

# Shared decision-making about treatments for early breast cancer : preferences of older patients and clinicians

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# CHAPTER 6

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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.<sup>1</sup> Approximately 30% of the cases are in women over 70 years of age.<sup>1</sup> 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.<sup>2</sup> Besides, those enrolled in trials are usually in better than average health, and therefore may not be representative for all older BC patients.<sup>3</sup> Elderly patients comprise a heterogeneous group due to differences in comorbid conditions, functional capacity, and social support.<sup>4</sup> 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<sup>5</sup> make treatment decision-making for these patients generally difficult.

The Dutch treatment guidelines for BC make little or no age-specific recommendations.<sup>6</sup> 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.<sup>7,8</sup> 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,<sup>5</sup> whilst others have suggested that clinicians play a notable role in treatment decision-making, particularly among older patients.<sup>9,10</sup>

Currently, it is unknown how clinicians weigh treatment options for patients aged  $\ge$ 70 years. Previous surveys using hypothetical scenarios explored how patient age or health status influenced clinicians' treatment recommendations,<sup>11-19</sup> but most only focused on adjuvant systemic therapy.<sup>11-15,18</sup> Furthermore, their recommendations were seldom compared for scenarios only involving patients aged over 70.<sup>12-15,19</sup> 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,<sup>2</sup> a better understanding of clinicians' recommendations and influencing factors become increasingly relevant.

This study aimed to examine the treatment recommendations of BC specialists for locoregional 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  $\geq$ 70 years (Appendix 1). The scenarios were based on the Dutch treatment guidelines for BC<sup>6</sup> and previous work.<sup>2,8</sup> 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.<sup>6</sup> 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.<sup>2</sup> 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.<sup>2</sup>

### 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  $\chi^2$  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  $\geq$ 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-relat	ed characterist	ics (n=174)		
	Total	Surgical oncologists	Radiation oncologists	Medical oncologists
	(n=174)	(n=106, 61%)	(n=37, 21%)	(n=31, 18%)
Variables	n (%)	n (%)	n (%)	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 <sup>a</sup>				
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 $\geq$ 70 years seen per mo	onth			
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)

<sup>a</sup> 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	f patient ag	e on specialists' trea	atment recon	mmendation for loco	-regional ther	apy (scenar	rio 1)				
A(n) (76- or 84-)year- invasive ductal adenