0	22	28	18	35	4	15	0.14
1	20	25	13	25	7	26	
2 or more	37	47	21	40	16	59	
Geriatric health condition[b]							
no	49	62	37	71	12	44	**0.02**
yes	30	38	15	29	15	56	
Tumour characteristics							
Morphology							
DCIS	16	20	10	19	6	22	0.75
invasive T_{1-2}	63	80	42	81	21	78	

DCIS= Ductal carcinoma in situ; BCS= Breast-conserving surgery; MAST= Mastectomy; T_{1-2}= Tumour size not larger than 5 cm

A p-value in bold means a significant difference between younger and older participants with respect to that variable

[a] Levels of education were categorized as low=completed no/primary school; intermediate=completed lower general secondary education/ vocational training; or high=completed pre-university education/high vocational training/university

[b] Presence of a geriatric health condition was defined as having one or more of the following characteristics: not able to carry out daily activities, incontinence, severe sensory impairment, depression, polypharmacy; difficulties with walking

Type of surgery

BCS (with radiotherapy) was most frequently preferred; by 69% (36/52) of the younger and 56% (15/27) of the older participants respectively. Nineteen percent (10/52) of the younger and 40% (11/27) of the older participants preferred MAST, and 12% (6/52) of the younger and 4% (1/27) of the older participants expressed no preference, or the preference was unknown. These differences were not significant (p=0.11).

Both age groups assigned the highest importance to the surgeon's treatment recommendation (Figure 1). Two factors significantly differed between the groups: younger participants rated the possibility of breast reconstruction as more important than older participants (2.6 versus 1.9, p=0.01), whereas older participants were more concerned about possible additional surgery (3.2 versus 2.7, p=0.04). Further, older participants tended to be more concerned about the side effects of radiotherapy (2.8 versus 2.4, p=0.07) and the frequent hospital visits for radiotherapy (2.6 versus 2.0, p=0.06).

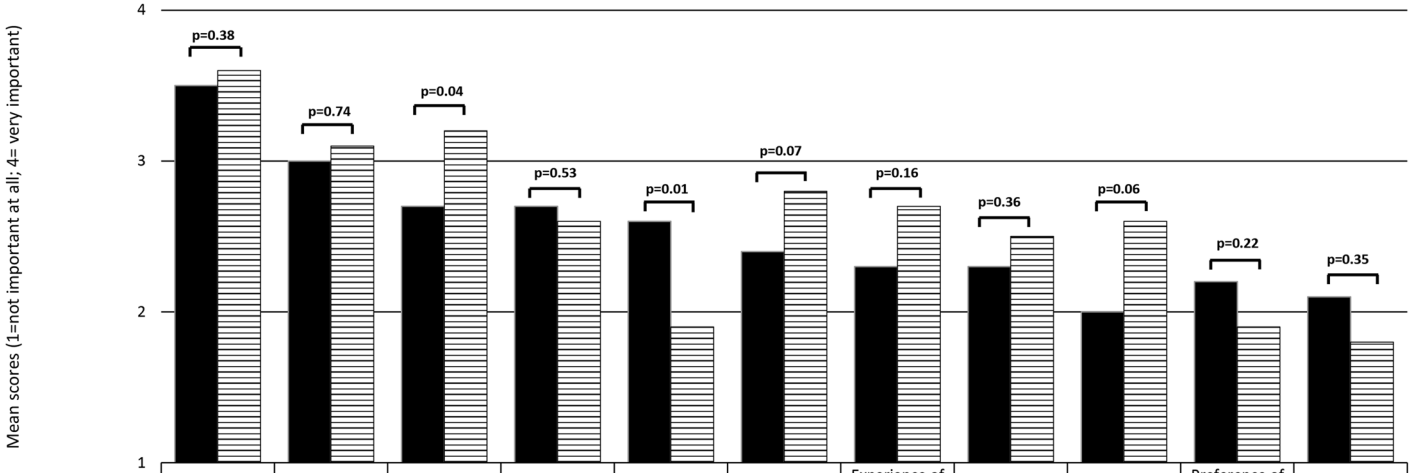
Breast reconstruction

Thirty-five percent (18/52) of the younger versus 26% (7/27) of the older participants did not know whether they would opt for post-MAST breast reconstruction or did not answer the question. Of those reporting a preference, significantly fewer older (40%; 8/20) than younger (77%; 26/34) participants would probably choose to have a reconstruction (p=0.01).

DISCUSSION

The current study is the first to prospectively compare younger and older patients' surgical treatment preferences. It is often assumed that MAST is the preferred choice among older women who are thought to be less interested in their physical appearance than younger women.[4] Indeed, our study showed that treatment preferences differed between the age groups, but not significantly so. Like the younger women, older participants also frequently preferred BCS to MAST, and both groups did not differ in their views on loss of a breast. A retrospective study[9] among patients aged ≥67 years found that body image was stated to be an important factor when deciding about treatment. These findings illustrate that older women require as much information as younger women about breast appearance after surgery when discussing each option.

Our findings suggest that treatment-related factors appear to play a larger role in decision-making. Older patients may want to avoid the extra daily hospital visits for radiotherapy that are needed to complete breast-conserving therapy.[9] Getting to radiotherapy appointments can be a larger burden at older age, as patients are more likely to experience mobility limitations and/or to rely on others. This may explain why older women may not choose BCS. Our findings indeed show a trend that frequent hospital visits for radiotherapy as



	The treatment recommendation of the surgeon	Fear of disease recurrence	Being reluctant to the possible need of undergoing an extra surgery	The possibility that I might lose a breast	Possibility of breast reconstruction	Side effects of radiation therapy	Experience of others who underwent a breast-conserving surgery	Experience of others who underwent a mastectomy	Frequent hospital visits for radiation therapy	Preference of significant others (partner, child[ren], environment)	Fear of radiotherapy
■ 40-64 years (n=46)	3.5 [b,c]	3.0	2.7	2.7	2.6 [b]	2.4 [b]	2.3 [b]	2.3	2.0	2.2	2.1
⊟ ≥65 years (n=26)[a]	3.6 [c]	3.1	3.2	2.6	1.9 [b]	2.8 [c]	2.7 [b]	2.5 [b]	2.6	1.9	1.8

Figure 1. Importance of factors for treatment preference among the participants preferring either breast-conserving surgery (with radiotherapy) or mastectomy

Differences in mean scores between younger and older participants were tested using Independent Samples t-test

[a] One out of 26 did not fill in any of these questions, and was excluded from all analyses

[b] One person did not answer this question

[c] For this item, participants' lowest score was 2 and the highest score was 4. For the remaining items, the scores ranged between 1 and 4

well as radiotherapy side effects are contributing factors to older patients' preference for MAST over BCS. Thus, the benefit of breast preservation may not outweigh the treatment inconvenience and the possible side effects. Another treatment-related factor that seemed relevant to older women is the wish to avoid the risk of having a second surgery.[9] The risk of undergoing another surgery after MAST is generally smaller than after BCS. In our study, older participants were indeed more concerned about the possible need of having to undergo additional surgery than younger participants.

Both age groups stated the surgeon's treatment recommendation to be the most important factor. Since the clinician's recommendation may possibly overrule other factors that patients also consider important,[10] this stresses the imperative for clinicians to avoid providing a recommendation before having assessed patients' concerns. Especially when deciding between BCS and MAST, patient preferences become increasingly relevant.

Unfortunately, the sample of older participants was small. Some differences that can be seen as relevant were therefore not statistically significant. Nonetheless, our findings demonstrate the need to discuss both surgical options, not just with younger patients. Similarly, although not all older patients may want a reconstructive surgery, before making a decision patients should know about the option of post-MAST reconstruction. Whether they consider having reconstruction and when (during/after MAST) should be preferably elicited in the first surgical consultation, as it may influence the choice between MAST and BCS. A visit to a plastic surgeon can then be scheduled before a surgical decision is reached.

Acknowledgements

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APPENDIX A. Preferences for type of surgery and for breast reconstruction following mastectomy

A.1 Breast-conserving surgery versus mastectomy

The content in the overview was based on patient education brochures[1] and on information provided on the website[2] of the Dutch Breast Cancer Association. The information about 10-year loco-regional recurrence risks after breast-conserving surgery with radiotherapy and mastectomy was based on data of the Early Breast Cancer Trialists' Collaborative Group.[3] Drawings of the breast after breast-conserving surgery and mastectomy were reprinted by permission of the American Society of Clinical Oncology.[4]

The content was checked after discussion with two surgical oncologists, one radiation oncologist, three research nurses/nurse specialists and one plastic surgeon. A pilot test was carried out among three healthy women and seven breast cancer patients to check for problems in understanding. During this process, the researcher encouraged them to think aloud as they answered the question, and to vocalize any thoughts, including difficulties, distress and suggestions for improvement. Based on their feedback, we rephrased the question and clarified the instruction.

In most situations there is a choice between:

- breast-conserving surgery
- mastectomy

The choice depends, amongst others, on the size and location of the tumour in the breast. A breast-conserving surgery is always followed by radiotherapy.

The chances of surviving breast cancer are the same for both breast-conserving surgery with radiotherapy and mastectomy.

On the next page you will find an overview with general information about both surgical options. The information is based on education material of the Dutch Cancer Society and Dutch Breast Cancer Association.

Please carefully read the overview and scan the differences between both surgical types. Then answer the question: **Imagine that both breast-conserving surgery (followed by radiotherapy) and mastectomy were available treatment options, which type of surgery would you prefer?**

1	2	3	4	5
Definitely prefer breast-conserving surgery followed by radiotherapy	Prefer breast-conserving surgery followed by radiotherapy	No preference between the two options	Prefer mastectomy	Definitely prefer mastectomy

	Breast-conserving surgery	Mastectomy
Surgical procedure *Length of time in hospital*	Only the cancer lump is removed. The remaining of the breast is preserved. Most patients are home within 24 hours of surgery or the next day.	The whole breast is removed. Most patients stay overnight at the hospital.
Complications after surgery	*Possible* complications include: • Bleeding • Wound infection • Pain and discomfort • Small collection of fluid under the wound	*Possible* complications include: • Bleeding • Wound infection • Pain and discomfort • Collection of fluid under the wound
A second surgery (more than one operation)	If there are still cancer cells after the surgery, another operation on the breast may be needed. The second surgical procedure may be a breast-conserving surgery or a mastectomy.	After a mastectomy, another operation is seldom to never required.
Radiotherapy	A breast-conserving surgery is *always* followed by radiotherapy to the breast. A course of radiotherapy can take 3 to 5 weeks. Most patients undergo radiotherapy 4 or 5 days a week. Radiotherapy usually begins within a few weeks after surgery and takes place at the hospital. You can go home after each session of radiotherapy.	After a mastectomy, radiotherapy is usually *not* given. Whether or not radiotherapy is given depends on the results of the surgery; 1 out of 10 women still need radiotherapy. In case radiotherapy is needed after a mastectomy, the procedure is the same as with a breast-conserving surgery (see left).
Side effects of radiotherapy	*Possible* side effects of radiation to the breast: • Redness of the skin. This is a temporary reaction. • Painful and/or tender breast. This is a temporary reaction. • A slight discoloration of the skin. This is irreversible and occurs rarely. • The breast tissue may feel permanently firmer. • Most patients experience fatigue during radiotherapy and in the first weeks afterwards.	In case radiotherapy is given after mastectomy, side effects can occur similar as to those of radiotherapy after breast-conserving surgery (see left).
page 1 of 2		

The chances of cancer coming back in the breast	About 14.4 out of 100 women will develop a recurrence in the breast and/ or armpit in the 10 years after a breast-conserving surgery.	About 13.8 out of 100 women will develop a recurrence in the chest region and/or armpit in the 10 years after a mastectomy.
Cosmetic results (what will my breast look like after surgery?)	The effect of the surgery on the appearance of the breast is minimal, but the breast can look different. The shape and size of the breast after surgery may differ somewhat from the other breast. 	The whole breast is removed and a large scar remains. There are options to undergo breast reconstruction or to wear an external prosthesis. 
Breast reconstruction (creating a 'new breast')	After a breast-conserving surgery, a breast reconstruction is usually not performed.	After a mastectomy, there are options for a breast reconstruction. In some cases a breast reconstruction can be carried out at the same time as the mastectomy. In some cases, in another operation, sometime later.
page 2 of 2		

A.2 Breast reconstruction

The information below was based on patient education brochures,[1] information of the Dutch Breast Cancer Association,[5] and expertise of two surgical oncologists and one plastic surgeon. A pilot study was conducted among three healthy women and seven breast cancer patients. Minor revisions were made based on their feedback.

It is possible to undergo a breast reconstruction following a mastectomy. This is an operation to create a new breast that matches the shape and size of the other breast as closely as possible. For this procedure the surgeon will refer you to a plastic surgeon.

The procedure differs from patient to patient. In some cases the reconstruction can be performed immediately after the mastectomy (during the same operation). In some cases the surgery is performed at a later time after the mastectomy. A breast reconstruction does not affect the chance of the cancer coming back or the ability to check for recurrence.

Breast reconstructive surgery usually requires a hospital stay of a few days. It will take a few weeks to heal fully.

As with any (breast) surgery, complications may occur after breast reconstruction.

After a reconstruction the new breast looks natural. However, the reconstructed breast feels different and the shape and size may differ from the original breast.

Imagine that you would undergo a mastectomy, which option would you prefer?

☐ After a mastectomy, I would probably choose to have a breast reconstruction

☐ After a mastectomy, I would probably not choose to have a breast reconstruction

☐ I do not know

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CHAPTER 4

A Prospective Comparison of Younger and Older Patients' Preferences for Adjuvant Chemotherapy and Hormonal Therapy in Early Breast Cancer

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ABSTRACT

Purpose | It is unknown what minimal benefit in disease-free survival older breast cancer patients require from adjuvant systemic therapy, and if this differs from that required by younger patients. We prospectively examined patients' preferences for adjuvant chemotherapy (aCT) and adjuvant hormonal therapy (aHT), factors related to minimally-required benefit, and patients' self-reported motivations.

Methods | Fifty-two younger (40-64 years) and 29 older (≥65 years) women with a first primary, invasive tumor were interviewed post-surgery, prior to receiving aCT/aHT recommendation.

Results | The proportions of younger versus older participants who would accept, refuse, or were undecided about therapy were 92% versus 62%, 4% versus 24%, and 4% versus 14% for aCT, and 92% versus 59%, 8% versus 17%, and 0% versus 24% for aHT. The proportion of older participants who would refuse rather than accept aCT was larger than that of younger participants (p=0.005). No significant difference was found for aHT (p=0.12). Younger and older participants' minimally-required benefit, in terms of additional 10-year disease-free survival, to accept aCT (median, 5% versus 4%; p=0.13) or aHT (median, 10% versus 8%; p=0.15) did not differ. Being single/divorced/widowed (odds ratio [OR], 0.16; p=0.005), presence of geriatric condition (inability to perform daily activities, incontinence, severe sensory impairment, depression, polypharmacy, difficulties with walking; OR, 0.27; p=0.047), and having a preference to make the treatment decision either alone or after considering the clinician's opinion (active role; OR, 0.15; p=0.012) were independently related to requiring larger benefits from aCT. The most frequent motivations for/against therapy included the wish to survive/avoid recurrence, clinician's recommendation, side effects, and treatment duration (only aHT).

Conclusion | Whereas older participants were less willing to accept aCT than younger participants, no significant difference was found for aHT. However, a majority of older participants would still accept both therapies. Adjuvant systemic therapy should be discussed with eligible patients regardless of age.

INTRODUCTION

Breast cancer (BC) is a disease affecting a large proportion of women over 65 years of age. In Western countries, approximately 40% of new cases occur in older women.[1] As the risk of developing BC increases with age and the general population is ageing, the number of older patients is expected to rise significantly.[1]

In most cases of early-stage (I-II) BC, adjuvant systemic therapy is recommended in addition to primary surgery with or without post-operative radiotherapy. The addition of adjuvant chemotherapy (aCT) or adjuvant hormonal therapy (aHT) can lower the risk of BC relapse and mortality.[2] However, these therapies are associated with short- and long-term side effects which, in turn, can cause physical, psychological and social problems.[3] Therefore, the expected benefits need to be carefully weighed against its side effects. With regard to older patients, making the decision for or against systemic therapy is generally difficult. Benefits of adjuvant systemic therapy in older patients, especially those of aCT, are uncertain because of small numbers of older women in trials.[2,4] Moreover, high rates of comorbid conditions and polypharmacy in this patient group pose additional challenges.[4] Consequently, treatment decisions in older patients should incorporate their valuation of potential benefits and side effects of treatment strategies.[5]

So far, data on older patients' preferences for aCT and aHT are limited. We performed a systematic review of patients' preferences,[6] and found that most patients judged small to modest survival benefits sufficient to consider these therapies worthwhile, regardless of the consequences. A limitation of the reviewed studies was that the women surveyed had already been treated or had already received a treatment recommendation, which could have had a strong influence on their reported treatment preferences.[7] Moreover, most patients were young or middle-aged (mean/median of 36-55 years),[7-12] and none of the studies on aHT included patients aged ≥65 years.[8,12]

A few studies have retrospectively explored factors that may affect the decisions about adjuvant systemic treatment of older patiens with BC.[13-15] These studies involved only patients aged 65-70 years and over, making it difficult to determine whether older patients place different values on benefits versus side effects of adjuvant systemic therapy than younger patients. To our knowledge, solely one retrospective study examined age differences in factors influencing treatment decisions for aCT and aHT.[16] Of the other existing studies involving patients of all ages, none specifically focused on differences in motivations between younger and older patients.[17-19]

Given the growing incidence of BC in older women, it will become increasingly relevant to establish a more complete picture of treatment preferences in this patient group, and to determine whether their preferences differ from those of younger women. A better understanding of older patients' preferences and the factors that distinctively affect their preferences will assist clinicians in determining the set of treatment options relevant to older patients and in tailoring their information provision better.

The objectives of this prospective study were threefold. First, to examine whether there are differences in the benefit that younger and older patients minimally require from aCT and aHT to consider it worthwhile. Second, to determine which factors are related to the minimally-required benefit. Lastly, to examine whether motivations for and against therapy differ between younger and older patients.

METHODS

Participants

This study took place at one academic and two non-academic teaching hospitals in the Netherlands. Between January 2012 and December 2013, women aged ≥40 years with a primary invasive tumor (clinical T_{1-2}) scheduled to undergo surgery with curative intent, were included. Exclusion criteria were bilateral BC, *BRCA 1/2* mutation, history of (non)invasive BC, history of other malignancies (other than non-melanoma skin cancer or cervical carcinoma in situ) within the past five years, insufficient knowledge of the Dutch language, cognitive/mental problems, inability to participate in a telephone interview (e.g., hearing impairment), and a diagnosis of metastatic BC after resection. The Medical Ethical Committee of the Leiden University Medical Center and the institutional review boards of the participating hospitals approved the study. All participants provided informed consent.

Procedure

In a telephone interview, we determined participants' minimally-required benefit from aCT and aHT and their motivations for/against both therapies. Eligible participants were approached following their diagnosis, and they received an informed consent form and a self-administered questionnaire on socio-demographic background. After the pre-surgical consultation and before surgery, consenting patients were handed out a questionnaire about their preferred involvement in decision-making as well as information to prepare for a telephone interview scheduled after their surgery. Participants were asked to read the information right before the interview. Patients usually receive a recommendation for or against adjuvant systemic therapy based on pathological findings following surgery, during a post-surgical consultation. To rule out that this recommendation could influence the participant's adjuvant treatment

preference, the interview was held before that post-surgical consultation. Three trained interviewers conducted the interviews, strictly adhering to a script.

Measures

Minimally-required benefit and motivations for/against adjuvant systemic therapy

The minimally-required absolute benefit, in terms of additional 10-year disease-free survival, from aCT and aHT was assessed using the probability trade-off method.[20] As part of this method, we developed two hypothetical scenarios: no aCT versus aCT, and no aHT versus aHT (see Appendix A for details). The scenarios were provided to the participant and included information about the treatment strategies and the accompanying health consequences and recurrence risks. During the interview, we read aloud the information, and asked the participant to read along. Next, participants were asked to imagine that their clinician had offered them two treatment strategies. We presented a 10% difference in BC recurrence risk at 10 years between no aCT (25 out of 100 women with a recurrence) and aCT (15 out of 100 with a recurrence), and asked the participants which treatment they preferred at this benefit of aCT of 10%. The participants were asked to indicate their preference each time in subsequent comparisons, in which the absolute benefit from aCT was systematically increased or decreased, depending on their answer. If their initial preference was aCT, we searched for their minimally-required benefit between the range of 0 (no benefit) and 10%. If their initial preference was no aCT, we searched for the minimally-required benefit between the ranges of 11 and 25% (maximum benefit). Participants could indicate to refuse aCT if they considered that, for a benefit of 25%, aCT was not worthwhile. After the aCT scenario, we similarly assessed participants' preferred benefit from aHT, except that we presented a 15% difference in 10-year recurrence risk between no aHT and aHT in the initial question. At the end of each scenario, we asked participants about their motivations for their preference.

Participants' demographic and medical characteristics

The first self-report questionnaire contained questions about socio-demographic details. Information with regard to type of surgery, comorbid conditions, and geriatric health conditions (i.e., inability to carry out daily activities, incontinence, severe sensory impairment, depression, polypharmacy, difficulty with walking[21]) were extracted from medical records. Comorbid conditions at the time of diagnosis were registered according to the 10th revision of the International Classification of Diseases.[22]

Decisional role preference

We assessed participants' preferred involvement in decision-making about aCT and aHT using an adapted version of the Control Preferences Scale.[23] Participants were asked to choose one of five decisional roles, ranging from (1) the patient making the decision, (2) the patient making the decision after considering the clinician's opinion, (3) the patient making the

decision jointly with the clinician, (4) the clinician making the decision after considering the patient's opinion, to (5) the clinician making the decision.

Statistical analyses

Participants were categorized into 'younger' (40-64 years) and 'older' (≥65 years) based on their age at diagnosis. The response options for decisional role preference were merged into three categories: active (1-2), shared (3), and passive (4-5). Comorbidity was defined as the sum of any comorbid disease (0, 1, or 2 or more diseases). Differences in patient characteristics and decisional role preferences between the groups were examined using the χ^2 or Fisher exact tests, as appropriate.

Participants' minimally-required benefits to accept aCT and aHT were categorized into 0%, 1-5%, 6-10%, 11-15%, 16-20%, and 21-25%. Participants who were undecided about the minimally-required benefit were excluded from further analyses. Younger versus older participants' minimally-required benefits and acceptance versus refusal of therapy were compared using the Fisher exact test.

Univariable logistic regression analyses were conducted to examine the association between minimally-required benefit and patient characteristics and decisional role preference. The minimally-required benefit of both aCT and aHT was dichotomized into 0-10% required benefit ('1') and 11-25% required benefit or refusal of therapy ('0'). A multivariable model was built with all significant factors ($p<0.05$) in univariable analysis.

Two researchers independently coded participants' motivations. Dissimilarities in coding were resolved through consensus. As this section was conducted for exploratory purposes, statistical differences in motivations between the age groups were not tested.

Analyses were conducted using SPSS version 20. A p-value below 0.05 was considered statistically significant.

RESULTS

Participants

Overall, 100 women with invasive BC were eligible for this study. Of them, 13 were not interviewed before the post-surgical consultation, and six withdrew before the interview. The reasons for withdrawal were no interest (n=3), being nervous about getting the pathology results within the next few days (n=2), and not being fully recovered from surgery (n=1). Eighty-one participants were included in the analyses. The median time between surgery and

the interview was six days (range, three to 12 days), and the telephone interview lasted on average 30 minutes (range, 10-50 minutes).

The participants' median age was 61 years (range, 42-86 years). Fifty-two (64%) participants were aged 40-64 years, and 29 (36%) were aged ≥65 years (Table 1). Overall, most women were married/lived together (51/81; 63%), had completed an intermediate-level education (35/81; 43%), were employed (38/81; 47%), and had children (not living at home) (49/81; 61%). Seventy-two (58/81) percent had ≥1 comorbid conditions, and 38% (31/81) suffered from ≥1 geriatric health conditions at diagnosis. Eighty percent (65/81) were treated with breast-conserving surgery. Most participants preferred to share the decision about aCT (42/73; 58%) and aHT (39/73; 53%) with the clinician.

Minimally-required benefit in 10-year disease-free survival from aCT

Some younger (2/52; 4%) and older (4/29; 14%) participants could not decide which benefit they would minimally require to consider the therapy worthwhile. In the remaining participants, 92% (48/52) of the younger and 62% (18/29) of the older participants, respectively, would accept aCT, and 4% (2/52) of the younger and 24% (7/29) of the older participants would refuse aCT at the maximum absolute benefit of 25% (Figure 1A). Older participants refused aCT significantly more often than younger participants (p=0.005). Of those who would accept therapy, the younger participants considered aCT worthwhile at an absolute median benefit of 5% (range, 1-25%) and the older participants at an absolute median benefit of 4% (range, 0-25%). These minimally-required benefits did not significantly differ (p=0.13).

Minimally-required benefit in 10-year disease-free survival from aHT

None of the younger and 24% (7/29) of the older participants were undecided about their minimally-required benefit. In the remaining group, the majority of younger (48/52; 92%) and older (17/29; 59%) participants would accept aHT (Figure 1B). Eight percent (4/52) of the younger and 17% (5/29) of the older participants would refuse aHT at an absolute benefit of 25%. Overall, acceptance versus refusal rates did not significantly differ between younger and older participants (p=0.12). Of the group accepting therapy, younger and older participants considered it worthwhile at a median of 10% (range, 1-25%) and 8% (range, 0-25%) absolute benefit, respectively. These minimally-required benefits did not significantly differ (p=0.15).

Table 1. Characteristics of the study population overall (N=81) and by age category

	Total (n=81)		**40-64 y** (n=52, 64%)		**≥65 y** (n=29, 36%)		
Variables	n	%	n	%	n	%	*p*
Marital status							
married/living together	51	63	33	63	18	62	0.90
single/divorced/widowed	30	37	19	37	11	38	
Educational level[a]							
low	20	25	13	25	7	24	0.19
intermediate	35	43	19	37	16	55	
high	26	32	20	39	6	21	
Employment status							
full/part-time	38	47	36	69	2	7	**<0.001**
housekeeper	9	11	3	6	6	21	
unemployed/long-term sick leave	8	10	8	15	0	0	
retired	26	32	5	10	21	72	
Having children							
no children	18	22	11	21	7	24	**0.044**
yes, children not living at home	49	61	28	54	21	72	
yes, children living at home	14	17	13	25	1	3	
Number of comorbid conditions							
0	23	28	19	37	4	14	0.08
1	21	26	13	25	8	28	
2 or more	37	46	20	39	17	59	
Geriatric health condition[b]							
no	50	62	35	67	15	52	0.17
yes	31	38	17	33	14	48	
Type of surgery							
BCS	65	80	43	83	22	76	0.46
MAST	16	20	9	17	7	24	
Decisional role preference[c]							
Adjuvant chemotherapy[d]							
active	19	26	12	26	7	26	0.71
shared	42	58	25	54	17	63	
passive	12	16	9	20	3	11	
Adjuvant hormonal therapy[d]							
active	21	29	14	30	7	26	0.42
shared	39	53	22	48	17	63	
passive	13	18	10	22	3	11	

A p-value in bold means a significant difference between younger and older participants with respect to that variable
BCS = Breast-conserving surgery; MAST = Mastectomy

[a] Levels of education were categorized as low=completed no/primary school; intermediate=completed lower general secondary education/vocational training; or high=completed pre-university education/high vocational training/university

[b] Presence of a geriatric health condition was defined as having one or more of the following characteristics: not able to carry out daily activities, incontinence, severe sensory impairment, depression, polypharmacy; difficulties with walking

[c] Decisional role preferences were merged into three categories: active (the patient makes the decision alone, the patient makes the decision after considering the clinician's opinion); shared (patient makes the decision together with the clinician); and passive (the clinician makes the decision after considering the patient's opinion, the clinician makes the decision alone)

[d] Eight participants did not fill out this question before the post-operative consultation

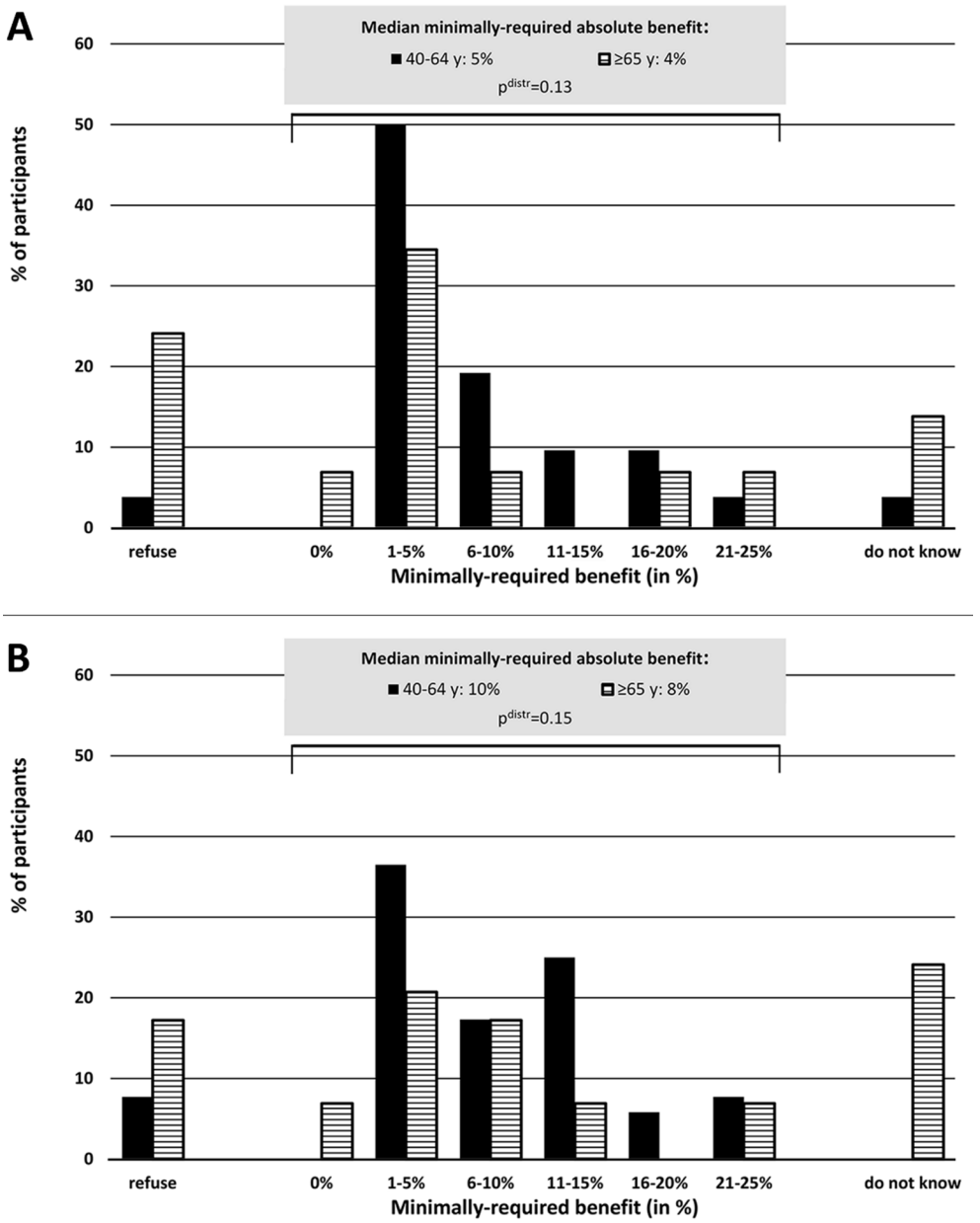

Figure 1. Minimum absolute increase in 10-year disease-free survival that younger (N=52) and older (N=29) participants would require to consider adjuvant chemotherapy (A) or hormonal therapy (B) worthwhile

In both scenarios, the 10-year disease-free survival without adjuvant systemic therapy was 75%, and the minimally-required benefit to accept therapy could range from 0 (no benefit) to 25% (maximum benefit)

Note: pdistr=p-value for distribution; refuse=women who would not accept therapy at any benefit; do not know=women who were undecided about the minimal benefit they would require to consider the therapy worthwhile

Factors related to minimally-required benefit

Univariable logistic regression analyses showed that participants who were single/divorced/widowed were significantly less likely to accept aCT (odds ratio [OR] 0.21; 95% confidence interval [CI] 0.08-0.59; p=0.003) or aHT (OR 0.34; 95% CI 0.13-0.92; p=0.033) for 10% benefit or less, compared to participants who were married/lived together (Table 2). For aHT, there were no other significant factors besides marital status. For aCT, participants with a geriatric health condition had lower odds of accepting therapy at a 0-10% benefit (OR 0.18; 95% CI 0.06-0.50; p=0.001). Furthermore, participants who preferred an active decisional role were less likely to accept aCT at a 0-10% benefit than participants who preferred a shared decisional role (OR 0.25; 95% CI 0.08-0.81; p=0.021).

Factors included in the multivariable model for aCT were marital status, geriatric health condition, and decisional role preference. The participants who were single/divorced/widowed had an odds of 0.16 (95% CI 0.04-0.57; p=0.005) for accepting aCT at a 0-10% benefit, compared to participants who were married/living together. Having a geriatric condition was related to requiring larger benefits to accept aCT (OR 0.27; 95% CI 0.07-0.98; p=0.047). Having an active decisional role preference was related with requiring larger benefits compared to having a shared decisional role preference (OR 0.15; 95% CI 0.04-0.67; p=0.012).

Table 2. Univariable logistic regression analysis between patient characteristics, type of surgery, and decisional role preferences, and accepting adjuvant chemotherapy (N=75)[a] and adjuvant hormonal therapy (N=74)[a] at a 0-10% benefit

	Participants who would accept aCT at a 0-10% benefit (%)	OR[b] 95% CI	*p*	Participants who would accept aHT at a 0-10% benefit (%)	OR[b] 95% CI	*p*
Patient characteristics						
Age in years						
40-49	78	1 (ref)		78	1 (ref)	
50-59	88	2.00 (0.28-14.53)	0.49	44	0.22 (0.04-1.30)	0.10
60-69	59	0.42 (0.07-2.39)	0.33	63	0.49 (0.08-2.81)	0.42
≥70	40	0.19 (0.03-1.25)	0.08	46	0.25 (0.04-1.66)	0.15
Marital status						
married/living together	79	1 (ref)		65	1 (ref)	
single/divorced/widowed	44	0.21 (0.08-0.59)	**0.003**	39	0.34 (0.13-0.92)	**0.033**
Educational level[c]						
low	79	1 (ref)		50	1 (ref)	
intermediate	64	0.47 (0.13-1.73)	0.26	59	1.46 (0.46-4.67)	0.52
high	61	0.42 (0.10-1.66)	0.21	54	1.18 (0.35-4.02)	0.79

Employment status						
full/part-time	75	1 (ref)		55	1 (ref)	
housekeeper	75	1.00 (0.17-5.87)	1.00	50	0.81 (0.18-3.73)	0.79
unemployed/long-term sick leave	50	0.33 (0.07-1.62)	0.17	50	0.81 (0.18-3.73)	0.79
retired	57	0.43 (0.14-1.33)	0.14	60	1.21 (0.40-3.65)	0.73
Having children						
no	63	1 (ref)		43	1 (ref)	
yes, children not living at home	65	1.13 (0.35-3.66)	0.85	57	1.73 (0.52-5.80)	0.37
yes, children living at home	77	2.00 (0.39-10.31)	0.41	64	2.40 (0.52-10.99)	0.26
Number of comorbid conditions						
0	81	1 (ref)		64	1 (ref)	
1	65	0.44 (0.11-1.82)	0.26	58	0.79 (0.22-2.77)	0.71
2 or more	59	0.34 (0.09-1.22)	0.10	49	0.54 (0.18-1.62)	0.27
Geriatric health condition[d]						
no	81	1 (ref)		64	1 (ref)	
yes	43	0.18 (0.06-0.50)	**0.001**	41	0.39 (0.15-1.03)	0.06
Treatment characteristics						
Type of surgery						
BCS	68	1 (ref)		51	1 (ref)	
MAST	60	0.70 (0.22-2.23)	0.54	73	2.66 (0.76-9.31)	0.13
Decisional role preference[e,f]						
shared	72	1 (ref)		56	1 (ref)	
active	39	0.25 (0.08-0.81)	**0.021**	40	0.53 (0.18-1.62)	0.27
passive	80	1.57 (0.29-8.60)	0.60	67	1.60 (0.41-6.29)	0.50

A p-value in bold means a significant difference beween that group and the reference group

aCT = Adjuvant chemotherapy; aHT = Adjuvant hormonal therapy; BCS = Breast-conserving surgery; MAST = Mastectomy; OR = Odds ratio; ref= reference; CI = Confidence interval

[a] Participants who could not decide upon their minimally-required benefit were excluded (aCT, n=6; aHT, n=7)

[b] An OR over 1 indicates a greater likelihood to accept therapy at a 0-10% benefit, an OR below 1 indicates a lower likelihood to accept therapy at a 0-10% benefit (and a greater likelihood to require a >10% benefit)

[c] Levels of education were categorized as low=completed no/primary school; intermediate=completed lower general secondary education/vocational training; or high=completed pre-university education/high vocational training/university

[d] Presence of a geriatric health condition was defined as having one or more of the following characteristics: not able to carry out daily activities, incontinence, severe sensory impairment, depression, polypharmacy; difficulties with walking

[e] Decisional role preferences were merged into three categories: active (the patient makes the decision alone, the patient makes the decision after considering the clinician's opinion); shared (patient makes the decision together with the clinician); and passive (the clinician makes the decision after considering the patient's opinion, the clinician makes the decision alone)

[f] Eight respondents did not fill out the questions about aCT and aHT before the post-operative consultation and were excluded from this analysis

Motivations in favor of or against adjuvant systemic therapy

Both younger and older participants frequently reported that the wish to survive/avoid recurrence and the treatment recommendation of their clinician were motivations in favor of aCT (Table 3). In the case of aHT, younger participants frequently cited the clinician's recommendation and wanting to survive/avoid recurrence as arguments for the therapy. For older participants, the clinician's recommendation was the predominant argument.

For both younger and older participants, the most often reported argument against aCT was concern about potential side effects. Older participants also commonly reported that the wish to maintain their current quality of life and independence, the negative treatment experience of others, the benefits not outweighing side effects, and their old age were arguments against aCT. Regarding aHT, both age groups frequently noted that side effects and the long duration of treatment were arguments against the therapy.

Table 3. Arguments in favor of and against adjuvant chemotherapy (N=75)[a] and adjuvant hormonal therapy (N=74)[a] according to age category[b]

	aCT		aHT	
	40-64 y (n=50) %	**≥65 y** (n=25) %	**40-64 y** (n=52) %	**≥65 y** (n=22) %
Arguments in favor of systemic therapy				
Wish to survive/avoid recurrence/ Do everything possible to fight the cancer	40	28	25	14
Clinician's recommendation for treatment	24	36	25	36
Downplays side effects/ not everybody will have side effects	14	16	13	18
Positive treatment experience of others	12	4	6	0
Age ("I am too young")	12	4	6	0
Potential benefits outweigh potential side effects	12	8	8	18
Someone (e.g., partner, (grand)children) to live for	6	4	6	5
Reduce possible (future) regret	6	4	4	5
Trust in (effectiveness) of treatment	2	4	2	5
Preference based on feeling (not further specified)	2	0	4	0
Trust in the capability of my body to deal with the drug	0	4	0	0
Specific for aCT:				
Short duration of treatment	2	0	-	-
Specific for aHT:				
Able to discontinue therapy in case of many/severe side effects	-	-	8	5
Is experiencing/has experienced little/no menopausal complaints	-	-	6	18
Not having to go to hospital to undergo treatment	-	-	2	0
Medication/life style changes possible to lessen the severity of side effects	-	-	2	0
Taking a daily pill is not a burden	-	-	2	9
Arguments against systemic therapy				
Concerns about short- and/or long-term side effects	50	40	42	36
Maintain quality of life/independence/ Continue work	12	24	10	18
Negative treatment experience of others	12	20	8	0

Health status/condition	12	12	8	14
Potential benefits do not outweigh potential side effects	8	24	0	5
Undergoing adjuvant systemic therapy does not guarantee no recurrence	6	8	0	5
Relies on regular check-ups/ option of new therapy in case of recurrence	4	0	2	0
Hopes to be cured without adjuvant systemic therapy	2	0	2	0
Age ("I am too old")	2	24	2	9
Lack of social support	2	8	2	5
Long duration of treatment	2	0	40	23
No or little trust in (effectiveness) of treatment	0	0	0	5
Specific for aCT:				
Frequent hospital visits for chemotherapy are a burden	2	4	-	-
Fear of needles	2	0	-	-
Specific for aHT:				
Is experiencing/has experienced many/severe menopausal complaints	-	-	6	0
Taking a daily pill is a burden	-	-	2	0
Negative experience with hormones	-	-	2	0

"—" indicates that the argument is not applicable to the therapy
aCT = Adjuvant chemotherapy; aHT = Adjuvant hormonal therapy

[a] Participants who could not decide upon their minimally-required benefit, were excluded (aCT: n=6; aHT: n=7)
[b] Participants could indicate more than one argument

DISCUSSION

This prospective study compared the minimal benefit in 10-year disease-free survival that younger and older patients with early BC would require to consider aCT and aHT worthwhile. Additionally, we assessed which factors were related to minimally-required benefit, and explored younger and older patients' motivations for and against these therapies. To our knowledge, this is the first study that examined preferences for aCT and aHT in older patients[24] and before patients received a recommendation for or against adjuvant systemic therapy, thereby minimizing the biasing influence of cognitive dissonance reduction. This cognitive mechanism of adaptation leads individuals to reduce inconsistencies between previous decisions (such as treatment decisions) and current beliefs. Thus, patients will tend to justify earlier decisions about how they will be treated in such ways that their current preferences are in accordance with that decision.[7] In this sample, participants did not know which treatment was indicated, and no treatment decision was yet made. We are aware that participants may already have had a treatment preference, based on clinical information they received after diagnosis (e.g., having a very large tumor), experiences from significant others, or on information found on the Internet or elsewhere. This is true also in daily practice.

Our results reveal that older participants would more often refuse aCT than younger participants, but no significant difference was found regarding aHT. However, the proportion of older participants willing to accept systemic therapy was large (three out of five women, for both aCT and aHT), and for these older women, the minimally-required benefit did not differ from that of younger women. The latter finding is in line with other studies on aCT that found no association between age and minimally-required benefit, in terms of overall[9-11] or disease-free survival,[7] but not with other studies demonstrating in contrast that higher age was related to higher minimally-required benefit from aCT[25,26] or aHT.[26] However, our study as well as earlier studies[7,9-11] showing no such association differ from the latter two[25,26] regarding design and population in the following way. Firstly, in the two latter studies it was unclear whether participants could refuse therapy. Secondly, the latter studies also involved more advanced BC stages, which could lead to different treatment preferences. Based on our results, it appears that for early-stage BC, age is not a factor in determining the minimally-required benefit, and that the majority of patients are willing to consider adjuvant systemic therapy. It is important for clinicians to be aware of these preferences.

Another finding was that some participants, predominantly older participants, were undecided about the minimal benefit they would require to consider adjuvant systemic therapy worthwhile. Participants primarily reported they would rely on the treatment advice of their clinician. It is important that clinicians themselves are aware of this finding, and they should try to ensure that information provision is clear and tailored to the needs of the patient. Additionally, patients should be made aware that they should voice their preferences and concerns.

Another finding was that being single, divorced, or widowed, having a geriatric health condition, and having a preference for an active decisional role predicted patients' preference for aCT. Women who were single/divorced/widowed had a five times higher odds of requiring a large benefit than women who were married/living together. This may be explained by either not having a partner for whom to consider a treatment worthwhile ("to live for"), or by lack of support from a partner during treatment. If a patient has one or more geriatric health conditions, she might be more likely to think that she might not cope with the side effects of adjuvant systemic therapy, and thus her minimally-required benefit should be higher to make it worthwhile. The association with role preference may be explained by two mechanisms with a different causal direction. On the one hand, patients who do not want aCT may want to be actively involved to ensure that no overtreatment occurs. That is, patients' existing treatment preference may determine their role preference. On the other hand, it has been found that patients who are more active, following the use of a decision aid, tend to choose more conservative treatment,[27] implying that decisional role may explain treatment preference.

As expected, the predominant motivation in favor of aCT was to survive/avoid recurrence, irrespective of age. Nevertheless, older participants seemed to value the clinician's recommendation more compared to younger participants. These two factors have often been noted in previous studies concerning older patients' decision-making about aCT[13,14] and about treatment for BC in general.[15,28] Further, our study indicated that motivations against aCT largely differed between younger and older participants. Both groups frequently reported concern about side effects as a motivation. Additionally, older participants reported the wish to maintain their current quality of life and independence and the belief that benefits do not outweigh side effects as concerns about aCT. As these concerns are specific to older patients, more focus should be placed on quality of life and independence when discussing treatment consequences, and sufficient information should be provided to help develop realistic expectations on side effects of aCT. This will better support older patients in developing an informed treatment preference. Interestingly, although age was not a factor in determining the minimally-required benefit to accept therapy, it was an important argument for women in deciding for or against adjuvant systemic therapy. The most striking observation was that older participants more frequently stated that their old age was an argument against aCT.

The motivations for aHT were similar to those found for aCT, except that the wish to survive/avoid recurrence was less frequently reported. An explanation may be that participants generally know less about this treatment compared with aCT, and thus possibly doubt or underestimate the effectiveness of aHT. The wish to survive/avoid recurrence and the clinician's recommendation were valued equally in younger participants. This was not found for older participants who considered the clinician's recommendation most important. With regard to arguments against aHT, no overt differences were found in the predominant motivations between the age groups.

Some limitations of this study need to be noted. Participants were approached before they actually faced a decision. Although they probably would be confronted with this decision, the preference they reported here might still differ from their preference once they had received a recommendation. Further, fewer older participants than anticipated could be included in the study. This was owing to the fact that primarily older participants were excluded based on the exclusion criterion of having a previous malignancy (11 older compared with 2 younger women). Nevertheless, comparison of our older participants with older patients with early-stage invasive BC enrolled in a population-based cohort study in the Netherlands[29] showed that our sample was compared favorably with the average older woman with BC with regard to median age and presence of comorbid and geriatric conditions. Finally, because our sample was small, further investigation about younger and older participants' preferences for aHT in a larger sample is required.

Conclusion

This prospective study revealed that whereas older participants were less willing to undergo aCT than younger participants, no significant difference was found for aHT. Still, a majority of older participants would accept both therapies, and these women required similar benefits in 10-year disease-free survival as younger women. The option of adjuvant systemic therapy should therefore be discussed with eligible patients regardless of age. Younger and older participants' motivations for and against therapy generally did not differ, except that, contrary to younger participants, older participants reported multiple motivations against aCT, which included fear of treatment-related toxicity, the wish to maintain current quality of life and independence, the negative treatment experience of others, benefits not outweighing side effects, and old age. Clinicians should explore what matters most to the patient, elicit their preference, and incorporate these evaluations in their treatment recommendation.

CLINICAL PRACTICE POINTS

- To date, little is known about older patients' preferences for aCT and aHT. Previous studies have mainly focused on young or middle-aged patients. The scarcity of evidence on older patients' treatment preferences indicates that clinicians have no clear guidance about what older patients generally desire. Several studies demonstrated that patient age often influences clinicians' advice about adjuvant systemic therapy.[30,31] This ageism may partially explain why older patients more often receive suboptimal therapy than younger patients, which might then be associated with lower survival rates.[32]
- Our prospective study has generated new knowledge that can be of help when making adjuvant treatment decisions with older patients. We found that the proportion of older women that would accept adjuvant systemic therapy was large, and for these women the minimally-required benefit for aCT and aHT did not differ from that of younger women. Also, we found a large variation in preferences within the older group, suggesting that each individual older patient may value the benefits and side effects of treatment strategies differently.
- It is necessary to involve older patients in the decision-making process. This requires patients to be made aware that adjuvant systemic therapy is an option. Next, the benefits and side effects involved, including the associated uncertainty given the individual's biological age, should be discussed. It is essential to explicitly explore the patient's consideration as to whether the expected benefit is worth the side effects.[33]

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APPENDIX A. Hypothetical scenario A.1: no adjuvant chemotherapy versus adjuvant chemotherapy; and hypothetical scenario A.2: no adjuvant hormonal therapy versus adjuvant hormonal therapy

The numbers represent the order in which the information about the treatment strategies was read aloud. Health consequences and side effects were based on a previous study about patient preferences (in the case of adjuvant chemotherapy only),[7] patient education brochures of the Dutch Cancer Society,[34,35] and expertise of two medical oncologists. Recurrence probabilities with and without adjuvant systemic therapy at 10 years were based on Early Breast Cancer Trialists' Collaborative Group data[36,37] and the Dutch treatment guidelines for BC.[38] The time period of 10 years differs from earlier studies,[7-9,11,12] but reflects current clinical practice. The treatment strategies were listed next to each other to ease comparability, and a combination of frequency formats and bar graphs was used to present the recurrence probabilities. This format was pilot-tested (face-to-face and by phone) among two healthy women and 23 patients, to assess readability, ease of understanding, and the level of distress the information might provoke. Based on the feedback, the wording of the interview questions was rephrased to improve understanding.

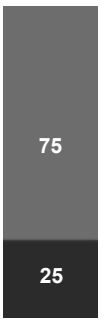
A.1 1. TREATMENT

No chemotherapy	Chemotherapy
The treatment consists of surgery (and possibly irradiation).	The treatment consists of surgery (and possibly irradiation), followed by chemotherapy. In most cases, chemotherapy is given once every three weeks for up to 6 months. It is administered by intravenous drip in the arm at the hospital, and each session lasts a few hours.
After surgery check-ups with the treating specialist take place.	After chemotherapy check-ups with the treating specialist take place.

2. HEALTH CONSEQUENCES AND SIDE EFFECTS

Both the disease and surgery (and irradiation) can cause physical, psychological and/or social problems.	Both the disease and surgery (and irradiation) can cause physical, psychological and/or social problems. Additionally *chemotherapy* can cause side effects, such as: *Hair loss, tiredness, feeling sick and vomiting, muscle and joint pain, diarrhea or constipation, decrease in the number of red blood cells, increased chance of infections, sores in the mouth, feeling of numbness or pins and needles, loss of appetite, skin rashes, itching, sore eyes, menopausal symptoms, infertility and (rarely) heart problems* The intensity of these side effects is impossible to predict; this varies from person to person.

3. PROBABILITY OF RECURRENCE AT 10 YEARS



75 out of 100 women

25 out of 100 women

Of the 100 women who do <u>not</u> undergo chemotherapy:

75 will have no recurrence of the disease
25 will have a recurrence of the disease

75 out of 100 women

10 out of 100 women

15 out of 100 women

Of the 100 women who do undergo chemotherapy:

75 will have no recurrence of the disease
10 will benefit from chemotherapy
15 will have a recurrence of the disease

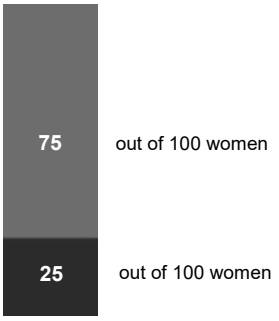
A.2 1. TREATMENT

No hormonal therapy	Hormonal therapy
The treatment consists of surgery (and possibly irradiation).	The treatment consists of surgery (and possibly irradiation), followed by hormonal therapy. Hormonal therapy is given for 5 years and consists of a tablet taken daily.
After surgery check-ups with the treating specialist take place.	During hormonal therapy check-ups with the treating specialist take place.

2. HEALTH CONSEQUENCES AND SIDE EFFECTS

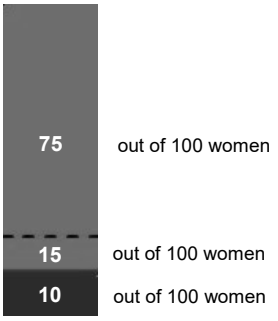
Both the disease and surgery (and irradiation) can cause physical, psychological and/or social problems.	Both the disease and surgery (and irradiation) can cause physical, psychological and/or social problems. Additionally *hormonal therapy* can cause side effects, such as: *Menopausal symptoms (hot flushes, feeling sick, muscle and joint pain, tiredness, breast pain or discomfort, hair thinning, mood changes, feeling sleepy, weight changes, vaginal bleeding and/or dryness) and (rarely) an increased risk of womb cancer, thrombosis –blood clots in veins- and bone loss* The intensity of these side effects is impossible to predict; this varies from person to person.

3. PROBABILITY OF RECURRENCE AT 10 YEARS



Of the 100 women who do <u>not</u> undergo hormonal therapy:

75 will have no recurrence of the disease
25 will have a recurrence of the disease



Of the 100 women who do undergo hormonal therapy:

75 will have no recurrence of the disease
15 will benefit from hormonal therapy
10 will have a recurrence of the disease

CHAPTER 5

Preferred and Perceived Participation of Younger and Older Patients in Decision-Making about Treatment for Early Breast Cancer: a Prospective Study

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ABSTRACT

Purpose | Older patients are believed to prefer a more passive role in treatment decision-making, but studies reporting this relation were conducted over a decade ago or were retrospective. We prospectively compared younger (40-64 years) versus older (≥65 years) breast cancer patients' preferences for decision-making roles and their perceived actual roles.

Methods | A prospective multicenter study was conducted in Leiden, The Hague and Tilburg over a two-year period. Early-stage breast cancer patients were surveyed about their preferred and perceived decision-making roles (active, shared, or passive) concerning surgery type (breast-conserving versus mastectomy) (n=74); adjuvant chemotherapy (aCT, n=43); and adjuvant hormonal therapy (aHT, n=39).

Results | For all decisions, both age groups most frequently preferred a shared role before consultation, except for decisions about aHT, for which younger patients more commonly preferred an active role. The proportion of patients favouring an active or passive role in each decision was lower for the older than the younger patients, but none of the differences was significant. Regarding perceived actual roles, both groups most frequently reported an active role in the surgical decision after consultation. In deciding about both aCT and aHT, a larger proportion of older patients perceived having had a passive role compared to younger patients, and a greater proportion of younger patients perceived to have been active. Again, differences were not statistically significant.

Conclusion | Most older patients preferred to decide together with their clinician, but preferences varied widely. Older patients more often than younger patients perceived they had not been involved in decisions about systemic therapy. Clinicians should invite all patients to participate in decision-making and elicit their preferred role.

INTRODUCTION

Over the last years, patient decisional role preferences in treatment decisions and shared decision-making (SDM) have been of central interest.[1] SDM entails clinicians helping patients to understand the potential benefits and risks of different treatment options, based on the best available medical evidence, and encouraging them to consider what matters most to them and to communicate their preferences. These preferences are then integrated with the clinical evidence to select the treatment option that best fits the patient.[2,3] SDM is strongly advocated in situations in which more than one option is medically appropriate and the choice strongly depends on patient preferences.[4] This is particularly true in early-stage breast cancer (BC). Primary treatment often involves a choice between breast-conserving surgery (BCS) and mastectomy (MAST). Both surgical options are equally effective in terms of survival,[5] but they have different consequences that may be valued differently by individual patients.[6,7] The importance of SDM has also been emphasized in the decisions about adjuvant systemic therapy in early-stage BC.[8] Adjuvant chemotherapy (aCT) or hormonal therapy (aHT) can improve disease-free survival,[9] but the benefits sometimes are only marginal and must be balanced against the large probability of side effects and inconveniences associated with treatment. Research has shown that large differences exist in preferences for adjuvant systemic therapy between individuals.[6] In these decisions, treatment choice therefore relies on a subjective weighing of the considerations.

Decision-making about treatment is complex for all patients, but it may be even more challenging when it comes to older patients. There is more uncertainty about the most appropriate treatment in this patient group, as clinical trials have frequently excluded older patients because of age or comorbid conditions,[10] and as shorter life expectancy decreases the benefit from treatment. Additionally, older patients often use multiple medications which may interact with treatment.[11] Further, a large heterogeneity exists among older patients in terms of general health status, physical and cognitive functioning, and tolerance to treatment toxicity.[12] Finally, non-clinical challenges (e.g., less social support) may affect treatment preferences of older patients differently compared to younger patients.[13] These reasons underscore the need to involve older patients in the decision-making process.[14,15]

A commonly reported argument against SDM with older patients is that they do not want a role in which they share the responsibility for the decision with the clinician, and that they would rather just receive information about their disease and treatment.[16-19] Studies that examined the preferred role of older patients in deciding about BC treatment have yielded inconsistent findings. Some found that a majority of older patients preferred a passive role like younger patients,[20] while others reported that a majority of the elderly wished a shared role[21-23] like younger patients.[24-27] It is noteworthy that most studies reporting a relation between older age and a passive decisional role preference were conducted over a decade ago.[20,28-31]

In the current era, in which patients are encouraged to be involved in treatment decision-making, it is conceivable that older patients have different decisional role preferences than older patients from previous generations.[32] It therefore remains unclear if and to what extent older patients prefer to be involved in decision-making, and how their preferences compare to that of younger patients. Furthermore, most studies assessed preferences following decision-making, whereby the patients' perceived role in the consultation could have strongly influenced their preferences, and whereby older patients in particular most likely had experienced passive roles.[16,33] Little is known about patients' decision-making preferences as assessed prospectively.

This prospective study aimed to compare the preferences of younger versus older patients for decision-making roles concerning three decisions (type of surgery, aCT, and aHT) in early BC. We also explored, for each decision, whether younger versus older patients differed in their perceived roles, and the concordance between preferred and perceived roles.

METHODS

Participants

This study was conducted at one academic and two non-academic teaching hospitals in the Netherlands, from January 2012 to December 2013. Eligible patients were aged ≥40 years, had a primary ductal carcinoma in situ or an invasive tumour (clinical T_{1-2}), and were candidates for both BCS (with radiotherapy) and MAST. Exclusion criteria were bilateral BC, *BRCA* 1/2 mutation, previous diagnosis of (non)invasive BC, other malignancies within the past five years (except non-melanoma skin cancer or cervical carcinoma in situ), poor comprehension of the Dutch language, mental/cognitive problems, intention to undergo neo-adjuvant therapy, any concurrent malignancy, and evidence of metastatic disease. Approval of the study protocol was obtained from the Medical Ethical Committee of the Leiden University Medical Center and the review boards of the other participating hospitals. Written informed consent was obtained from all participants.

Additional criteria were applied to each treatment decision. For surgery, patients who underwent a re-operation due to tumour positive surgical margins were excluded. For adjuvant systemic therapy, only patients eligible to receive aCT, aHT, or both were included. We first selected the patients who were referred to a medical oncologist. Subsequently, patients with hormone receptor (HR)-negative tumours were excluded from the aHT-related analysis, as they are ineligible to be treated with aHT. Finally, based on the national treatment guidelines,[34] patients aged ≥70 years were only included in the aCT analysis if they presented with highly unfavourable prognostic features (i.e., positive nodes and/or HR-negative tumours, or an intermediate- or a high-grade, HR-positive tumour ≥2.0 cm in size).

Procedure

Eligible patients were informed about the study during the first surgical consultation, after having been informed about the diagnosis and their eligibility for both BCS and MAST. Those who were interested received a questionnaire that contained a short comparative overview of the surgical options (see Hamelinck et al.[35] for more details), and one question to determine the participant's role preference in decision-making. They were instructed to complete the questionnaire before the second surgical consultation, in which the surgical options are usually discussed more in detail, a treatment recommendation is given, and a decision is made.

Before surgery, only the participants with invasive disease received another questionnaire. This questionnaire contained information on aCT and aHT (see Hamelinck et al.[13] for more details) and two questions to determine their preferred role in decision-making about these treatments. They had to complete the questionnaire after surgery but before the post-surgical consultation. During that consultation, patients are informed whether adjuvant systemic therapy is recommended based on pathology results, and that in case of eligibility, a consultation with the medical oncologist follows to discuss the systemic therapy options. We purposively asked participants to complete the questionnaire about surgery before the second surgical consultation, and the questionnaire about adjuvant systemic therapy before the post-surgical consultation, to prevent the surgeon's recommendation for type of surgery and for referral to the medical oncologist, respectively, from influencing the participant's decisional role preference. Six weeks after surgery, all participants received a mailed follow-up questionnaire containing questions regarding participants' perceptions of their role during decision-making about surgery, and if applicable, about aCT and/or aHT. By then, it was expected that patients with an indication for adjuvant systemic therapy had been referred to the medical oncologist and that a treatment plan had been determined.

Measures

Preferred and perceived role in decision-making

A modified version of the Control Preferences Scale[36] was used to assess decisional role preferences. For each treatment decision, participants were asked to indicate their preferred role for involvement in decision-making from the following five roles: (1) the patient decides, (2) the patient decides after considering the clinician's opinion, (3) the patient decides jointly with the clinician, (4) the clinician decides after considering the patient's opinion, and (5) the clinician decides. Perceived role in decision-making was assessed by asking participants to indicate the role they had played in each decision, by choosing from the same five roles (presented in the past tense).

Participants' characteristics

Self-report data on socio-demographic details were collected in the pre-surgery questionnaire.

Medical charts were reviewed for information on tumour and treatment characteristics, date of first medical oncology visit (in which a decision about systemic therapy is usually made), and geriatric conditions.[37] Comorbid conditions were also registered using the 10th revision of the International Classification of Diseases.[38]

Statistical analyses

Participants were divided into younger (aged 40-64 years) and older (aged ≥65 years) patients. For each decision, only participants who filled in both their preferred and perceived role were included. Responses regarding preferred and perceived roles were categorized as active (responses of 1-2), shared (3), and passive (4-5). Each participant's preferred role was compared to her perceived role, resulting into two categories: concordance (preferred and perceived role were similar) and discordance (preferred role differed from perceived role). In case of discordance, we noted whether more (from passive to shared/active; from shared to active) or less (from active to shared/passive; from shared to passive) involvement was perceived than preferred. Descriptive statistics were used to present participants' characteristics, preferred and perceived roles, and concordance. Differences in characteristics, roles, and concordance among the age groups were assessed by the χ^2 or Fisher Exact tests. Data were analysed using SPSS version 22. A p-value <0.05 was considered statistically significant.

RESULTS

Participants

Type of surgery

Overall, 132 eligible patients agreed to participate (75% response). Of them, 92 answered the question about preferred role in surgical decision-making before the second surgical consultation. No significant differences were found between characteristics of participants who did versus who did not return the questionnaire before the consultation (data not shown). As three patients subsequently withdrew from the study, 89 were sent the follow-up questionnaire and 83 of these returned it. Nine of them were excluded for the following reasons: underwent a reoperation (n=7), had a concurrent malignancy discovered after surgery (n=1), or did not answer the question about perceived role (n=1). In total, 74 participants completed the questionnaire at a median of 60 days after the consultation (range, 45-115; Table 1 and Figure 1). A majority had invasive disease (85%) and underwent BCS (72%). The sample included 49 younger (66%) and 25 older (34%) patients. Younger and older patients did not differ on most variables, with the exception that older versus younger participants were less often employed (p<0.001) and had less often children living at home (p=0.05). Further, older patients more often experienced one specific geriatric health condition: severe sensory impairment (p=0.02). Although a greater proportion of the older patients had one or more comorbid conditions than younger patients, there were no significant differences between the three most common types (cardiovascular, endocrine, and musculoskeletal diseases).

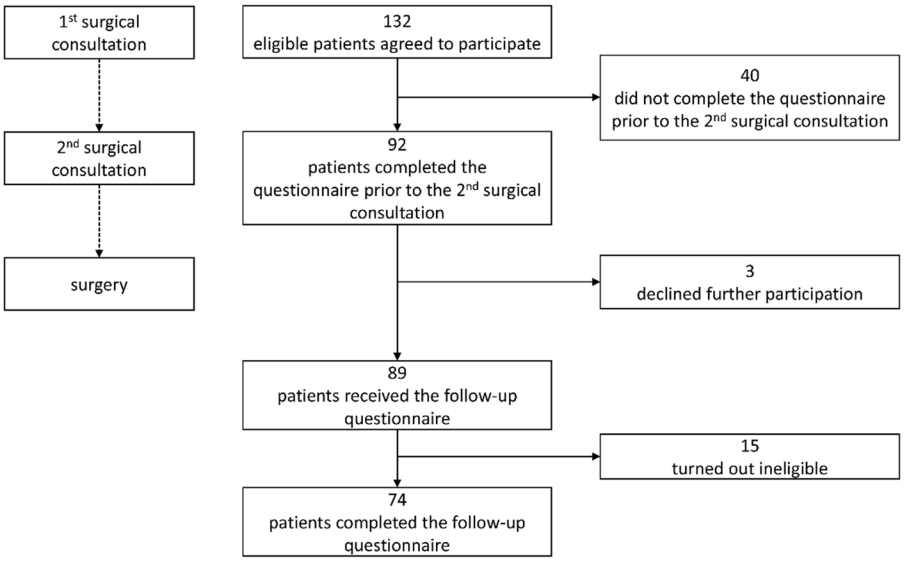

Figure 1. Flow chart of selection of patients included in analysis for decision-making about type of surgery

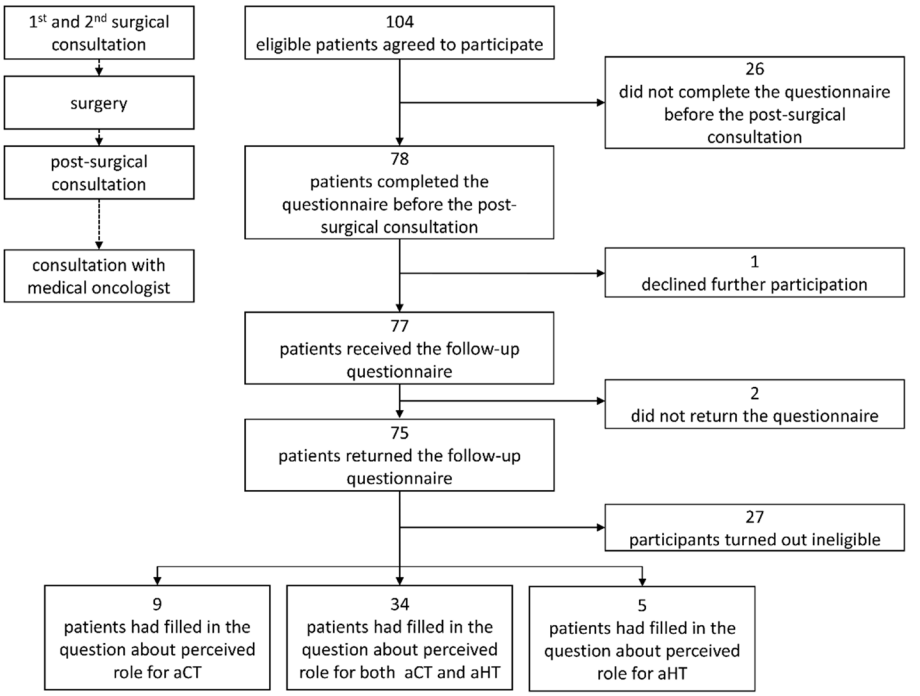

Figure 2. Flow chart of selection of patients included in analysis for decision-making about adjuvant chemotherapy (aCT) and adjuvant hormonal therapy (aHT)

Adjuvant systemic therapy

In total, 104 participants received the questionnaire about preferred roles in aCT and aHT decision-making, and 78 completed the questions before the post-surgical consultation. No significant differences were found for patients' age between those who did versus did not return the questionnaire before the consultation. One participant dropped out after filling out the questionnaire, and 77 received the follow-up questionnaire. Of the 75 who returned it, 52 had visited a medical oncologist. Participants were excluded if they had a concurrent malignancy (n=1), if the perceived role question was answered before their medical oncology visit (n=2), or if the question was not answered (n=1). Of the remaining 48 patients, 34 had an indication for both aCT and aHT, 9 had an indication for only aCT and 5 for only aHT. Thus, 43 participants were included in the aCT analysis and 39 in the aHT analysis (Figure 2). Participants completed the aCT questionnaire on average 29 days after consultation (range, 9-89, Table 1) and the aHT questionnaire on average 31 days (range, 8-58) after consultation. In the aCT analysis, 11 patients (26%) were aged ≥65 years, and in the aHT analysis, 12 patients (31%) were aged ≥65 years.

Table 1. Patient characteristics by age group and decision type

	Total		40-64 y		≥65 y	
Variables	n	%	n	%	n	%
Surgery[a]	(n=74)		(n=49, 66%)		(n=25, 34%)	
Patient characteristics						
Age (y)	60 (42-80)		55 (42-64)		70 (65-80)	
Time from second surgical consultation to filling in the follow-up questionnaire (d)	60 (45-115)[b]		60 (46-105)[b]		61 (45-115)	
Marital status						
married/living together	50	68	33	67	17	68
single/divorced/widowed	24	32	16	33	8	32
Educational level[c]						
low	19	26	11	22	8	32
intermediate	34	46	20	41	14	56
high	21	28	18	37	3	12
Employment status						
full/part-time	36	49	34	69	2	8
housekeeper	9	12	2	4	7	28
unemployed/long-term sick leave	7	10	7	14	0	0
retired	22	30	6	12	16	64
Having children						
no children	16	22	10	20	6	24
yes, children not living at home	40	54	23	47	17	68
yes, children living at home	18	24	16	33	2	8
Number of comorbid conditions						
0	25	34	21	43	4	16
1	16	22	9	18	7	28
2 or more	33	45	19	39	14	56
Type of comorbid conditions						
cardiovascular diseases (ICD10-9; yes)	30	41	16	33	14	56

endocrine diseases (ICD10-4; yes)	18	24	10	20	8	32
musculoskeletal diseases (ICD10-13; yes)	15	20	8	16	7	28
other diseases (yes)[d]	30	41	19	39	11	44
Geriatric health condition[e]						
no	49	66	36	73	13	52
yes	25	34	13	27	12	48
Specific geriatric health condition[f]						
incontinence (yes)	3	12	1	8	2	17
severe sensory impairment (yes)	10	40	2	15	8	67
depression (yes)	4	16	3	23	1	8
polypharmacy (yes)	17	68	11	85	6	50
difficulties with walking (yes)	6	24	2	15	4	33
Preoperative tumor morphology						
DCIS	11	15	7	14	4	16
invasive	63	85	42	86	21	84
Type of surgery performed						
BCS	53	72	38	78	15	60
MAST	21	28	11	22	10	40
Adjuvant chemotherapy[a]	(n=43)		(n=32, 74%)		(n=11, 26%)	
Patient characteristics						
Age (y)	60 (42-76)		55 (42-63)		70 (65-76)	
Time from medical oncologist consultation to filling in the follow-up questionnaire (d)	29 (9-89)[g]		30 (9-58)[g]		24 (18-89)	
Received chemotherapy						
no	19	44	11	34	8	73
yes	24	56	21	66	3	27
Had initiated therapy at time of filling in the follow-up questionnaire						
no	12	50	10	48	2	67
yes	12	50	11	52	1	33
Adjuvant hormonal therapy[a]	(n=39)		(n=27, 69%)		(n=12, 31%)	
Patient characteristics						
Age (y)	60 (42-86)		55 (42-63)		73 (65-86)	
Time from medical oncologist consultation to filling in the follow-up questionnaire (d)	31 (8-58)[g]		31 (9-58)[g]		28 (8-53)	
Received hormonal therapy						
no	4	10	2	7	2	17
yes	35	90	25	93	10	83
Had initiated therapy at time of filling in the follow-up questionnaire						
no	18	51	18	72	0	0
yes	17	49	7	28	10	100

Data are presented as n (n%) or median (ranges)
DCIS= Ductal carcinoma in situ; BCS= Breast-conserving surgery; MAST= Mastectomy; ICD= International Classification of Disease; y = years; d=days

[a] Three patient groups because of three different inclusion criteria
[b] Two participants did not fill in date of completion
[c] Levels of education were categorized as low=completed no/primary school; intermediate=completed lower general secondary education/vocational training; or high=completed pre-university education/high vocational training/university
[d] Other comorbid diseases included respiratory diseases (ICD10-10), neurologic diseases (ICD10-6), psychiatric diseases (ICD10-5), digestive diseases (ICD10-11), genitourinary diseases (ICD10-14) and blood diseases (ICD10-3)
[e] Presence of a geriatric health condition was defined as having one or more of the following characteristics: not able to carry out daily activities, incontinence, severe sensory impairment, depression, polypharmacy; difficulty walking
[f] No participant had difficulties carrying out daily activities
[g] One participant did not fill in date of completion

Preferred and perceived roles in decision-making

Type of surgery

Differences in both preferred and perceived roles between the age groups were found, but the differences were not significant (p=0.62 and p=0.94, respectively). Both younger and older participants most often preferred a shared role (49% and 60%, respectively) before consultation (Table 2A). Fewer members of both groups wished an active role (35% and 32%, respectively), and only 16% of younger and 8% of older participants preferred a passive role. After consultation, both younger and older participants most frequently reported to have perceived they had had an active role (49% and 56%, respectively), followed by shared (37% and 32%) and passive (14% and 12%) roles. Comparison of preferred and perceived roles showed that 32% of the younger and 36% of the older participants had participated to their preferred extent, 43% of the younger and 40% of the older participants had played a greater role in the decision than initially preferred, and 25% of the younger and 24% of the older participants had been less involved than preferred. The differences in concordance between the groups did not significantly differ (p=0.77).

Adjuvant chemotherapy

Again, both preferred and perceived roles varied between the age groups, but the differences were not significant (p=0.41 and p=0.82, respectively). Younger and older participants most frequently indicated a preference for a shared role (47% and 73%, respectively), followed by a preference for an active (34% and 18%) or a passive (19% and 9%) role (Table 2B). After consultation, younger participants more often perceived to have had an active role than older participants (41% versus 36%), and older participants more often indicated to have perceived a passive role (36% versus 25%). In 50% of the younger and 54% of the older participants, their perceived role matched their preferred role (p=0.80). The remainder of the younger participants were most often more involved than initially desired (28%), whereas older participants were most often less involved (27%).

Adjuvant hormonal therapy

As earlier, differences in preferred and perceived roles between the age groups were not significant (p=0.43 and p=0.52, respectively). Younger participants often preferred an active role (44%), whereas older participants more often had a preference for a shared role (58%) (Table 2C). Younger participants most often perceived to have had an active role (44%) and older participants most often a passive role (42%). Fifty percent of the older participants had their preferred role match their perceived role, compared to 37% of the younger participants, but this difference was not significant (p=0.45). Also in this decision, younger participants were most often more involved than initially desired (33%) and older participants most often less involved than desired (41%).

Table 2. Preferred (pre-consultation) and perceived (post-consultation) roles and concordance between the roles by decision type

A. Type of surgery (breast-conserving surgery vs. mastectomy)								
	40-64 y (n=49)				**≥65 y** (n=25)			
	Perceived role				**Perceived role**			
Preferred role	active	shared	passive	total	active	shared	passive	total
active	**8 (16)**	5 (10)	4 (8)	17 (35)	**5 (20)**	3 (12)	0 (0)	8 (32)
shared	13 (27)	**8 (16)**	3 (6)	24 (49)	8 (32)	**4 (16)**	3 (12)	15 (60)
passive	3 (6)	5 (10)	**0 (0)**	8 (16)	1 (4)	1 (4)	**0 (0)**	2 (8)
total	24 (49)	18 (37)	7 (14)	49 (100)	14 (56)	8 (32)	3 (12)	25 (100)
B. Adjuvant chemotherapy (yes/no)								
	40-64 y (n=32)				**≥65 y** (n=11)			
	Perceived role				**Perceived role**			
Preferred role	active	shared	passive	total	active	shared	passive	total
active	**6 (19)**	2 (6)	3 (9)	11 (34)	**2 (18)**	0 (0)	0 (0)	2 (18)
shared	6 (19)	**7 (22)**	2 (6)	15 (47)	2 (18)	**3 (27)**	3 (27)	8 (73)
passive	1 (3)	2 (6)	**3 (9)**	6 (19)	0 (0)	0 (0)	**1 (9)**	1 (9)
total	13 (41)	11 (34)	8 (25)	32 (100)	4 (36)	3 (27)	4 (36)	11 (100)
C. Adjuvant hormonal therapy (yes/no)								
	40-64 y (n=27)				**≥65 y** (n=12)			
	Perceived role				**Perceived role**			
Preferred role	active	shared	passive	total	active	shared	passive	total
active	**5 (19)**	2 (7)	5 (19)	12 (44)	**2 (17)**	1 (8)	0 (0)	3 (25)
shared	6 (22)	**3 (11)**	1 (4)	10 (37)	0 (0)	**3 (25)**	4 (33)	7 (58)
passive	1 (4)	2 (7)	**2 (7)**	5 (19)	1 (8)	0 (0)	**1 (8)**	2 (17)
total	12 (44)	7 (26)	8 (30)	27 (100)	3 (25)	4 (33)	5 (42)	12 (100)

Data are presented as n (%)

Numbers and proportions in bold add up to numbers and proportions of concordance between preferred and perceived role; Numbers and proportions below the diagonal bold line add up to numbers and proportion of participants who experienced a greater role than initially preferred; Numbers and proportions above the diagonal bold line add up to numbers and proportions of participants who experienced a lesser role than initially preferred

DISCUSSION

In this prospective study of patients with early BC, we compared the preferred and perceived roles of younger and older patients in decisions about type of surgery, aCT and aHT, as well as the concordance between their preferred versus perceived decision-making roles.

Our findings challenge the belief that older patients often prefer to leave treatment decisions to their clinician. Only few older patients wished a passive role, and most preferred to make

the decision themselves or together with their oncologist, in line with another recent study[39] showing that most older patients preferred a shared or active role over a passive role. In our study, about three in five older patients preferred to make the decision together with their clinician. Our finding that both younger and older patients most often preferred to be involved in making the decision about type of surgery is in line with one of the few other prospective studies among newly-diagnosed patients with early-stage disease eligible for BCS and MAST.[25] In contrast, a retrospective study found that preferring a passive role was related to being older.[40] Patients' experiences of the decision-making process may possibly have influenced their reported preferences in the latter study. Our results suggest that patients of all ages prefer to be involved in decision-making and thus that one should not automatically assume that older patients wish to defer the decision to the clinician. This is particularly important because clinicians often underestimate patients' decisional role preferences[41] and rarely ask patients for their preferences.[42]

Although decisional role preferences did not significantly differ between age groups, preferred roles in deciding whether to undergo aHT stand out, with relatively more younger than older patients preferring to make the decision themselves. Premenopausal patients may perceive aHT as having a greater impact on their daily lives than older patients, given that aHT can cause menopausal symptoms. We found in our previous study[13] that both age groups, but more so in younger patients, frequently reported that concern about the short- and long-term side-effects was an important factor in their preferences for aHT (of 74 patients in our previous study, 35 participated in the present study).

We also found that older patients' perceived roles varied from those of younger patients and varied across the different decisions. Because BCS and MAST are equivalent options in terms of survival, and are presented as such in national guidelines,[34] we may expect that clinicians offer patients a choice between these two surgical options. It is, not surprising then, that both older and younger patients frequently perceived to have had an active role in making the decision. In contrast, older patients more often than younger patients felt that they had not been involved in making the decision concerning aCT. The treatment guidelines indeed state that aCT may not be a reasonable treatment option for patients over 70 years of age.[34] Similarly, older patients more often perceived to have had a passive role in deciding about aHT. In clinical practice, patients with HR-positive tumours, irrespective of their age, are rarely offered a choice about aHT.[43] Younger patients may ask more questions after being informed about aHT, which could result in more communication about treatment characteristics. As a result, younger patients may have felt more involved in decision-making,[44] thereby explaining why they more frequently perceived an active role. More research is needed to better explain these findings.

For each decision, we found an overall difference between patients' preferred versus perceived decisional roles in 40% of the younger patients and 47% of the older patients. For both age groups, the largest difference was observed with respect to the decision about surgery. Differences in these gaps between the age groups were minimal, except for the decision about aHT. Discordance can negatively impact patients' treatment outcomes and experiences of care[45,46] and it is therefore important that future studies examine how the occurrence of discordant roles can be minimized.

To our knowledge, our study is the first to prospectively explore patients' preferences regarding decisional roles for three common breast cancer treatment decisions with a specific focus on age-differences. A strength is that data were prospectively collected from patients. A potential limitation is that the decisional role preferences were regarded as if these remained stable; however, a patient's preference can change during or between consultations (e.g., a more active decisional role preference after receiving information about treatment options than before the consultation[47]). Also, recall bias could have affected participants' perception of their role during the consultation. Another limitation is the small number of older participants. We did not find significant differences between the age groups, as the sample size may not have been large enough to detect these. We believe it to be worthwhile to examine whether our findings also hold with a larger sample of older patients. Regardless of this limitation, this study provides valuable insights into the decision-making roles of this growing patient group.

It is important for clinicians to know that most older patients are willing to be involved in decision-making. However, we also want to stress the variation in role preferences among older patients and across the different decisions. As clinicians set the agenda for the consultation, it is reasonable to expect that the responsibility for inviting patients to participate in decision-making lies with clinicians. They should explicitly inform patients that a decision needs to be made and explain why patient involvement is relevant.[2,48] Older patients who feel they are not (yet) ready or able to engage in deliberation about different treatment options should be offered more time and support (e.g., an appointment with a nurse specialist, patient decision aids[49,50] or other support tools if available). This approach could improve their participation in decision-making. In the end, of course, at the patient's wish, the clinician can make the final decision, as long as he/she has elicited the patient's concerns and goals.[2] In addition, health care as a whole should empower older patients to become more involved in the decision-making process. The use of interventions that guide older patients through topics that are important to ask can help them better prepare for the consultation and may give them encouragement to be involved,[51] such as campaigns like 'Ask3' (e.g.. http://www.cardiffandvaleuhb.wales.nhs.uk/ask3).

Conclusion

Older patients, like younger patients, often favoured participation in decision-making about treatments for early BC. Also, both age groups mostly perceived more involvement than they preferred in the decision about surgery. Some older patients perceived less involvement than they preferred in aCT and aHT decision-making, and these patients may therefore need more encouragement to participate. Our results underscore the need for clinicians to invite all patients to participate in decision-making for each decision, and to retrieve to what extent patients want to be involved in making the final decision.

CLINICAL PRACTICE POINTS

- Older patients are believed to prefer a more passive role in treatment decision-making than younger patients. However, studies showing this relation were conducted over a decade ago, or were retrospective. In this era of increased attention to shared decision-making, it is conceivable that older patients have different decisional role preferences than older patients from previous generations.
- This prospective study found that older patients, like younger patients, often favoured to participate in decision-making. However, older patients more often than younger patients perceived they had not been involved in decisions about systemic therapy.
- Clinicians need to know that most older patients are willing to be involved in making treatment decisions, although role preferences varied within older – as in younger – patients and across decisions. It is therefore important that clinicians invite all patients to participate in decision-making, regardless of their age. Aside from the clinician's role, it is also important to stimulate older patients themselves to become more involved in decisions about their treatment, for example by directing patients to key questions to help them prepare better for the consultation.

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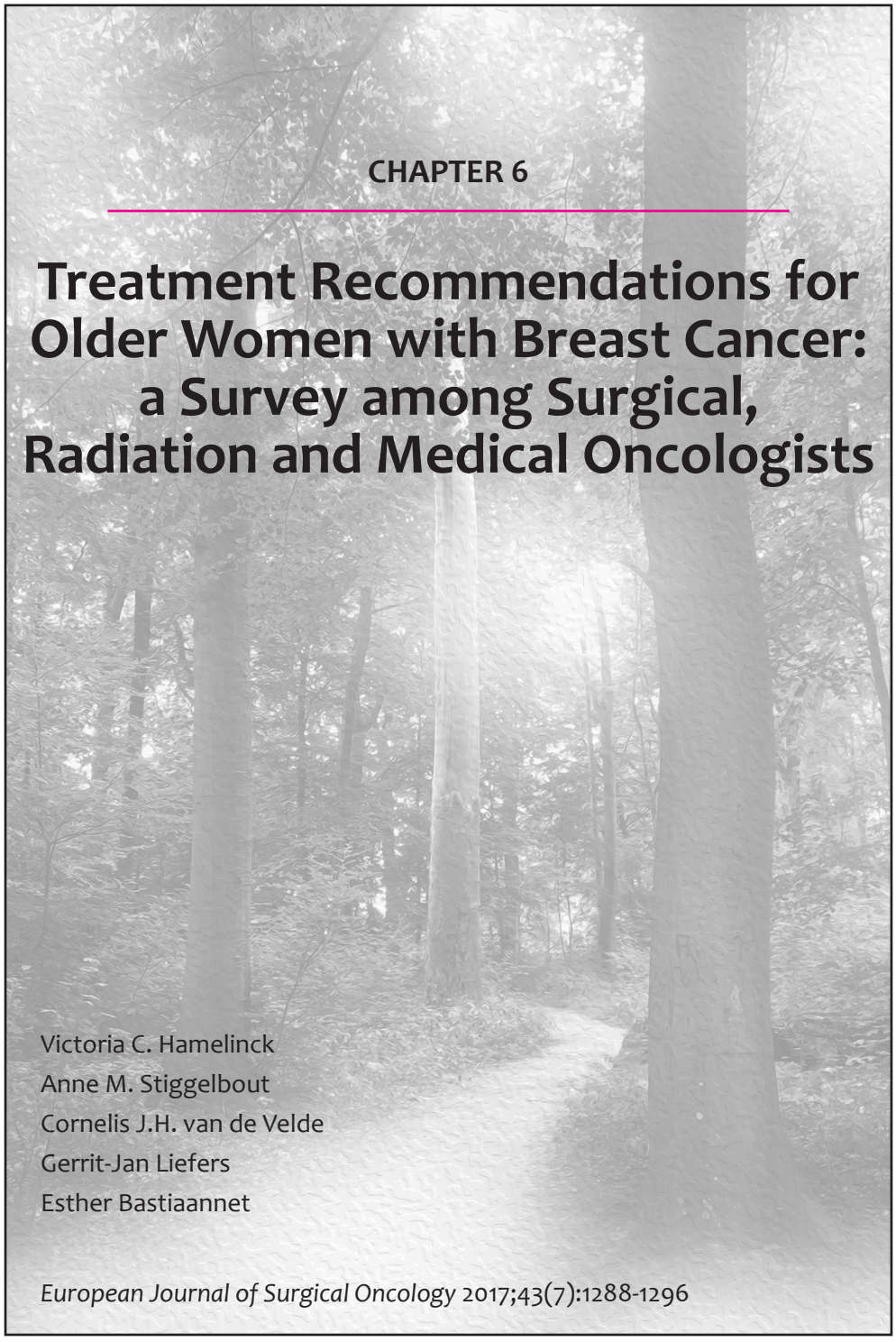

CHAPTER 6

Treatment Recommendations for Older Women with Breast Cancer: a Survey among Surgical, Radiation and Medical Oncologists

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ABSTRACT

Purpose | As older women with breast cancer (BC) are underrepresented in trials, it is often unclear what represents the best treatment option for this patient group. To understand how oncologists approach the management of BC in older patients, we assessed their treatment recommendations.

Methods | In an online survey, 106 surgical, 37 radiation and 31 medical oncologists provided a treatment recommendation for hypothetical patients aged >70 years. Scenarios included loco-regional therapy with patient age varying at 76 and 84 years; systemic therapy with Karnofsky performance score varying at 90% and 50%; neo-adjuvant therapy; and adjuvant chemotherapy in triple-negative BC.

Results | Participants would less often recommend breast-conserving surgery plus radiotherapy for an 84 versus a 76-year-old patient (56% versus 73%, p=0.001). They would more often accept omission of radiotherapy after breast-conserving surgery in older than in younger patients, if the patient wished to avoid this therapy (26% versus 4%, p<0.001). All participants would propose systemic therapy for a high-recurrence risk patient with a good performance score, and 92% would still recommend therapy if the patient had a poor score (p<0.001). Neo-adjuvant hormonal therapy followed by breast-conserving surgery for a large tumour was recommended by 27% of the participants. Adjuvant chemotherapy for an otherwise healthy woman with triple-negative BC was considered by 83% of the participants.

Conclusion | Patient age and performance status influenced specialists' treatment recommendations. The observed recommendations for the treatment scenarios under investigation differ from older women's actual treatment. This discrepancy highlights the need for studies specifically targeting older patients.

INTRODUCTION

With over 14,000 new cases in 2013, breast cancer (BC) is the most common malignancy among women in the Netherlands.[1] Approximately 30% of the cases are in women over 70 years of age.[1] Although BC in older women is a common health problem, optimal treatment of this patient group remains unclear, since older patients are often excluded from clinical trials.[2] Besides, those enrolled in trials are usually in better than average health, and therefore may not be representative for all older BC patients.[3] Elderly patients comprise a heterogeneous group due to differences in comorbid conditions, functional capacity, and social support.[4] The large variety in characteristics within this population, together with the lack of evidence on treatment approach and the limited data on older patients' preferences[5] make treatment decision-making for these patients generally difficult.

The Dutch treatment guidelines for BC make little or no age-specific recommendations.[6] This provides room for variation in the treatment of older patients. Studies have demonstrated that older patients are less likely than younger patients to undergo breast-conserving surgery and radiotherapy after breast-conserving surgery. They also less often receive adjuvant chemotherapy compared to younger patients with similar disease severity.[7,8] The reasons for these age-differences in treatment are unclear and could result from either patients' or clinicians' preferences. It has been shown that individual patient's treatment preferences vary greatly,[5] whilst others have suggested that clinicians play a notable role in treatment decision-making, particularly among older patients.[9,10]

Currently, it is unknown how clinicians weigh treatment options for patients aged ≥70 years. Previous surveys using hypothetical scenarios explored how patient age or health status influenced clinicians' treatment recommendations,[11-19] but most only focused on adjuvant systemic therapy.[11-15,18] Furthermore, their recommendations were seldom compared for scenarios only involving patients aged over 70.[12-15,19] Of these latter studies, none compared the recommendations of oncologists of different specialties, despite multidisciplinary team decision-making becoming the norm in BC. Surgical, radiation and medical oncologists are ought to decide together what could be the best treatment for the patient. With the increasing incidence of BC in older women,[2] a better understanding of clinicians' recommendations and influencing factors become increasingly relevant.

This study aimed to examine the treatment recommendations of BC specialists for loco-regional and (neo-)adjuvant systemic therapy in older patients, and to explore whether the recommendations are influenced by patient age and performance status, and by clinician speciality.

METHODS

Participants

Eligible participants were surgical, radiation, and medical oncologists (including doctors in training) involved in BC treatment. Between October 2013-February 2014, members of the Dutch Society of Surgical Oncology (n=~550), the Dutch Society of Radiotherapy and Oncology (n=525) and the Dutch Society of Medical Oncology (n=418) received an emailed newsletter of their society which contained an invitation to participate. As it was not possible to select BC specialists only, the emailed newsletter was sent to all members, irrespective of their cancer type specialism. The invitation was addressed to BC specialists only, and briefly described the study and provided a link to the anonymous online questionnaire. Four weeks after, all members were once again informed via a newsletter. Between July-November 2014, collaborating partners (Comprehensive Cancer Centre Leiden Region, the Netherlands, and three medical oncologists) forwarded our invitation directly to medical oncologists within their network to increase their response. Consequently, 37 oncologists of the regional medical oncology working party, and a random sample of 40 medical oncologists were approached. As this study did not involve patients, no ethical approval was required for this study.

Questionnaire

The two-part questionnaire consisted of participants' socio-demographic and work-related characteristics and of hypothetical scenarios, which resembled situations for which there is currently little or no consensus about the best treatment for patients aged ≥70 years (Appendix 1). The scenarios were based on the Dutch treatment guidelines for BC[6] and previous work.[2,8] We pilot-tested the scenarios for clarity among seven health professionals and five BC researchers. Minor modifications to the phrasing of the questions and lay-out of the questionnaire were made. We used NetQ software to create the questionnaire.

Participants were presented the scenarios and asked to choose a treatment recommendation from a list of options. Each scenario included a description of patient (e.g., age and Karnofsky Performance Status [KPS]) and clinical characteristics (e.g., hormone receptor status) that would usually be available at decision-making. Scenario 1 explored whether a patient's chronological age influenced the recommendation for loco-regional therapy. Two identical sub-scenarios (1A and 1B) were developed, except the age of the patient differed (76 versus 84 years). Scenario 2 examined whether a patient's performance status influenced the recommendation for adjuvant systemic therapy, by decreasing the KPS score from 90% (2A) to 50% (2B), keeping all other characteristics identical. Scenario 3 focused on neo-adjuvant hormonal therapy. The guidelines state that this therapy should only be prescribed to old and frail patients who are unsuitable for neo-adjuvant chemotherapy or surgery.[6] In recent years, neo-adjuvant hormonal therapy gained interest, because it increases the feasibility of breast-

conserving surgery in patients who would otherwise undergo a mastectomy. This therapy could be appropriate for older patients, as most have hormone receptor-positive BC.[2] Scenario 4 concerned adjuvant chemotherapy for hormone receptor-negative and HER2-negative BC. Triple-negative BC in older patients is particularly challenging, because chemotherapy is the only systemic option, but most (e.g., who are unfit) are ineligible for this therapy.[2]

Analyses

Participants were included in the analyses if the first question of the scenarios was completed. Regarding scenarios 1 and 2, we excluded participants who did not complete questions about both sub-scenarios (1A and 1B, or 2A and 2B). Free-text responses (i.e., 'other, namely:') were independently reviewed by three investigators and were recoded appropriately if it corresponded to an already available answering option; otherwise they were considered as 'other' and excluded from further analyses. Descriptive statistics were used to describe participants' characteristics, and responses to the scenarios. Differences in the proportions of the recommendations between sub-scenarios, and between speciality groups (in scenarios 3 and 4) were assessed using χ^2 or Fisher Exact test. A p-value below 0.05 was considered statistically significant. Analyses were conducted using SPSS version 22.

RESULTS

Participants

Overall, 243 oncologists opened the link to the questionnaire and 190 eligible participants began the survey. Of them, 16 dropped out after the socio-demographic questions. In total, 164/174 participants completed all questions. Socio-demographic and work-related characteristics did not significantly differ between participants who had fully/partly completed the questions (data not shown). The median age of the participants was 47 years (range, 27-68), and most were male (55%, Table 1). The participants comprised of 106 (61%) surgical, 37 (21%) radiation, and 31 (18%) medical oncologists. Nearly half (49%) practiced in general teaching hospitals, and 58% had been specialized in BC treatment for more than ten years. All, except one, reported to see at least one newly-diagnosed woman aged ≥70 years per month.

Hypothetical scenarios

Overall, 167 (96%) participants responded to scenarios 1A and 1B, and 164 (94%) to all scenarios (1A, 1B, 2A, 2B, 3, and 4).

Influence of age on recommendation for loco-regional therapy (scenario 1)

The scenario portrayed a woman, aged either 76 (1A) or 84 (1B) years, who was otherwise in good health, and had a clinically small, node-negative, hormone receptor-positive tumour. She was eligible for both surgical options.

Table 1. Participants' socio-demographic and work-related characteristics (n=174)

Variables	Total (n=174) n (%)	Surgical oncologists (n=106, 61%) n (%)	Radiation oncologists (n=37, 21%) n (%)	Medical oncologists (n=31, 18%) n (%)
Median age in years (range)	47 (27-68)	46 (32-64)	48 (27-64)	48 (30-68)
Gender				
male	95 (55)	65 (61)	17 (46)	13 (42)
female	79 (45)	41 (39)	20 (54)	18 (58)
Practice setting				
general non-teaching hospital	42 (24)	37 (35)	0 (0)	5 (16)
general teaching hospital	86 (49)	55 (52)	8 (22)	23 (74)
university medical center/specialized oncology center	46 (26)	14 (13)	29 (78)	3 (10)
Region[a]				
North (i.e. Groningen, Friesland, Drenthe)	19 (11)	12 (11)	4 (11)	3 (10)
East (i.e. Gelderland, Overijssel, Flevoland)	30 (17)	18 (17)	7 (19)	5 (16)
West (i.e. Noord-Holland, Zuid-Holland, Utrecht)	83 (48)	52 (49)	18 (49)	13 (42)
South (i.e. Zeeland, Brabant, Limburg)	39 (22)	22 (21)	7 (19)	10 (32)
I prefer not to disclose this	3 (2)	2 (2)	1 (3)	0 (0)
No. of years of experience treating breast cancer patients				
<2 years	6 (3)	2 (2)	3 (8)	1 (3)
2-5 years	32 (18)	22 (21)	2 (5)	8 (26)
6-10 years	36 (21)	24 (23)	9 (24)	3 (10)
>10 years	100 (58)	58 (55)	23 (62)	19 (61)
No. of new breast cancer patients seen per month				
1-2 patients	5 (3)	2 (2)	1 (3)	2 (6)
3-5 patients	43 (25)	21 (20)	10 (27)	12 (39)
6-10 patients	69 (40)	44 (42)	11 (30)	14 (45)
11-15 patients	32 (18)	18 (17)	11 (30)	3 (10)
>15 patients	25 (14)	21 (20)	4 (11)	0 (0)
No. of new breast cancer patients aged ≥70 years seen per month				
none	1 (1)	0 (0)	0 (0)	1 (3)
1-2 patients	64 (37)	31 (29)	15 (41)	18 (58)
3-5 patients	82 (47)	54 (51)	18 (49)	10 (32)
6-10 patients	23 (13)	17 (16)	4 (11)	2 (7)
11-15 patients	3 (2)	3 (3)	0 (0)	0 (0)
>15 patients	1 (1)	1 (1)	0 (0)	0 (0)

[a] One participant did not respond to this question

Type of surgery:

Participants' treatment recommendation regarding surgical resection differed significantly by patient age (p=0.001, Table 2; Question 1). For a 76-year-old patient, 73% of the participants reported to recommend breast-conserving surgery plus radiotherapy. If this patient was 84-years-old, only 56% would give this recommendation. Conversely, the proportion recommending a mastectomy (7% vs 1%), or leaving the choice to the patient (37% vs 26%) was greater if this patient was 84-years-old.

Consistent with the overall results, the influence of patient age was observed among surgical oncologists (p=0.003), and to a lesser extent among medical oncologists (p=0.07). The recommendations of radiation oncologists did not differ by age (p=0.81).

Radiotherapy omission after breast-conserving surgery:

Next, participants were asked whether they would accept the omission of radiotherapy if the patient indicated to prefer a breast-conserving surgery but wished to avoid radiotherapy. Responses varied significantly by patient age (p<0.001, Table 2; Question 2). If the patient was 84-years-old, 26% would accept this without question. Only 4% would accept this if the same patient was 76. On the contrary, the proportion who would accept it, but would still try to convince the patient of the benefit of radiotherapy was greater if she was 76-years-old rather than 84-years-old (62% vs 57%). The proportion simply not accepting radiotherapy omission (16% vs 13%), or recommending a mastectomy with breast reconstruction instead (19% vs 4%) was greater for the younger patient.

The recommendations of surgical (p<0.001) and medical oncologists (p=0.004) differed significantly by age, those of radiation oncologists did not (p=0.26).

Influence of performance status on recommendation regarding adjuvant systemic therapy (scenario 2)

This scenario described a 77-year-old woman who underwent a mastectomy, and whose pathology results revealed positive lymph nodes, and a T_2, high grade, hormone receptor-positive tumour. Participants significantly differed in their recommendation for a woman with a good (KPS 90%; 2A) versus a poor (KPS 50%; 2B) performance status (p<0.001, Table 3). If the patient had a good performance score, all participants would advise some form of systemic therapy: 86% would recommend hormonal therapy alone and 14% a combination of chemotherapy and hormonal therapy. If the same patient had a poor performance score, 92% would advise adjuvant systemic therapy, with all of them recommending hormonal therapy alone.

Both surgical (p<0.001) and radiation oncologists' (p=0.020) treatment recommendation significantly varied based on performance status. Similar differences in the recommendation of medical oncologists by age were found, but were not significant (p=0.06).

Table 2. Influence of patient age on specialists' treatment recommendation for loco-regional therapy (scenario 1)

A(n) (76- or 84-)year-old female, KPS score of 90% (able to carry on normal activity; minor signs or symptoms of disease), right-sided breast cancer, one lesion of 1.7 cm in the upper outer quadrant, invasive ductal adenocarcinoma, cT1c, cN0, ER+, PR+, Her2neu−, no contraindications to breast-conserving therapy, no comorbidities

	A 76-year-old female (1A)			An 84-year-old female (1B)			
Question 1: What would be your treatment recommendation regarding resection of the tumour?							
	I would not give any advice, I leave the choice to the patient	Breast-conserving surgery, followed by radiotherapy	Mastectomy	I would not give any advice, I leave the choice to the patient	Breast-conserving surgery, followed by radiotherapy	Mastectomy	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	*p*
Total (n=167)	43 (26)	122 (73)	2 (1)	61 (37)	94 (56)	12 (7)	**0.001**
Surgical oncologists (n=104)	22 (21)	81 (78)	1 (1)	37 (36)	60 (58)	7 (7)	**0.003**
Radiation oncologists (n=34)	17 (50)	17 (50)	0 (0)	16 (47)	18 (53)	0 (0)	0.81
Medical oncologists (n=29)	4 (14)	24 (83)	1 (3)	8 (28)	16 (55)	5 (17)	0.07
Question 2: Suppose the patient indicates that she would like to undergo breast-conserving surgery, but no radiotherapy. Would you accept this?							
	Yes, without question	Yes, but I would still try to convince her of the benefit of radiotherapy	No, I would recommend her a mastectomy with reconstruction	No	Yes, without question	Yes, but I would still try to convince her of the benefit of radiotherapy	No, I would recommend her a mastectomy with reconstruction	No	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	*p*
Total (n=167)	7 (4)	103 (62)	31 (19)	26 (16)	44 (26)	95 (57)	7 (4)	21 (13)	**<0.001**
Surgical oncologists (n=104)	6 (6)	66 (63)	14 (14)	18 (17)	30 (29)	60 (58)	1 (1)	13 (13)	**<0.001**
Radiation oncologists (n=34)	0 (0)	22 (65)	7 (21)	5 (15)	3 (9)	23 (68)	3 (9)	5 (15)	0.26
Medical oncologists (n=29)	1 (3)	15 (52)	10 (35)	3 (10)	11 (38)	12 (41)	3 (10)	3 (10)	**0.004**

KPS = Karnofsky Performance Status

A p-value in bold means a significant difference in treatment recommendation between scenario 1A and 1B

Table 3. Influence of patient performance status on specialists' treatment recommendation for adjuvant systemic therapy (scenario 2)

A 77-year-old female, KPS score of (90 or 50) %, right-sided breast cancer, one lesion of 3.0 cm in the upper outer quadrant, invasive ductal adenocarcinoma, a modified radical mastectomy was performed, pT2, pN1, grade 3, ER+, PR+, Her2neu−, no comorbidities

	KPS score of 90%[a] (2A)			KPS score of 50%[b] (2B)			
What would be your treatment recommendation?							
	No adjuvant systemic therapy	Adjuvant hormonal therapy	Adjuvant chemo-therapy, followed by adjuvant hormonal therapy	No adjuvant systemic therapy	Adjuvant hormonal therapy	Adjuvant chemo-therapy, followed by adjuvant hormonal therapy	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	*p*
Total (n=164)[c]	0 (0)	137 (86)	22 (14)	13 (8)	145 (92)	0 (0)	**<0.001**
Surgical oncologists (n=101)[d]	0 (0)	81 (83)	16 (17)	6 (6)	94 (94)	0 (0)	**<0.001**
Radiation oncologists (n=34)[e]	0 (0)	31 (91)	3 (9)	4 (13)	27 (87)	0 (0)	**0.020**
Medical oncologists (n=29)[f]	0 (0)	25 (89)	3 (11)	3 (11)	24 (89)	0 (0)	0.06

KPS = Karnofsky Performance Status
A p-value in bold means a significant difference in treatment recommendation between scenario 2A and 2B

[a] Able to carry on normal activity; minor signs or symptoms of disease
[b] Requires considerable assistance and frequent medical care
[c] Participants who filled in 'other' for scenario 2A (n=5) or 2B (n=6) were excluded
[d] Participants who filled in 'other' for scenario 2A (n=4) or 2B (n=1) were excluded
[e] Three participants who filled in 'other' for scenario 2B were excluded
[f] Participants who filled in 'other' for scenario 2A (n=1) or 2B (n=2) were excluded

Neo-adjuvant hormonal therapy (scenario 3)

For an otherwise healthy 75-year-old woman who was not initially a candidate for breast-conserving surgery because of a large hormone receptor-positive tumour in relation to her breast size, 27% would recommend neo-adjuvant hormonal therapy followed by breast-conserving surgery (Table 4). Fifty percent of the participants would recommend a mastectomy, and the remaining 23% would not give a treatment recommendation, but would leave the choice to the patient. No relevant differences in the recommendation between the specialities were observed (p=0.12).

Adjuvant chemotherapy for triple-negative BC (scenario 4)

The scenario described a 75-year-old woman, in otherwise good health, who underwent a mastectomy and was diagnosed with a T_2, high grade, node-positive, triple-negative BC. Most (83%) would consider adjuvant chemotherapy, of which 56% (72/129) would only consider it if the patient indicated to have a strong preference to be treated with chemotherapy (Table 5). There were no significant differences among the specialities (p=0.30).

Table 4. Specialists' treatment recommendation for neo-adjuvant hormonal therapy (scenario 3)

A 75-year-old female, KPS score of 90% (able to carry on normal activity; minor signs or symptoms of disease), right-sided breast cancer, one lesion of 3.5 cm in the upper outer quadrant, cup size 36A, invasive ductal adenocarcinoma, cT2, cN0, ER+, PR+, Her2neu–, no comorbidities

What would be your treatment recommendation?

	I would not give any advice, I leave the choice to the patient	Mastectomy	Neo-adjuvant hormonal therapy, followed by breast-conserving surgery	
	n (%)	n (%)	n (%)	*p*
Total (n=164)[a]	36 (23)	80 (50)	43 (27)	-
Surgical oncologists (n=101)[b]	21 (21)	51 (52)	26 (27)	0.12
Radiation oncologists (n=34)[c]	12 (37)	14 (44)	6 (19)	
Medical oncologists (n=29)	3 (10)	15 (52)	11 (38)	

KPS = Karnofsky Performance Status

[a] Five participants who filled in 'other' were excluded from the analyses
[b] Three participants who filled in 'other' were excluded from the analyses
[c] Two participants who filled in 'other' were excluded from the analyses

Table 5. Specialists' treatment recommendation for adjuvant chemotherapy in case of triple-negative BC (scenario 4)

A 75-year-old female, KPS score of 90% (able to carry on normal activity; minor signs or symptoms of disease), right-sided breast cancer, one lesion of 3.0 cm in the upper outer quadrant, invasive ductal adenocarcinoma, a modified radical mastectomy was performed, pT2, pN1, grade 3, ER–, PR–, Her2neu–, no comorbidities

Would you consider adjuvant chemotherapy?

	No, I would not consider adjuvant chemotherapy	Yes	Yes, but only if the patient has a strong preference for chemotherapy treatment	
	n (%)	n (%)	n (%)	*p*
Total (n=164)[a]	27 (17)	57 (37)	72 (46)	-
Surgical oncologists (n=101)[b]	13 (14)	39 (41)	43 (45)	0.30
Radiation oncologists (n=34)[c]	8 (25)	7 (22)	17 (53)	
Medical oncologists (n=29)	6 (21)	11 (38)	12 (41)	

KPS = Karnofsky performance status

[a] Eight participants who filled in 'other' were excluded from the analyses
[b] Six participants who filled in 'other' were excluded from the analyses
[c] Two participants who filled in 'other' were excluded from the analyses

DISCUSSION

This study explored the treatment recommendations of different BC specialists for hypothetical patients aged >70 years. We found that patients' chronological age influenced specialists' recommendations for loco-regional therapy. This is in line with other comparable work. Warner et al.[19] also found that radiation oncologists would be more comfortable with the option of omitting radiotherapy after breast-conserving surgery if a patient who chose to not undergo radiotherapy was 80-years-old rather than 70-years-old. Further, we found that patients' performance status influenced participants' recommendations for adjuvant systemic therapy: participants proposed hormonal therapy with or without chemotherapy for an older patient at high recurrence risk with a good performance score, and hormonal therapy without chemotherapy if she had a poor score. Previous studies among medical oncologists also reported that participants were less likely to recommend systemic therapy for hypothetical older women in poor health with node-positive, hormone receptor-positive tumours, compared to those in good health.[12,13,15]

Interestingly, a large proportion of the specialists would accept radiotherapy omission after breast-conserving surgery. Data from trials in older patients with small, node-negative, hormone receptor-positive tumours, who underwent breast-conserving surgery and were receiving hormonal therapy showed that the addition of radiotherapy had a small absolute benefit in terms of loco-regional control, but no impact on distant disease-free or overall survival.[20,21] Since the absolute recurrence risk was low, these results suggested that

radiotherapy omission can be considered for selected groups of older, hormone receptor-positive patients. Consistent with the evidence, a majority stated they would be willing to omit radiotherapy (66% for the 76-year-old and 83% for the 84-year-old woman, Table 2), despite the guidelines which recommend radiotherapy after breast-conserving surgery regardless of patient age.[6] However, participants' recommendations do not correspond with the low rates of radiotherapy omission in older patients, as observed in population-based data from the Netherlands Cancer Registry. In 2013, only 9% of the patients aged ≥70 years who underwent breast-conserving surgery for small (T_{1-2}), node-negative, hormone receptor-positive tumours, were not treated with adjuvant radiotherapy.[22] An explanation for this discrepancy is that, in practice, clinicians may find it difficult to omit treatments that are considered standard of care because of fear that the patient may develop a recurrence.[23] As radiotherapy is generally well-tolerated by most older women,[24] the threshold is low to recommend this treatment. Further, the introduction of equally effective and more convenient alternatives of standard radiotherapy, including hypofractionated and intraoperative radiotherapy, may explain why clinicians prefer to opt for radiotherapy rather than to omit the therapy for older patients with low-risk recurrence.[23]

Differences were also observed between specialists' recommendations for use of adjuvant chemotherapy (followed by hormonal therapy) in node-positive, high grade, hormone receptor-positive tumours (14% versus 5%[22]), and use of neo-adjuvant hormonal therapy for a clinically large hormone receptor-positive tumour (27% versus 6%[22]) and actual treatment of older patients. The proportion of participants recommending adjuvant chemotherapy and neo-adjuvant hormonal therapy was higher than anticipated, since the guidelines advise to consider this recommendation and do not mention this recommendation, respectively.[6] Another difference was found between the recommendation of use of adjuvant chemotherapy for triple-negative BC and actual practice (83% versus 27%[22]). The proportion considering adjuvant chemotherapy in this scenario is in accordance to the guidelines.[6]

The currently available evidence might explain the differences between specialists' recommendations and actual practice. In case of the radiotherapy scenario, there has been growing evidence since 2004 that the benefits of radiotherapy are limited in selected groups of older patients. Most participants seemed to be aware of this evidence, but seem to be reluctant to omit radiotherapy in clinical practice as this is not in line with the guidelines. In case of the other scenarios, the specialists we questioned might either not be convinced by currently available evidence, or feel that the evidence is insufficient or inadequate to determine which treatment options are appropriate. Another explanation to the differences is social desirability bias. The participants may have had a tendency to report a recommendation that is consistent with current evidence, rather than to report their true preferences.

Our findings raise the question whether adherence to the current treatment guideline is desirable concerning the treatment of older patients. Studies on adherence to BC guidelines in older patients demonstrated that large variation in loco-regional and systemic treatments did not result in differences in survival.[25,26] The large heterogeneity of this patient group in terms of functional capacity, comorbid conditions, and social support implies that a one-size-fits-all approach may not be justified, but that emphasis needs to be placed on an individualized treatment approach, taking into account the older patient's individual characteristics, including the patient's treatment preference.

A difference between the three specialities emerged when we analysed the influence of age on the recommendations regarding loco-regional therapy. Contrary to the other specialities, the recommendations of radiation oncologists were similar irrespective of patient age. They would more often offer a choice of surgery type to both the 76 and 84-year-old woman than surgical and medical oncologists, and if they did consider a treatment recommendation, all proposed breast-conserving surgery plus radiotherapy. Also, although they were somewhat more willing to accept without question the omission of radiotherapy for the older patient, they still had a greater tendency than the other specialities to convince a patient to undergo radiotherapy. These differences in recommendations are in line with previous work[27] that show that specialists tend to favour the treatments they themselves provide.

Strengths of this study include the comparison of the three main specialities involved in BC treatment, and an insight into their perspectives of multiple treatment modalities. Its innovative aspect is the exploration of other current challenges in the treatment of older patients, namely neo-adjuvant hormonal therapy and triple-negative BC. A limitation is the lower response of radiation and medical oncologists as compared to that of surgical oncologists. Unfortunately, we had no information about the total number of potentially eligible participants for this study and their characteristics. Therefore, we were unable to calculate an overall response rate and analyse to what extent our sample is representative for the general population of oncologists specialized in BC. Another limitation, as previously mentioned, is that participants' responses may have been influenced by social desirability bias.

Our results have important implications for future research. The difference between the reported recommendations and actual treatment of older women leads us to believe that more studies among older patients are needed to better define which subgroups are appropriate to receive further treatment. Although the need to improve the evidence on the treatment for older patients has often been addressed, a review demonstrated that only 2% of all currently running trials on BC treatment specifically target older patients (i.e., aged ≥60 years).[28] Additionally, trials in older patients do not often incorporate patient-related

endpoints (e.g., preservation of functional capacity). This implies that current trials will result in little improvement in our knowledge regarding the treatment of older patients. More randomized and prospective observational studies (as an alternative to trials provided that methodology is adequate) examining relevant end points in the older patient population may trigger a change in or help fine-tune treatment guidelines, and aid clinicians in providing their older patients an evidence-based treatment recommendation.

In conclusion, this study showed that patient chronological age and performance status are factors that influence clinicians' recommendations regarding loco-regional and adjuvant systemic therapy in older patients. Differences in recommendations between the three specialities were minimal, except for the influence of patient age on the recommendation for loco-regional therapy. The observed treatment recommendations for the scenarios under investigation do not match the actual treatment of older patients. This discrepancy could imply that specialists need more outcome data on the elderly, before they feel comfortable making recommendations in practice. Our results imply the need for trials and observational studies targeted at older patients to better inform and support decision-making and to develop evidence-based treatment guidelines for this growing group.

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APPENDIX 1. Questionnaire

Your answers will be analysed anonymously. For this study, it is important to have insight into the characteristics of the participants. Therefore, we ask you to fill in the questions below.

Fill in date: …..... / …..... / …..... (day/month/year)

1. What is your specialism? *(please choose one answer)*

- ☐ Surgical oncologist
- ☐ Medical oncologist
- ☐ Radiation oncologist
- ☐ Surgical oncologist in training
- ☐ Medical oncologist in training
- ☐ Radiation oncologist in training
- ☐ Other, namely: ……..

2. In which region do you practice? *(please choose one answer)*

- ☐ Regio North (i.e. Groningen, Friesland, Drenthe)
- ☐ Regio East (i.e. Gelderland, Overijssel, Flevoland)
- ☐ Regio West (i.e. Noord-Holland, Zuid-Holland, Utrecht)
- ☐ Regio South (i.e. Zeeland, Brabant, Limburg)
- ☐ I prefer not to disclose this

3. In what type of hospital do you work? *(please choose one answer)*

- ☐ General hospital (non-teaching)
- ☐ General hospital (teaching)
- ☐ University medical center, or specialized oncology center
- ☐ Other, namely: ……..

4. What is your gender? *(please choose one answer)*

- ☐ Male
- ☐ Female

5. What is your age? ..... years old

6. Do you have experience treating breast cancer patients?

- ☐ Yes *(Go to question 7)*
- ☐ No *(No further questions need to be answered. We would like to thank you for your interest in this survey.)*

7. How many years of experience do you have treating breast cancer patients? *(please choose one answer)*

☐ < 2 years
☐ 2-5 years
☐ 6-10 years
☐ >10 years

8. Approximately how many new breast cancer patients do you see per month, where initially the treatment intent is curative? *(please choose one answer)*

☐ 0
☐ 1-2 patients
☐ 3-5 patients
☐ 6-10 patients
☐ 11-15 patients
☐ >15 patients

9. Approximately how many new breast cancer patients of 70 years of age or older do you see per month, where initially the treatment intent is curative? *(please choose one answer)*

☐ 0
☐ 1-2 patients
☐ 3-5 patients
☐ 6-10 patients
☐ 11-15 patients
☐ >15 patients

On the following pages you will be presented with a clinical case scenario and asked to indicate your treatment recommendation. At the beginning of each case scenario the patient and tumour characteristics will be described. We kindly request you to carefully read each scenario and all possible responses, and then to answer the questions. We are interested in your treatment recommendation regardless of the treatment guideline.

CASE SCENARIO 1 A – Type of surgery and adjuvant radiotherapy

Below you find the patient and tumour characteristics. Please read these carefully and then answer the questions.

- A 76-year-old female
- Karnofsky score: 90% (able to carry on normal activity; minor signs or symptoms of disease)
- Right-sided breast cancer
- One lesion of 1.7 cm in the upper outer quadrant
- Invasive ductal adenocarcinoma
- cT1c, cN0
- ER+, PR+, Her2neu−
- No contraindications to breast-conserving therapy
- No comorbidities

1. What would be your treatment recommendation regarding resection of the tumour? *(please choose one answer*
   - ☐ I would not give any recommendation, I leave the choice to the patient
   - ☐ Breast-conserving surgery, followed by radiotherapy
   - ☐ Mastectomy

2. Suppose the patient indicates that she would like to undergo breast-conserving surgery, but no radiotherapy. Would you accept this? *(please choose one answer)*
   - ☐ Yes, without question
   - ☐ Yes, but I would still try to convince her of the benefit of radiotherapy
   - ☐ No, I would recommend her a mastectomy with reconstruction
   - ☐ No

CASE SCENARIO 1 B – Type of surgery and adjuvant radiotherapy

Suppose that the same patient is 84-years-old.

- An 84-year-old female
- Karnofsky score: 90% (able to carry on normal activity; minor signs or symptoms of disease)
- Right-sided breast cancer
- One lesion of 1.7 cm in the upper outer quadrant
- Invasive ductal adenocarcinoma
- cT1c, cN0
- ER+, PR+, Her2neu−
- No contraindications to breast-conserving therapy
- No comorbidities

1. What would be your treatment recommendation regarding resection of the tumour? *(please choose one answer*
   - ☐ I would not give any recommendation, I leave the choice to the patient
   - ☐ Breast-conserving surgery, followed by radiotherapy
   - ☐ Mastectomy

2. Suppose the patient indicates that she would like to undergo breast-conserving surgery, but no radiotherapy. Would you accept this? *(please choose one answer)*
   - ☐ Yes, without question
   - ☐ Yes, but I would still try to convince her of the benefit of radiotherapy
   - ☐ No, I would recommend her a mastectomy with reconstruction
   - ☐ No

CASE SCENARIO 2 A – Adjuvant systemic treatment

- A 77-year-old female
- Karnofsky score: 90% (able to carry on normal activity; minor signs or symptoms of disease)
- Right-sided breast cancer
- One lesion of 3.0 cm in the upper outer quadrant
- Invasive ductal adenocarcinoma
- A modified radical mastectomy was performed
- pT2, pN1
- Grade 3
- ER+, PR+, Her2neu−
- No comorbidities

1. What would be your treatment recommendation? *(please choose one answer)*

☐ No adjuvant systemic treatment
☐ Adjuvant hormonal therapy
☐ Adjuvant chemotherapy, followed by adjuvant hormonal therapy
☐ Other, namely:

……

……

……

CASE SCENARIO 2 B – Adjuvant systemic therapy

Suppose that the same patient has a Karnofsky score of 50%.

- A 77-year-old female
- Karnofsky score: 50% (requires considerable assistance and frequent medical care)
- Right-sided breast cancer
- One lesion of 3.0 cm in the upper outer quadrant
- Invasive ductal adenocarcinoma
- A modified radical mastectomy was performed
- pT2, pN1
- Grade 3
- ER+, PR+, Her2neu−

1. What would be your treatment recommendation? *(please choose one answer)*

☐ No adjuvant systemic treatment
☐ Adjuvant hormonal therapy
☐ Adjuvant chemotherapy, followed by adjuvant hormonal therapy
☐ Other, namely:

……

……

……

CASE SCENARIO 3 – Neo-adjuvant therapy

- A 75-year-old female
- Karnofsky score: 90% (able to carry on normal activity; minor signs or symptoms of disease)
- Right-sided breast cancer
- One lesion of 3.5 cm in the upper outer quadrant, size 36A
- Invasive ductal adenocarcinoma
- cT2, cN0
- ER+, PR+, Her2neu−
- No comorbidities

1. What would be your treatment recommendation? *(please choose one answer)*

☐ I would not give any recommendation, I leave the choice to the patient
☐ Mastectomy
☐ Neo-adjuvant hormonal therapy, followed by breast-conserving surgery
☐ Other, namely:

……
……
……

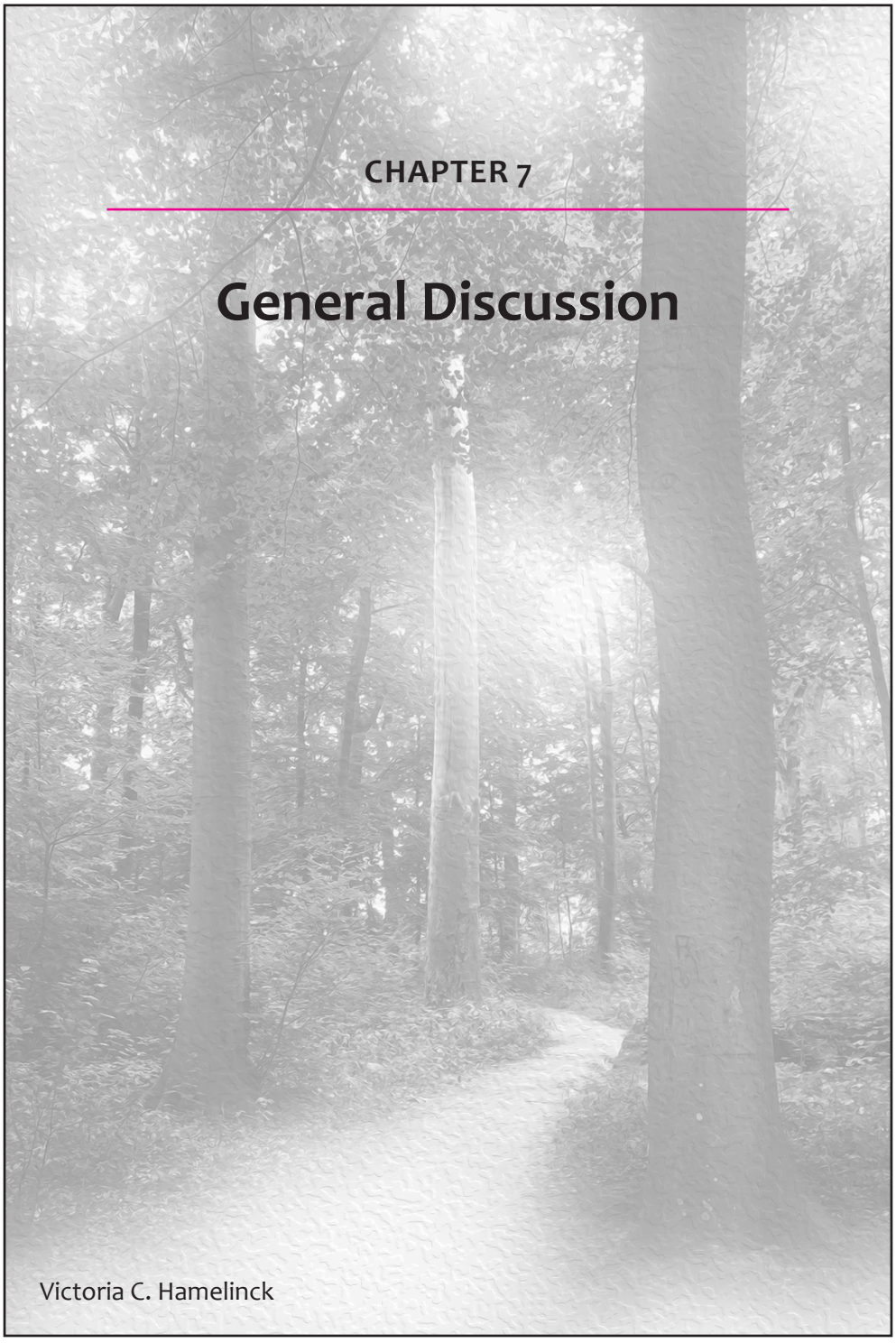
CASE SCENARIO 4 – Adjuvant systemic therapy

- A 75-year-old female
- Karnofsky score: 90% (able to carry on normal activity; minor signs or symptoms of disease)
- Right-sided breast cancer
- One lesion of 3.0 cm in the upper outer quadrant
- Invasive ductal adenocarcinoma
- A modified radical mastectomy was performed
- pT2, pN1
- Grade 3
- ER−, PR−, Her2neu−
- No comorbidities

1. Would you consider adjuvant chemotherapy? *(please choose one answer)*

☐ No, I would not consider adjuvant chemotherapy
☐ Yes
☐ Yes, but only if the patient has a strong preference for chemotherapy treatment
☐ Other, namely:

……
……
……



CHAPTER 7

General Discussion

Victoria C. Hamelinck

Background

Older patients with breast cancer and their clinicians often face difficult treatment decisions, including a decision between a mastectomy (MAST) or a breast-conserving surgery (BCS), and whether to add systemic therapy (i.e., chemotherapy or hormonal therapy). Treatment decision-making for older patients generally presents a challenge, as scientific evidence for the best treatment option is often limited,[1] older patients differ in a number of important aspects from younger patients, and as the older patient population itself is characterized by a wide diversity in health and functional status.[2] Consequently, a shared decision-making process has been advocated as the preferred way to individualize breast cancer treatment for older patients.[1,3,4]

Studies have shown that older patients are less likely to receive the same treatments as younger patients[5,6]: they less often undergo BCS, radiotherapy (following BCS) and adjuvant chemotherapy (aCT). It is unclear whether age-related differences in treatment reflect older patients' preferences or clinicians' preferences, or a combination of these. To optimize care for older breast cancer patients, knowledge about the treatment decision-making process with older women is urgently needed.

The research in this thesis aimed to gain insight into the preferences of older patients and breast cancer specialists, with a focus on the first group. We started by reviewing the literature on patient preferences for surgical and adjuvant systemic therapy. We then carried out a prospective study in which we included older patients with newly-diagnosed early-stage breast cancer and compared their preferences for treatment and participation in decision-making with those of younger patients. Finally, we explored the treatment recommendations of clinicians for older breast cancer patients, including how their recommendations were influenced by patient age and performance status, and by clinician specialty. In this chapter, the main findings are discussed and put into perspective. Subsequently, recommendations for practice, policy and future research are provided.

Main findings

The systematic review (**chapter 2**) showed that factors related to body image and survival/recurrence determined the preferences of early-stage breast cancer patients for, respectively, BCS or MAST. A majority of patients considered small/moderate benefits in survival rate/life extension sufficient to make both aCT and aHT worthwhile, although individual preferences varied widely. Determinants of patient preference were most often significantly related to quality of life: a better perceived well-being during treatment was related to more willingness to accept systemic therapy. Socio-demographic (e.g., patient age) and disease characteristics were not consistent predictors of systemic treatment preference.

Results from the prospective study showed that both younger and older patients most frequently preferred BCS plus radiotherapy (69% and 56%, respectively) (**chapter 3**). Both age groups considered the clinicians' recommendation to be the most important influencing factor. However, older patients were more concerned than younger patients about the possible need for additional surgery and they attached less importance to the possibility of breast reconstruction. The latter was also reflected in their lower preference for breast reconstruction following MAST.

Further, older patients were less willing to undergo aCT (62% versus 92%, respectively) and aHT (59% versus 92%) than younger patients, although this was not statistically significant for aHT (**chapter 4**). The older patients willing to undergo aCT required similar benefits in 10-year disease-free survival as younger patients from aCT (median: 5% versus 4%) and aHT (median: 10% versus 8%). Main motivations for undergoing therapy included the wish to survive/avoid a disease recurrence and the clinician's advice (more often affecting older patients). Motivations against therapy were concerns about the treatment duration (mainly referring to aHT) and side effects. Older patients cited additional motivations against aCT including the wish to maintain quality of life/independence. Overall, patients who were single/divorced/widowed, who had a geriatric condition, or who preferred an active role were less likely to prefer aCT.

Finally, our results showed that older patients more frequently preferred to share the decision about type of surgery, aCT and aHT with the clinician (**chapter 5**). In contrast, younger patients more often preferred to make these decisions themselves or to defer these decisions. Regarding perceived actual roles, both age groups most frequently reported an active role in the decision between BCS versus MAST. Contrary to younger patients, older patients more often reported to have had a passive role in the decisions about adjuvant systemic therapy. The differences in preferred and perceived roles between the groups were not statistically significant.

The online survey among breast cancer specialists showed that treatment recommendations about radiation, surgical and medical oncology treatments did not differ much among the different specialties (**chapter 6**). In the hypothetical scenarios representing only patients >70 years of age, clinicians were more likely to recommend MAST for an older than for a younger patient with a small tumour, and more willing to omit radiotherapy after BCS in the older patient if this was the patient's preference. Also, all clinicians would recommend either aHT with or without chemotherapy for a patient at high risk of recurrence in good health, whereas they would less often propose therapy (and if so, their recommendation always involved only aHT) for the same patient in poor health. In other scenarios, neo-adjuvant hormonal therapy followed by BCS for a patient with a large tumour was recommended by one-third of the

clinicians, and aCT in case of triple-negative breast cancer would be considered by four in five clinicians (either with or without a strong treatment preference of the patient).

Discussion of the main findings

Patient preferences for early-stage breast cancer treatments

The elicitation of patient preferences for treatment and values regarding the benefits and risks of different treatment options is an essential component of shared decision-making between clinicians and patients. In decisions where there is no obvious best option, the patient's own values become more important.[7] Our systematic review of the literature identified numerous factors that breast cancer patients reported to influence their preferences for type of surgery (**chapter 2**). A main finding was that different decisive factors were found, namely patients who preferred BCS mostly valued body image-related factors, whereas patients who preferred MAST were mostly driven by concerns about survival or disease recurrence. The fact that early-stage breast cancer patients reported preferring MAST over BCS because they believe MAST will offer a better chance of survival is disconcerting as this may indicate that patients received inadequate information or, alternatively, that they were unconvinced about the equivalence of the options, despite being fully informed. It is therefore important that patients who are in a position to choose between BCS and MAST receive complete and balanced information about both surgical options and that their understanding of what they were told is checked to correct possible misconceptions. The results of the review showed that patient concerns about body image and disease recurrence are important topics that should be discussed between the patient and her clinician. Treatment-related factors, including the follow-up with radiotherapy, also appeared to be influential factors. However, most studies in the review included patients who had already made a treatment decision or who had already undergone surgery and radiotherapy. Factors that determined preferences may therefore not be extrapolated to patients who have yet to face the decision. Findings of the prospective study involving newly-diagnosed patients (**chapter 3**) support that fear of disease recurrence and concern about the loss of a breast are predominant concerns, but also show that patient preferences are strongly influenced by an aversion to more surgery, and to a smaller extent, by concerns about radiotherapy.

Patients with early-stage invasive breast cancer also often face the dilemma of whether to undergo a treatment that could potentially improve disease-free survival but is associated with unpleasant side effects. **Chapter 2** described the finding that a majority of patients who were treated or had already made a treatment decision, were willing to undergo a systemic therapy for small or moderate chances of benefit, regardless of the side effects and inconvenience of the treatment. This is in line with findings of the prospective study (**chapter 4**), where we found that overall, most newly-diagnosed patients would accept aCT for small benefits and aHT for moderate benefits. Both the systematic review and the

prospective study showed that some patients would even choose therapy if there was no additional benefit, a finding also found in many other cancer contexts.[8-12] Patients often reported to do everything possible to fight the cancer in order to live as long as possible and/or to minimize their risk of local recurrence (**chapter 4**). Still, willingness to accept treatment for no or small extra chances of survival seems illogical or irrational, and clinicians should carefully question whether treatment should be given in these cases. Clinicians should know about their patient's reasons for wanting or not wanting a burdensome treatment.

Another important finding was the large variation in patient preferences for surgical and adjuvant systemic therapy and the different factors that shape their preferences (**chapters 2-4**). Together, these findings suggest that clinicians should be aware of the different preferences between individual patients. However, evidence shows that patients rarely have individualized discussions with their clinicians and that exploration of patients' treatment preferences is often done implicitly.[13-17] Clinicians seldom inform patients of different treatment options or that a treatment decision needs to be made and seldom ask about their preferences. Other studies show that treatment plans often appear to have been already made at the multidisciplinary team meetings without knowing the patient's preference.[18] It is known that patients and clinicians think about different determinants when making treatment decisions,[11,19,20] with clinicians mainly focusing on the medical aspects of treatment. Consequently, there is a high probability that the recommended treatment plan will be unworkable in case the plan needs a revision if a patient becomes involved in a later stage.[18] The failure to incorporate patient preferences in clinical decision-making is disconcerting, given the preference-sensitive nature of the decisions in early breast cancer,[21,22] but also in light of growing consensus that patients should be actively involved in their healthcare.[23] We also found that the input of the clinician was a highly influential factor for patients' preference (**chapter 3 and 4**). Patients often tend to ask for guidance from their clinician as they believe that their clinician would know best. However, clinicians need to be aware that the preferences of patients might be different from theirs[19,24] and that the preferences of (new) patients are not easily predicted based on their socio-demographic characteristics (e.g., patient age) or on actual health status (**chapter 2-4**). It is therefore crucial for clinicians to explicitly explore the values and preferences of their patients. Even though a strong influence of clinicians on patient's preference does not automatically imply that patients' values are left out in the treatment plan, we recommend that clinicians carefully plan communicating a treatment recommendation. Providing treatment advice early in the consultation may lead to patients believing that their own preferences and values no longer matter in the decision process, that the doctor knows what is best. It is also important that treatment information is provided without implicit persuasion. A recent oncology study[14] regarding the decision about adjuvant systemic therapy demonstrated that clinicians often steered patients towards a particular treatment choice by the way they presented the information about the treatment

during the consultation. Even though clinicians are most likely unaware of this behaviour, patients may have the impression that they are pushed towards an option, possibly leading to an undesired decision. Therefore, only after balanced presentation about the treatment options, and patients' preferences have been adequately discussed, clinicians could explicitly recommend a treatment that reflects the concerns of the patient.

The influence of age on patients' preferences for treatment

Although the need to gain insight into the treatment preferences of older patients is evident, only one study in our systematic review provided information on older patients and none of the included studies specifically explored age-related differences (**chapter 2**). Understanding which factors drive older patients' preferences is important to tailor information provision and to assist clinicians in helping older patients in making treatment choices that fits their preferences. In daily practice, it is often assumed that older patients more frequently prefer MAST than younger patients. Potential explanations assumed are that older patients are less concerned about body image, are less willing to attend the subsequent visits for radiotherapy they would receive after BCS (due to limiting mobility or reliance on others for transportation), and that they do not desire more surgery.[25] According to the results of our prospective study (**chapter 3**), older patients most frequently preferred BCS, although to a lesser extent compared to younger patients. Perhaps more importantly, the proportion of older participants preferring BCS was larger than those preferring MAST. We also found that both age groups attached high importance to the same influencing factors, including body image. In line with other studies,[26-29] breast conservation appears to be relevant to older patients during the last decades of life as well. Its importance should therefore not be underestimated and body image and the option of breast reconstruction should be a part of the conversation with older patients. Our findings do confirm the assumption that older patients may have a stronger aversion to possibly requiring further surgical procedures. In addition, older patients seemed to be more concerned about the possible side effects from radiotherapy and the frequent hospital visits, although they were not overly put off by these factors. These factors should also receive attention in discussions with older patients. The opinions of older patients about the omission of radiotherapy (after breast-conserving surgery) is a topic that is currently explored in the Tailored Treatment in Older patients study (TOP[30]), a research project initiated at the Leiden University Medical Center and in collaboration with the Dutch Breast Cancer Association. Based on our findings, BCS is something that older patients are interested in discussing and considering in a similar way as younger patients and when indicated, BCS should therefore be offered to eligible patients alongside the option of MAST.

Another prevailing presumption among clinicians is that older patients have a lower willingness to undergo systemic therapy, because they consider their quality of life to be

more important than a small, possible gain in disease-free survival.[31,32] Our study seems to confirm the finding that older patients are less willing to add a systemic therapy than younger patients (**chapter 4**), but the difference in willingness was only statistically significant for aCT, and not for aHT. On the other hand, we also found that the older patients who would accept therapy, desired it as strongly as younger patients, and some even considering therapy for a 1% benefit. This finding may be considered somewhat surprising, but corresponds with the finding that many older patients would be willing to accept burdensome treatment. Like younger patients, older patients placed much importance on the possibility to reduce their risk of disease recurrence as well as on avoiding possible side effects. Based on our findings, the option of adjuvant systemic therapy should be discussed with them, and information on benefits and risks concerning a treatment with or without systemic therapy should be fully and neutrally delivered, so that patients can make an informed treatment preference. Both age groups considered the same main motivations for and against systemic therapy, but regarding aCT, older patients had reported that they wanted to keep their current quality of life and to continue their daily life activities. They also feared losing their independence after undergoing aCT. When communicating the risks and benefits of adjuvant systemic therapy with older patients, the impact of treatment on these aspects should deserve specific attention.

There were no overt differences regarding aHT between the age groups, and it was notable that older – like younger - patients also reported to be concerned about the side effects and treatment duration. Adjuvant hormonal therapy is often regarded as a treatment that is milder and easier to use than aCT, although treatment lasts for a considerably longer time. It is often the only available systemic treatment option for older patients, in particular for those with comorbid conditions. However, higher discontinuation and nonadherence rates have been observed in older patients,[33-36] with up to 49% discontinuation rate reported.[37] Research has shown that patients find the side effects to be burdensome,[38] and that the side effects were the most common reason for discontinuing treatment before completion of the recommended five years.[39] As aHT is an important option for older patients, more attention should be given to the impact of treatment before they start treatment in order for them to better cope with the possible side effects and to improve therapy adherence/persistence.[40]

An essential question arising from these findings is whether treatment decision-making with older patients requires a different approach than that with of younger patients. It is important to acknowledge that reasons unique to this age group were found, but also that many influencing factors were the same for both younger and older patients. Older patients may have a lower willingness to undergo BCS or adjuvant systemic therapy than younger patients, but the variation in preferences and the weight put on different factors within the older – as within the younger – patient population illustrate the importance of eliciting and

taking into account older patients' preferences, not just those of younger patients. That such an approach is needed is strengthened by the finding that patient preferences were influenced more by social support, health status and decisional role preference than by their age (**chapter 4**). Older patients were more likely to indicate the clinician's advice as the most significant influence on treatment preference. Because the treatment recommendation of the clinician is more highly valued by older patients (also slightly seen in **chapter 3**) and by those who were undecisive about their preference (who were in particular older patients), clinicians should be aware of the factors that older patients consider important (and that are different than those of younger patients). For example, older patients differed most in their preferences from younger patients with regard to aCT, which indicates the need for age-specific information provision about aCT. Our findings fits the current shift seen in oncology from a 'one-size-fits-all' approach towards personalized medicine.

The influence of clinician's preference on treatment of older patients

Understanding the variation in treatment between younger and older patients also requires insight into the ideas that clinicians have regarding the management of breast cancer in older patients. Using hypothetical scenarios, we found that most clinicians of the different breast cancer specialties seemed to take a similar approach to our treatment scenarios under investigation. However, the discrepancy between the overall selected treatment recommendations and the actual treatment of older breast cancer patients (**chapter 6**) raised the question which factors may lead clinicians in deciding whether or not to treat older patients. In the scenario about locoregional therapy, a majority of the clinicians would be willing to omit radiotherapy for a patient over the age of 70 years, but in practice older patients, like younger patients, almost always receive radiotherapy.[41] The TOP study will assess whether radiotherapy after BCS can be omitted in specific older breast cancer patients without negatively affecting their disease recurrence or survival, and possibly resulting in reduced costs. To that end, comparative effectiveness research will be performed, as well as surveys among older breast cancer patients and specialists about their opinions regarding omission of treatment.[30] Results of this study will provide more clarity regarding this topic. It is possible that clinicians find it difficult to advice omission of a treatment that is well-established in clinical guidelines, despite the fact that there is strong scientific proof from trials that the option of radiotherapy may be questioned in certain selected older patients.[42] Our findings imply that although clinicians seemed to acknowledge this evidence, they have a strong tendency to adhere to the guidelines. Possibly, we might have to consider to change current guidelines by incorporating age- or subgroup-specific sections.

Another finding was that some clinicians would recommend or consider aCT for an older patient in otherwise good health at high-risk for recurrence, however, the actual uptake of aCT in older patients is very low.[41] A barrier that clinicians may encounter is that the

guidelines advocate the consideration of chemotherapy for 'fit' older patients without specifying this definition. Consequently, this lack of information may hinder the application of this recommendation.[43] Clinicians may also be particularly reluctant to recommend current recommendation in older patients because they are uncertain about the benefits. Although clinicians selected treatment in accordance with current evidence, their uncertainty to recommend aCT seems to be a reflection of the guidelines. Possibly, more trials are needed to guide decisions about extensive treatment and to fine-tune current guidelines for chemotherapy at older age.

While abovementioned factors may contribute to the age-based variation in treatment, recent attention has been directed to the strong influence of a patient's chronological age on treatment options presented to patients by clinicians.[44-46] A study showed that although performance status was cited the most important factor affecting their treatment decisions, 96% of the clinicians would choose an intensive treatment for a 60-year-old breast cancer patient, compared to only 13% for an 85-year-old patient who had the same characteristics as the younger patient.[47] Other vignette studies also found that patient's age was considered the most influential factor when making treatment decisions for older patients.[48] Similarly, clinicians in our study made different recommendations for locoregional therapy based on patient age. Although it was quite obvious for them to notice that we were interested in the age factor, they still provided different treatment recommendations, which raises the possibility of a different approach towards older adults based on their chronological age. Although it is inarguable that ageing is associated with an increase in medical and social problems, and that older patients may generally not benefit as much as younger patients from certain treatment, ageism can lead to misconceptions as to what is best for the patient.

A number of potential explanations have been offered for a different approach.[44] It is often expected by society that older adults are mentally and physically weak, and are dependent on others.[18] These negative perceptions are further strengthened by the portrayal of older patients in the media. Further, breast cancer in older patients is often portrayed to be less agressive and less deadly compared to younger patients, although some studies show otherwise.[49,50] Also, perceptions about older patients not wanting certain treatments or not wanting to share decision-making[51] may lead to clinicians behaving – consciously or unconsciously – differently towards older patients. It may result in elderspeak (speaking slower/louder when talking to an older individual[44]), less consultation time spent with older patients,[52] and being directer about their own preferences.[3,53-55] Despite best intentions (e.g., protecting older patients from unacceptably harmful treatments), making unilateral decisions or witholding treatment options based on unsounded beliefs about an entire group of patients may jeopardize clinicians in fullfilling their obligations to inform eligible patients about available options, and also denies older patients becoming involved in decision-making.

It is important to be aware of this, because most older adults are different from how they are stereotyped, and most are still independent and fully capable of cognitive and physical activities. In addition, there are indications that older patients are becoming more assertive during consultations, desire more information and want to be above all kept informed about their disease and treatment options.[56,57] Also, they use the Internet more to seek health information.[58,59] As discussed earlier, results of the prospective study (**chapters 3-5**) run counter to the prevailing presumptions about the preferences of older breast cancer patients. Altogether, this raises interesting questions on how to approach older patients in clinical care and how to change the current views about older patients. Suggestions to improve clinical practice and health care policy are discussed in the following paragraphs.

Methodological considerations

In the previous chapters, we described the various strengths and limitations of the studies in this thesis. In the following paragraphs, some general strengths and limitations are discussed in detail.

An important strength of this thesis is that we captured the perspectives of older patients and clinicians. A strength of the studies performed among patients was its prospective design. The innovative aspect was that preferences were assessed even before patients received a treatment recommendation from the surgical oncologist or information about a possible referral to a medical oncologist. In retrospective studies, the patients may have had a strong preference for the treatment they underwent, which may be caused by a psychological mechanism (i.e., cognitive dissonance reduction or post-hoc justification[60]). Even in previous prospective studies, in which preferences were assessed before the start of treatment, but after a treatment decision had been made, patients may already have had a more positive attitude towards their recommended treatment.[60] As a result of our study design, we could minimize the possible influence of cognitive dissonance reduction or justification.

Nonetheless, several limitations should be considered. A main shortcoming of the studies among patients is the smaller number of older patients who participated in the study compared to that of younger patients. In two studies, one third of the sample were aged ≥65 years and in one study, the percentage of older patients was around 30%. These percentages are smaller than the estimated 40% of the new breast cancer cases in older women. As earlier addressed, we were unable to include more older patients, as many of the older patients who were approached and participated in the study, were identified with a previous malignancy later on, after review of their medical records. This previous experience could have influenced their opinion about the treatment under investigation. We acknowledge that comparisons between younger and older patients could have been more properly explored using a larger sample of older patients (to increase statistical power). However, we did compare the

characteristics of our older patients with those older patients in a population-based cohort study in the Netherlands[61] and this showed that the samples were comparable with regard to median age and presence of comorbid and geriatric conditions.

Second, in the study among clinicians, the number of radiation and medical oncologists was lower than the number of surgical oncologists. Consequently, results may greater imply the views of the latter group. Further, we did not directly assess agreements between what clinicians report to recommend versus what they actually recommend. Therefore, it is not clear from our work which factors may lead clinicians in deciding whether or not to treat older patients.

Next steps to further improve decision-making in older women with breast cancer

In the Netherlands, approximately 60,000 (60%) of all newly-diagnosed cancers currently occur in older adults.[62,63] This number will rise due to the ageing of the Dutch population. Consequently, a trend will be seen in which all subspecialties of oncology will primarily deal with the care of older patients. Paradoxically, there is limited knowledge about the treatment and psychosocial needs of older cancer patients.[64,65] Fortunately, it has become well-recognized that the focus needs to be on this patient group. Between 2011 and 2014, the Dutch Cancer Society prioritized its agenda onto geriatric oncology and funded projects involving older individuals with cancer.[58] Similarly, the Dutch Breast Cancer Association focused their policy on older patients between 2012 and 2014 and conducted a project to explore their information needs.[66] Further, national (e.g., Geriatric Oncology Netherlands[67]) and international (e.g., SIOG[1]) societies and organizations committed to geriatric oncology have made great efforts to raise awareness in the medical community and to exchange information about best care between clinicians, patient associations and researchers with an interest in geriatric oncology. However, it is clear that still much work is to be done, especially in the field of breast cancer. If current demographic trends continue, older patients will comprise 52% of the new breast cancer cases by 2030, compared to 40% in 2012.[68] Consequently, more data are required to guide treatment decision-making; however, still only 2% of the ongoing clinical trials specifically focus on older patients.[64]

In the following sections, implications for health policy and clinical practice are discussed based on the findings of this thesis. Also, recommendations for future research are given.

Implications for practice and policy

Our findings prove the need for clinicians to explicitly explore older patients' preferences, as their preferences varied widely. Even more so important, older patients reported preferences that deviated from previous assumptions (e.g., older patients would be willing to undergo breast-conserving surgery or adjuvant chemotherapy). If clinicians assume that they know their older patients' preferences based on the patient's age without explicitly asking them,

they may erroneously believe that older patients do not want certain treatments and propose a treatment plan that is not consistent with their preferences. Therefore, it is important that clinicians discuss all available treatment options and explicitly explore the older patient's wishes, regardless of whether or not the patient defers the final decision.[69] They need to be asked about their wishes as early as possible in the decision process, so that their preferences can be taken into account in multidisciplinary team meetings as much as possible.

What can be done to help clinicians to further optimize elicitation of older patients' preferences? A practical step could include the development and use of patient decision aids tailored to the needs of older patients. Decision aids are tools that help make the decision explicit by outlining the available treatment options and associated benefits and risks, and have been overall successful in clarifying patients' values and preferences.[70] These tools may well be effective in supporting older patients' decision-making and improving patient-clinician communication.[71-73] Our results on the unique concerns of older patients could inform on the benefits and risks to be included in new[71,74] or existing[75] patient decision aids (**chapters 3 and 4**).

It may also be useful to add a separate module dedicated to older patients to the current breast cancer treatment guidelines. Such an addition would likely create more awareness among clinicians about the severity of the disease in this patient group. Throughout the module the emphasis should be on the older patient's preference, especially in decisions for which there is limited scientific evidence about the best treatment option. It would be helpful to mention the specific treatment decision points for which there is a high need to explicitly explore the older patient's preference. The current breast cancer guidelines briefly remark that patient preference should be taken into account for the decision between breast-conserving surgery versus mastectomy, but do not elaborate on the reason to inform patients about treatment options and to discuss their values, nor acknowledge that an individualized approach may lead to different treatment advices. Additionally, a comment that older patients' expectations, preferences and motivations can be different from those of previous generations of elderly could be helpful, supported by a description of research data about current older patients' preferences. Our results have highlighted which topics clinicians should clearly consider bringing into their conversations with older patients (**chapters 3 and 4**).

As described above, we argued that clinicians should more intensively ask the older patient about her preferences. However, this may not be sufficient to improve shared decision-making between the clinician and older patient. Most importantly, the mindset of clinicians needs to be changed with regard to older patients. It is important for them to acknowledge that views of older patients about their desired role in decision-making may have changed over time,[76,77] and that their treatment preferences may deviate from what was previously

expected. This change in the current group of older patients means that, consequently, a change in the perceptions among clinicians about older patients is required to reflect this reality. If clinicians fail to recognize this, then all abovementioned recommendations will most likely not be followed or considered. Implementation strategies must therefore rather focus on making clinicians aware of the possible impact of their attitude towards older patients, and on educating them about communication methods with older patients through training sessions. These sessions could be done by using role playing to practice communication skills. Previous research has shown that such interventions may result in increased knowledge about and a more positive attitude towards older patients.[40,78] More general, clinicians can be trained more thoroughly in shared decision-making to create awareness about their important role therein.[79] Current national campaigns stimulating the implementation of shared decision-making in hospitals (Beslist Samen! and Betere zorg begint met een goed gesprek[80]) are great initiatives to better equip clinicians with the tools to facilitate a shared decision-making conversation.

Aside from the clinician's role, it is also important to stimulate older patients themselves to become more involved in decision-making. Older women are especially in need of support since they seem more likely to experience lower levels of patient involvement than younger patients (**chapter 5**) and also more likely encounter specific barriers (e.g., not really allowed to decide, lower health literacy[81]) next to general and well-known barriers (e.g., time constraints). Further, older patients may be exposed to negative stereotypes, but they themselves may also be biased (e.g., breast reconstruction is not appropriate at older age[43]), which may prevent them from bringing up important topics. As shared decision-making starts with the clinician inviting the patient to make the decision together, the clinician is according to our belief the most important person to empower older patients and to guide them in the decision-making process. It has been shown that clinicians serve as a useful first resource of information[58,82,83] and that clinicians create a trustful environment in which the patient feels comfortable to express her values and concerns.[69,84] Additionally, there are general initiatives to help older patients prepare better for their consultation, such as the ask-three-questions ('what are my options?'; 'what are the possible benefits and harms of those options?'; 'how likely are each of those benefits and harms to happen to me?'[85]). Encouraging patients to ask a few key questions can already lead to higher quality information about treatment options from their clinician and thus greater patient involvement.[86] Also, decision support tools may be helpful in supporting the participation of the older patient in decision-making. Therein also lies in part a responsibility of the Dutch Breast Cancer Association to stimulate them in taking an active role in their healthcare. Based on their information needs project, they have undertaken several actions to provide older patients with tailored patient education, one of which included the addition of segments about breast cancer at older age on their webpage and to their magazine.[87] Further, they developed a checklist of relevant questions for older

patients during the consultation (i.e., B-bewust checklist[88]).

Implications for research

An important area for future research would be to assess the preferences within the older patient population itself. Due to the low number of patients above the age of 75 years, we were unable to compare preferences between different age groups within the older patient sample. Since the heterogeneity of older patients drastically increases with increasing age, it would be important to know which factors may be more relevant for the older-old (often referred to as adults aged over 75) compared to the young-old (those aged 65-74 years). Further, it could be argued that with the changing demographic population, another cut-off for older patients (e.g., 75 years and above) would provide greater meaning. It would be important for future research to recruit sufficient older-old patients to take into account their larger possibility of being excluded from the study, as in our case based on a previous malignancy. Possible solutions could be to recruit at more hospital sites (within the limits of financial resources and time available), or to recruit more older-old compared to young-old patients (for example, according to a 2:1 ratio). The findings of such studies can be compared with the findings of the patients in our studies, and could provide insight into whether our observed (dis)similarities hold in a larger sample. Aside from comparing age categories, it would be particularly relevant to assess whether treatment preferences are related to different levels of comorbid conditions, activities of daily living, social environment and quality of life in an older patient population.

More research is needed on the factors that frequently affect older patients' decision about whether to have breast reconstruction following a mastectomy. We noticed that the proportion of older patients who would prefer breast reconstruction was much lower than that of younger patients, but we had no information on the reasons for their different preferences. Based on our findings regarding their surgical treatment preference, older patients were less willing to deal with multiple surgeries, and this factor could be carefully extrapolated to breast reconstruction, as this procedure often entails multiple surgeries and is also a more extensive surgery. Other reasons of breast cancer patients, including being content with a prosthesis, could particularly apply to older patients,[89] but it is also possible that older patients may believe that a breast reconstruction at old age is inappropriate.[90] It is therefore necessary to enhance our study with results of other studies, to gain insight in reasons unique to older patients, and to (better) educate older patients about the possibility of breast reconstruction.

Another important recommendation for future research is to more fully assess the decision-making process by clinicians. If we want to stimulate the occurence of shared decision-making with older patients, it is not only relevant to assess how patients make decisions,

but also how clinicians make these. We would therefore argue for a combination of clinical encounters studies and self-reported data from clinicians to gain more insight into the decision-making process with older patients. Such findings could provide valuable insights for the development of interventions to optimize treatment decision-making with this patient group.

Another key priority of future research is the development a decision tool, which not only predicts (disease-free) survival with or without therapy for an older patient, but also provides information on other outcomes, such as the quality of life or functional decline after specific breast cancer treatments. Such patient-centred outcomes are likely to be equally or more important to older patients and can be important considerations in decision-making. Current prediction models that are frequently used to communicate prognosis to patients, such as Adjuvant! Online, are based on basic patient and tumour characteristics and do not include outcomes such as functional decline. A prediction tool that not only includes traditional outcomes, but also focuses on other highly relevant outcomes for older patients could be particularly useful for both clinician and older patient in evaluating treatment options and in making more individualized treatment decisions.

Finally, a general recommendation is to conduct more randomized clinical trials and prospective observational studies in older breast cancer patients to increase the evidence base. Fortunately, several (observational) studies have recently been initiated, such as the Climb Every Mountain study (functional, psychological, social and cognitive decline after treatment in older breast cancer patients[91]) and the TOP study.[92] The studies described in this thesis were part of one of the largest studies among older patients, namely the FOCUS study (Female breast cancer in the elderly: Optimizing Clinical guidelines USing clinico-pathological and molecular data[93]), which combined information from various sources (e.g., population-based national cancer registries, clinical trials and tumor tissues). The FOCUS study has recently been granted funding by the Dutch Cancer Society for a research project to develop a prediction tool, as earlier described, that should include both traditional and patient-centred endpoints.[94] Findings of these and future studies in older patients will hopefully advance our knowledge and better guide clinicians and older patients in deciding which treatment option is best.

CONCLUDING REMARKS

The findings that this thesis brought to light will help in providing more understanding to the preferences of older patients and will assist clinicians in tailoring their information provision for this growing patient group. It showed that younger and older patients had many similar – but also some dissimilar – preferences. Although age-related differences need to be kept in mind, it is even more crucially important that an individualized approach is followed in older –

as in younger – patients. We consider it necessary that older patients are invited in treatment decision-making too, are informed about the risks and benefits of available treatment options, and are asked about their individual preferences and concerns. Our findings indicate that older patients may have certain preferences that run counter to the assumptions prevailing in oncologic clinical practice. Our findings suggest that this patient group could therefore profit considerably from the assessment of their preferences. In this process, a change in the behavorial culture of the medical community towards geriatric oncology is needed. More work is also needed on research level. Until then, the practical and policy recommendations mentioned in this thesis provide guidance to clinicians and policy makers, and contribute to improving the quality of care for older breast cancer patients in the very near future.

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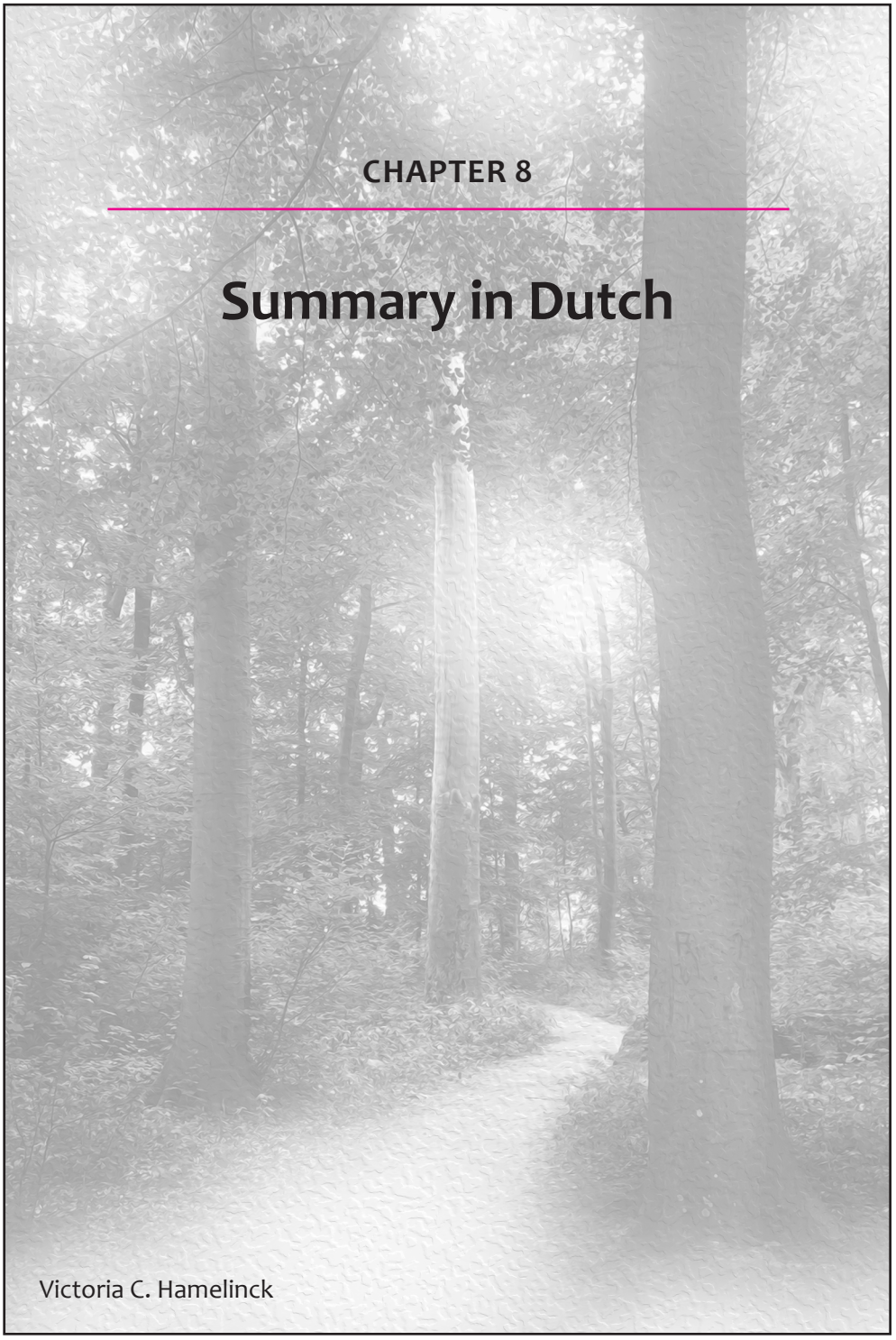


CHAPTER 8

Summary in Dutch

Victoria C. Hamelinck

Algemene inleiding

In Nederland werden in 2016 ongeveer 17.000 vrouwen gediagnosticeerd met borstkanker. Ongeveer 40% van de patiënten was 65 jaar of ouder ten tijde van de diagnose. Ondanks dat borstkanker een veelvoorkomend probleem is onder deze groep vrouwen, in het vervolg aangeduid als 'oudere patiënten', is de beste behandeling voor deze patiëntengroep vaak niet duidelijk. Het is belangrijk op te merken dat deze groep vaak wordt weggelaten uit klinische studies op basis van leeftijd of comorbiditeit. De behandeling van oudere patiënten met borstkanker wordt overigens bemoeilijkt doordat er geen leeftijdsspecifieke behandelrichtlijnen zijn en doordat de ouderenpopulatie zeer heterogeen is in termen van gezondheid, functioneren en sociaal welbevinden. Juist omdat er nog vrij weinig bekend is over de behandeleffecten, is het van belang om deze patiëntengroep zoveel mogelijk te betrekken in de besluitvorming, zodat deze een weloverwogen beslissing kan maken over de beste aanpak. Het proces waarbij arts en patiënt samen beslissen welk beleid het beste bij de patiënt past, oftewel de zogenaamde gedeelde besluitvorming, is in het bijzonder van belang bij beslissingen waarbij er meerdere behandelopties zijn.

In dit proefschrift worden de voorkeuren van zowel de oudere patiëntengroep als de borstkankerspecialisten onderzocht om de huidige zorg voor deze patiëntengroep te verbeteren. Met het snel stijgend aantal borstkankerpatiënten boven de 65 neemt het belang van inzicht in hun voorkeuren toe. Al in een vroeg stadium van borstkanker moeten moeilijke beslissingen genomen worden, die betrekking hebben op de keuze tussen twee chirurgische opties en de keuze tussen het wel of niet ondergaan van een adjuvante systeembehandeling. Evenals jongere patiënten staan ook oudere patiënten vaak voor deze lastige keuzes. Beide groepen worden hierin bijgestaan door de arts. Bij borstkanker in een vroeg stadium verschilt de behandeling echter aanzienlijk tussen de jongere en de oudere patiëntengroep, wat mogelijk verklaard kan worden door de voorkeuren van de oudere patiëntengroep of door die van hun artsen. Op dit moment is nog weinig bekend over de voorkeuren van deze oudere patiëntengroep, terwijl kennis over de voorkeuren juist van grote waarde is.

Om te ontdekken hoe de huidige zorg voor de oudere patiëntengroep en de besluitvorming met deze patiëntengroep verbeterd kan worden, onderzoeken wij (i) wat de behandelingsvoorkeuren en overwegingen zijn van oudere patiënten met een vroeg stadium van borstkanker; (ii) of en hoe die behandelingsvoorkeuren en hun betrokkenheid in de besluitvorming verschillen met die van jongere patiënten; en (iii) wat de behandelingsvoorkeuren van borstkankerspecialisten zijn ten aanzien van oudere vrouwen met borstkanker. Dit hoofdstuk vat de inhoud van het proefschrift samen.

Belangrijkste bevindingen

Omdat de overlevingskans na een borstsparende operatie even groot is als na een

borstverwijderende operatie en de chirurgische opties daarom vanuit medisch perspectief gelijkwaardig zijn, hangt de beste behandeling voornamelijk af van de waarden en preferenties van de patiënt. In **hoofdstuk 2** beschrijven wij de resultaten van een systematisch literatuuronderzoek naar de behandelingsvoorkeuren van patiënten met een vroeg stadium van borstkanker. Het eerste doel van het literatuuronderzoek is om een overzicht te geven van de factoren die een rol spelen bij de patiëntvoorkeuren voor een borstsparende versus een borstverwijderende operatie. Wij hebben vijftien relevante studies gevonden. Uit ons overzicht blijkt dat zorgen over lichaamsbeeld en (ziektevrije) overleving doorslaggevende factoren zijn bij de beslissing voor een bepaald type operatie. Patiënten die lichaamsbeeld belangrijk vinden, geven de voorkeur aan een borstsparende therapie. Patiënten die zich zorgen maken om ziektevrije overleving prefereren daarentegen een borstverwijderende operatie.

Het tweede deel van het literatuuronderzoek geeft een overzicht van de extra voordelen die patiënten met een vroeg stadium van borstkanker verlangen van een adjuvante behandeling om deze de moeite waard te vinden. Adjuvante systeembehandelingen, zoals chemotherapie en hormoontherapie, worden aan de behandeling toegevoegd met als doel de kans op ziektevrije of totale overleving te vergroten. Deze behandelingen hebben echter mogelijk bijwerkingen. Medisch gezien kan het niet ondergaan van een adjuvante behandeling dan ook een acceptabele keuze zijn, vooral als de kans relatief klein is op terugkeer van de ziekte of op overlijden door de ziekte. Zes studies blijken hiervoor relevant. De resultaten geven aan dat het extra voordeel dat de patiënten rapporteren over het algemeen klein is, maar dat de onderlinge voorkeuren sterk verschillen. Een deel van de patiënten zou namelijk voor de behandeling kiezen zonder enige voordeel, terwijl een ander deel de behandeling zou weigeren ondanks zeer veel voordeel. Verder komt in de meeste studies naar voren dat 'de ervaren kwaliteit van leven tijdens de betreffende behandeling' een voorspellende factor is. Patiënten die een betere kwaliteit van leven rapporteren kiezen namelijk eerder voor de behandeling. Een andere bevinding is dat de voorkeur voor een extra klein voordeel niet consistent samenhangt met sociaal-demografische kenmerken (bijv. leeftijd) of ziektekenmerken (bijv. stadium).

Al met al geven de resultaten van het literatuuronderzoek aan dat het voor de dagelijkse praktijk van belang is dat clinici zich bewust zijn van de wensen en voorkeuren van individuele patiënten. Daarnaast dienen clinici vooraf naar deze wensen en voorkeuren te vragen om de behandeling beter aan te laten sluiten bij de voorkeuren van de patiënt. Uit **hoofdstuk 2** blijkt ook dat de meeste studies een retrospectief karakter hebben, waarbij de patiënten de chirurgische of adjuvante behandeling al hebben ondergaan. Maar ook in het merendeel van de prospectieve studies is de behandelingsbeslissing al gemaakt. Een beperking van deze studies is dat de patiënten mogelijk geneigd zijn te geloven dat hun keuze de beste is,

om zo de eventuele verschillen tussen de gekozen behandeling en hun mening daarover te beperken. De resultaten van deze studies weerspiegelen mogelijk dus niet de voorkeuren van patiënten die nog vóór de beslissing staan. Bovendien blijkt uit het literatuuronderzoek dat studies niet of nauwelijks zijn toegespitst op de oudere patiëntengroep: slechts één studie ging kort in op de voorkeuren van patiënten boven de 70 jaar. De voorkeuren van de oudere patiëntengroep zijn volgens clinici bekend, maar bewijs is er veelal nog niet.

De resultaten van het literatuuroverzicht pleiten voor een prospectieve studieopzet (**hoofdstuk 3, 4 en 5**) waarbij nieuw-gediagnosticeerde patiënten met een vroeg stadium van borstkanker (0, I en II) worden geïncludeerd vlak na de voorlopige diagnose. Van januari 2012 tot en met december 2013 hebben wij een onderzoek uitgevoerd in meerdere onderzoekscentra. Nog strikter dan in eerdere prospectieve studies, werden in de analyses alleen de voorkeuren van patiënten meegenomen die vooraf aan het behandelplan gemeten waren. Het doel daarvan was het voorkomen van beïnvloeding van hun behandelend arts binnen het behandeladvies. In deze studies werd een vergelijking gemaakt tussen de jongere patiëntengroep (40 jaar tot en met 64 jaar) en de oudere patiëntengroep (gedefinieerd als 65 jaar en ouder aan de hand van de criteria van de World Health Organization).

Hoofdstuk 3 beschrijft de voorkeuren van beide patiëntengroepen voor een bepaald type operatie. Patiënten die in aanmerking kwamen voor zowel een borstsparende als een borstverwijderende operatie kregen na de diagnose een vragenlijst mee met een kort overzicht van beide type operaties, gevolgd door een vooraf gedefinieerde lijst van mogelijke beïnvloedbare factoren. Uit ons onderzoek blijkt dat beide patiëntengroepen voornamelijk een voorkeur hebben voor een borstsparende operatie: namelijk 56% van de oudere patiëntengroep en 69% van de jongere patiëntengroep. Wel heeft de oudere patiëntengroep vaker dan de jongere patiëntengroep een voorkeur voor een borstverwijderende operatie (40% versus 19%). Aan de andere kant heeft slechts 4% van de oudere patiëntengroep geen voorkeur of is hun voorkeur onbekend vergeleken met 12% van de jongere patiëntengroep. Deze verschillen zijn niet significant. Daarnaast blijkt dat voor beide patiëntengroepen het behandeladvies van de chirurg de belangrijkste factor is. Andere factoren die belangrijk worden geacht zijn angst voor terugkeer van de ziekte en het mogelijk missen van een borst. De mening van anderen (zoals de partner en familieleden) en angst voor radiotherapie worden door beide patiëntengroepen als het minst belangrijk beschouwd. Opmerkelijk is dat de oudere patiëntengroep significant vaker heeft aangegeven op te zien tegen de mogelijkheid dat er opnieuw geopereerd zou moeten worden. Mogelijk spelen factoren met betrekking tot de behandeling een grotere rol in de besluitvorming bij de oudere patiëntengroep en kan dit een doorslaggevende factor zijn in de voorkeur voor een borstverwijderende operatie. Ook zien we bij de oudere patiëntengroep de trend dat zij de bijwerkingen van de radiotherapie en de frequente ziekenhuisbezoeken voor de radiotherapie zwaarder

laat meewegen dan de jongere patiëntengroep. Tevens hecht zij minder waarde aan de mogelijkheid tot borstreconstructie dan de jongere patiëntengroep. Dit bleek nogmaals toen een lager percentage van de oudere patiëntengroep aangaf dat zij hoogstwaarschijnlijk voor een borstreconstructie na een mastectomie zou kiezen (40% versus 77%). Naar aanleiding van deze resultaten concluderen wij dat het bij oudere patiënten – net als bij jongere patiënten - ook van belang is om beide chirurgische opties (met hun voor- en nadelen) te bespreken, zodat zij een geïnformeerde voorkeur kunnen ontwikkelen. Gezien de variatie in voorkeuren binnen de oudere patiëntengroep, is het belangrijk om inzicht te krijgen in de beweegredenen van de oudere patiënten op individueel niveau. Ook adviseren wij dat oudere patiënten in ieder geval geïnformeerd moeten worden over de mogelijkheid tot een borstreconstructie, zodat zij van deze optie afweten.

Hoofdstuk 4 beschrijft een studie die als doel had te onderzoeken of er een verschil is in de bereidheid van de jongere en oudere patiëntengroep om een adjuvante systeemtherapie te ondergaan. Hiervoor gebruikten we gegevens uit zowel vragenlijsten als interviews. Patiënten met invasieve borstkanker (uit dezelfde patiëntengroep als in **hoofdstuk 3**) werden in de week na hun operatie geïnterviewd, maar nog voordat zij geïnformeerd werden over een mogelijke indicatie voor adjuvante systeemtherapie. Voorafgaand aan het telefonisch interview ontvingen zij een overzicht met twee hypothetische scenario's. In het eerste scenario werd de keuze tussen wel of geen nabehandeling met chemotherapie beschreven en in het tweede scenario tussen wel of geen nabehandeling met hormoontherapie. In elk scenario werden de algemene kansen op terugkeer van de ziekte binnen tien jaar (met of zonder aanvullende behandeling) en de mogelijke bijwerkingen beschreven. Het interview bestond uit de volgende onderdelen: het extra voordeel dat de patiënt wilde hebben van de behandeling om deze de moeite waard te vinden (aan de hand van een veelgebruikte probability trade-off methode) en de factoren die de patiënt zou laten meewegen bij deze afweging. Uit de analyses blijkt dat de oudere patiëntengroep vaker een adjuvante systeemtherapie zou weigeren dan de jongere patiëntengroep (een significant verschil wordt alleen gevonden voor chemotherapie). Ook blijkt uit ons onderzoek dat een groter percentage van de oudere patiëntengroep het voordeel niet weet aan te geven. Drie op de vijf oudere patiënten zou echter kiezen voor beide aanvullende behandelingen. Toen men bij deze groep navroeg hoeveel voordeel (extra kans op tien-jaars ziektevrije overleving) de behandeling minimaal zou moeten opleveren, bleek het extra voordeel voor beide therapieën niet significant te verschillen met die van jongere patiënten (minimaal 4% en 5% extra kans bij chemotherapie; 8% en 10% bij hormoontherapie). Toen men vroeg naar de factoren die een rol speelden bij de voorkeur van beide patiëntengroepen, beschouwden zowel de jongere als oudere patiëntengroep dezelfde factoren relevant (o.a. de wens om te overleven/geen recidief te krijgen) om voor een nabehandeling te kiezen. Uit ons onderzoek blijkt echter dat er grote verschillen zijn in de redenen om niet voor chemotherapie te kiezen.

Waar de jongere patiëntengroep de bijwerkingen als voornaamste reden noemt om niet voor chemotherapie te kiezen, noemt de oudere patiëntengroep bovendien als reden de wens hun onafhankelijkheid en huidige kwaliteit van leven te behouden. In de voorlichting aan oudere vrouwen dienen deze factoren meer aandacht te krijgen. Ook blijkt uit ons onderzoek dat patiënten die alleenstaand zijn, een geriatrische conditie hebben, of een actieve rol in de besluitvorming wensen een hoger voordeel van de chemotherapie willen om deze de moeite waard te vinden. Uit dit onderzoek concluderen wij dat de meerderheid van de oudere patiënten bereid is om een adjuvante systeemtherapie te ondergaan. Omdat er nog weinig wetenschappelijk bewijs is of chemotherapie bij oudere patiënten aanslaat, is het extra van belang om de verschillende behandelopties expliciet te bespreken (ook het niet ondergaan van behandeling) en naar hun overwegingen en voorkeuren te vragen, zoals al opgemerkt is in **hoofdstuk 3**. In aanvulling daarop constateren wij dat de leeftijd van de patiënt niet bepalend is voor het minimale voordeel en dat clinici zich hiervan bewust moeten zijn. Omdat voorkeuren kunnen verschillen tussen de jongere en oudere patiënten, tussen patiënten met verschillende persoonlijke kenmerken, maar ook binnen de oudere patiëntgroep zelf, is het van groot belang om de behandeling zoveel mogelijk af te stemmen op de individuele patiënt.

Hoofdstuk 5 onderzoekt in hoeverre jongere en oudere patiënten willen meebeslissen over hun behandeling. Hierbij zijn vragenlijstdata ingezet. Patiënten kregen voorafgaand aan het behandeladvies van de arts informatie uitgereikt over een borstsparende of borstverwijderende operatie (dezelfde informatie als in **hoofdstuk 3**) en over een nabehandeling met chemotherapie of hormoontherapie (wederom dezelfde informatie als in **hoofdstuk 4**). In de vragenlijsten werd de patiënt vervolgens gevraagd om per beslissing aan te geven of zijzelf die beslissing zou willen nemen, de arts wou laten beslissen of zij samen met de arts de beslissing wou nemen. Een klein aantal van de oudere patiëntengroep kiest ervoor de arts te laten beslissen, maar de meeste oudere patiënten hebben, net als jongere patiëntengroep, de voorkeur om deze beslissingen alleen of gezamenlijk met hun behandelend arts te nemen. Hoewel uit ons onderzoek blijkt dat jongere patiënten vaker dan oudere patiënten de beslissing zelf willen nemen of die aan de arts willen overlaten, zijn deze verschillen niet significant. We vergeleken ook per beslissing of er verschillen waren in de ervaren rol (vanuit het perspectief van de patiënt) tussen jongere en oudere patiënten. Onze analyses laten geen opvallende verschillen zien met betrekking tot de beslissing over het type operatie: beide patiëntgroepen geven aan dat zij vaak een actieve rol ervaren in de beslissing over het type operatie. Er blijken opvallende verschillen te zijn in de beslissingen over de nabehandeling. Oudere patiënten geven vaker aan een passieve rol te ervaren dan jongere patiënten, maar deze verschillen zijn niet statistisch significant. Onze resultaten maken duidelijk dat oudere patiënten betrokken moeten worden in het besluitvormingsproces en dat zij deze rol ook wensen. Een andere conclusie is dat oudere patiënten met name bij de beslissingen over adjuvante systeemtherapie meer betrokken mogen worden, indien zij een

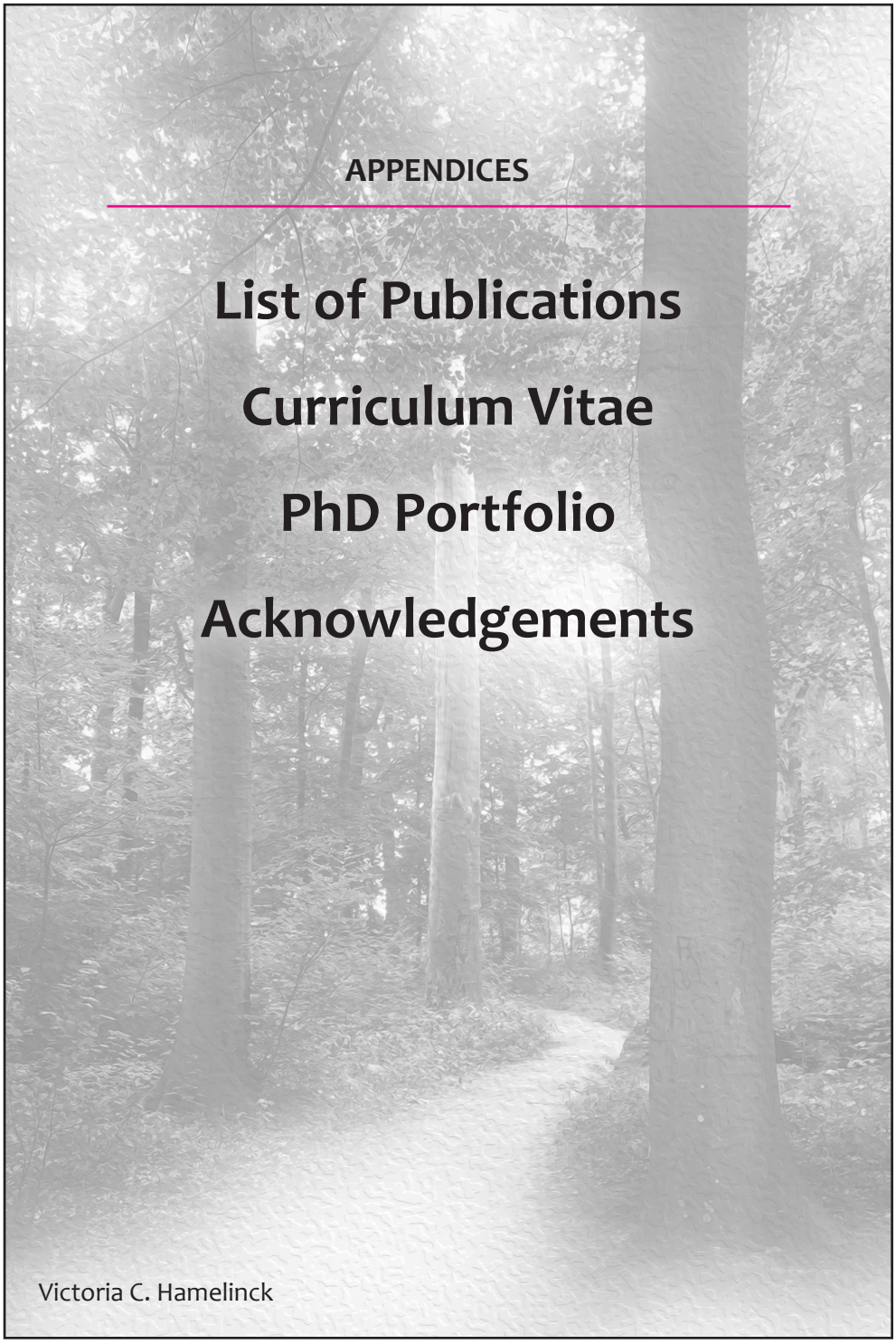
grotere rol wensen. Daarnaast suggereren wij dat de verantwoordelijkheid voor het vergroten van deelname aan de besluitvorming van oudere patiënten met borstkanker voornamelijk bij clinici ligt, aangezien zij bepalen welke onderwerpen in het consult besproken worden. Het is belangrijk om tijdens het consult na te vragen of patiënten zelf een beslissing kunnen/willen nemen, zodat de besluitvorming beter kan worden afgestemd op de voorkeuren van de individuele patiënt. Tot slot benadrukken wij dat er ook een rol voor de patiënt zelf is weggelegd om meer betrokken te zijn in beslissingen over hun behandeling.

Ons laatste onderzoek, dat beschreven staat in **hoofdstuk 6**, heeft als doel inzicht te krijgen in de voorkeuren van verschillende borstkankerspecialisten voor het type behandeling bij oudere patiënten boven de zeventig jaar. Het is van belang bij de implementatie van nieuwe voorstellen of richtlijnen inzicht te hebben in de ideeën die onder clinici leven, om eventuele barrières weg te kunnen nemen. Hiertoe zijn de leden van de Nederlandse Verenigingen voor Chirurgische Oncologie, Radiotherapie en Oncologie, en voor Medische Oncologie via een online nieuwsbrief benaderd voor het invullen van een korte vragenlijst. De deelnemers werd een viertal scenario's voorgelegd, waarbij hen gevraagd werd hun behandeladvies aan te geven. De resultaten laten zien dat patiëntkenmerken een significante invloed hebben op het behandeladvies van de artsen. Specialisten zouden minder vaak een borstsparende behandeling met radiotherapie adviseren voor een 84-jarige patiënte dan voor een 76-jarige patiënte met dezelfde tumorkenmerken. Ook zouden de specialisten vaker radiotherapie na een borstsparende operatie achterwege laten, indien de 84-jarige patiënte deze nabehandeling niet wenste te ondergaan. Voor chirurgisch en medisch oncologen blijkt de leeftijd van de patiënt van relatief groot belang, in tegenstelling tot radiotherapeut-oncologen die hetzelfde advies zouden geven ongeacht de leeftijd. In de drie andere casussen komt bij de specialisten duidelijke consensus naar voren over de beste behandeling. De algemene gezondheid van de patiënt is significant bepalend voor het behandeladvies. Het merendeel van de specialisten blijkt aanvullende hormoontherapie met of zonder chemotherapie aan te raden voor een oudere patiënte in goede algemene conditie, terwijl voor eenzelfde patiënte in matige of slechte conditie alleen hormoontherapie wordt aanbevolen. Ook komt naar voren dat één op de vier specialisten pre-operatieve hormoontherapie zou adviseren voor een patiënte met een grote, hormoongevoelige tumor, waarbij een borstsparende ingreep in eerste instantie niet mogelijk is. Vier van de vijf deelnemers geeft aan een aanvullende chemotherapie te overwegen in geval van een triple-negatieve borstkanker. Wij merken op dat de adviezen van de specialisten sterk verschillen met de huidige behandeling van de oudere patiëntengroep op basis van data van de Nederlandse Kankerregistratie. Een conclusie die wij hieruit trekken is dat er meer onderzoek nodig is om veranderingen in de bestaande behandelrichtlijnen te (kunnen) bewerkstelligen of te verfijnen en om clinici beter te ondersteunen in het geven van evidence-based behandeladviezen.

Algemene discussie en slotopmerkingen

Ondanks dat de oudere patiëntengroep met borstkanker in de klinische praktijk steeds meer aandacht krijgt, is er momenteel nog vrij weinig bekend over hun voorkeuren. De voorkeuren van borstkankerpatiënten worden momenteel geregeld onderzocht, maar met de bestaande kennis lijkt het raadzaam om de focus te verschuiven naar de oudere patiëntengroep, aangezien het aantal oudere patiënten met borstkanker sterk zal stijgen de komende jaren. Gezien de grote heterogeniteit binnen deze patiëntengroep, ondervinden oudere patiënten moeilijkheden bij beslissingen over hun behandeling. Daarom is er voor deze groep nog veel te winnen bij een onderzoek naar hun voorkeuren. In de onderzoeken in dit proefschrift is in kaart gebracht wat de specifieke voorkeuren zijn en welke factoren belangrijk worden geacht (bij het maken van beslissingen over type operatie en nabehandeling) en in hoeverre de voorkeuren van oudere patiënten verschillen met die van jongere patiënten. Ook is onderzocht welke patiënt- en artskenmerken bepalend zijn voor het behandeladvies van borstkankerspecialisten. Dit proefschrift beschrijft resultaten waarin zowel patiënten als clinici, waaronder oncologisch chirurgen, radiotherapeut-oncologen en medisch oncologen, zijn betrokken. Ook de prospectieve studieopzet onder nieuw-gediagnosticeerde patiënten die nog geen beslissing hebben genomen, is van grote meerwaarde voor de klinische praktijk. Door het kleiner aantal oudere patiënten (leeftijd >65 jaar), zijn enkele methodologische uitdagingen ondervonden bij het vergelijken van de twee leeftijdsgroepen.

Uit de resultaten van de studies blijkt de noodzaak om de oudere patiënt te betrekken bij de besluitvorming en deze de ruimte te bieden om haar individuele voorkeuren aan te geven. De resultaten in dit proefschrift kunnen gebruikt worden bij het vormgeven van toekomstige studies over besluitvorming bij oudere patiënten. De aanbevelingen voor de praktijk en beleid bevatten bruikbare aanknopingspunten om het huidige besluitvormingsproces met oudere borstkankerpatiënten in de dagelijkse praktijk te optimaliseren. In de algemene discussie pleiten wij er ook voor dat clinici meer kennis zouden moeten hebben van de verschillende voorkeuren en overwegingen van oudere patiënten, maar ook dat er meer aandacht moet worden besteed aan de impliciete verwachtingen van artsen over (de behandelingsvoorkeuren van) de oudere patiënt. Een investering in laatstgenoemde en het vergroten van het bewustzijn van bepaalde denkbeelden over deze patiëntengroep, zal van belang zijn om gedeelde besluitvorming te stimuleren. De behandelrichtlijn kan hier aandacht aan besteden door modules op te nemen met betrekking tot de oudere patiëntengroep en gezamenlijke besluitvorming. Daarnaast kan het aanbieden van communicatietrainingen aan clinici het besluitvormingsproces met de oudere patiëntengroep optimaliseren. Bovendien zou de focus erop gericht moeten zijn de individuele oudere patiënt meer te betrekken in het besluitvormingsproces.



APPENDICES

List of Publications

Curriculum Vitae

PhD Portfolio

Acknowledgements

Victoria C. Hamelinck

LIST OF PUBLICATIONS

Hamelinck VC, Bastiaannet E, Pieterse AH, Van de Velde CJH, Liefers GJ, Stiggelbout AM. Preferred and perceived participation of younger and older patients in decision-making about treatment for early breast cancer: a prospective study. *Clin Breast Cancer* 2018;18(2):e245-e253.

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CURRICULUM VITAE

Victoria Chantal Hamelinck werd op 23 augustus 1986 geboren in Oostburg (Zeeuws-Vlaanderen). Na het behalen van haar Gymnasium diploma aan het Zwin College begon zij in 2004 aan haar studie Algemene Gezondheidswetenschappen aan de Vrije Universiteit in Amsterdam. In 2007 startte zij haar masteropleiding Management, Policy-Analysis & Entrepreneurship in the Health and Life Sciences en koos zij voor de specialisatie International Public Health. Zij heeft stage gelopen bij expertisecentrum gezondheidsverschillen Pharos, met als onderwerp borstkankerscreening bij migrantenvrouwen, en bij een voedings- en onderzoeksinstituut in Guatemala City. Na haar studie werkte zij enige tijd als onderzoeksassistent bij het Dutch Cochrane Centre in het Academisch Medisch Centrum, waar haar interesse voor wetenschappelijk onderzoek versterkt werd. Vanaf februari 2011 was zij werkzaam als promovendus bij de afdeling Heelkunde in het Leids Universiteir Medisch Centrum. Onder leiding van Prof. Dr. C.J.H. van de Velde, Dr. G.J. Liefers en Prof. Dr. A.M. Stiggelbout (Medische Besliskunde) deed zij onderzoek naar oudere vrouwen met borstkanker, met als focus de preferenties voor behandeling van deze patiëntengroep (genaamd 'FOCUS op Keuze studie'). Begin 2012 heeft zij voor dit project een Pink Ribbon subsidie binnengehaald. Tijdens haar promotieonderzoek heeft zij haar onderzoeksresultaten op verschillende internationale congressen gepresenteerd. De resultaten van haar onderzoeken staan beschreven in dit proefschrift.

PHD PORTFOLIO

PhD student:	Victoria Chantal Hamelinck
Primary thesis advisor:	Prof. Dr. Cornelis J.H. van de Velde
Other thesis advisor(s):	Prof. Dr. Anne M. Stiggelbout
	Dr. Gerrit-Jan Liefers
Research program:	10202 Surgical oncology
Title of Thesis:	Shared decision-making about treatments for early breast cancer: preferences of older patients and clinicians

	Year
Mandatory courses	
• Basiscursus Regelgeving en Organisatie voor Klinisch onderzoekers	2013
• Basic Methods and Reasoning in Biostatistics	2012
• PhD Introductory Meeting	2011
Generic courses	
• Van klinisch probleem tot succesvolle aanvraag	2013
• Klinische Epidemiologie Schiermonnikoog	2013
• Design, Management and Analysis of Clinical Trials	2013
• Survival Analysis	2012
• Meta Analysis	2012
• Cancer Epidemiology, NIHES	2012
• Analysis of Repeated Measurements	2011
• Regression Analysis	2011
(Inter)national congress attendance	
• 16th World Congress of Psycho-Oncology and Psychosocial Academy, Lisbon, Portugal	2014
• 14th Meeting of the International Society of Geriatric Oncology, Lisbon, Portugal	2014
• 7th International Shared Decision Making Conference, Lima, Peru	2013
• 13th Meeting of the International Society of Geriatric Oncology, Copenhagen, Denmark	2013
• 17th ECCO, 38th ESMO, 32nd ESTRO European Cancer Congress, Amsterdam, The Netherlands	2013
• Dutch Epidemiology Conference (WEON), Utrecht, The Netherlands	2013
• 8th European Breast Cancer Conference, Vienna, Austria	2012
• 12th Meeting of the International Society of Geriatric Oncology, Manchester, United Kingdom	2012

- Dutch Epidemiology Conference (WEON), Rotterdam, The Netherlands 2012
- 32nd Congress of the European Society of Surgical Oncology, Valencia, Spain 2012
- 11th Meeting of the International Society of Geriatric Oncology, Paris, France 2011
- 16th ECCO, 36th ESMO, 30th ESTRO Congresses, Stockholm, Sweden 2011
- 9th Bossche Mamma Conference, Vught, The Netherlands 2011
- Dutch Epidemiology Conference (WEON), IJmuiden, The Netherlands 2011

Oral presentations

A prospective comparison of younger and older patients' preferences for adjuvant chemotherapy and hormonal therapy in early breast cancer

- International Society for Evidence Based Health Care and the International Shared Decision-Making, Sydney, Australia 2015
- 16th World Congress of Psycho-Oncology and Psychosocial Academy, Lisbon, Portugal 2014
- 15th Biennial Society for Medical Decision Making European Meeting, Antwerp, Belgium 2014

Patients' preferences for surgical and adjuvant systemic treatment in early breast cancer: A systematic review

- 7th International Shared Decision Making Conference, Lima, Peru 2013

Underweight as a predictor of recurrence and survival in elderly breast cancer patients

- 32nd Congress of the European Society of Surgical Oncology, Valencia, Spain 2012

Poster presentations

A prospective comparison of younger and older patients' preferences for adjuvant chemotherapy and hormonal therapy in early breast cancer

- 14th Meeting of the International Society of Geriatric Oncology, Lisbon, Portugal 2014
- 16th World Congress of Psycho-Oncology and Psychosocial Academy, Lisbon, Portugal 2014

Older patients' preferences for surgical treatment in early breast cancer: A systematic review

- 8th European Breast Cancer Conference, Vienna, Austria 2012

Parameters of esteem

- Pink Ribbon Foundation grant for project: Elderly patients' preferences for early stage breast cancer treatment: are there differences in treatment preferences between younger and older patients? (grant number 2011.WO06.C107) 2011

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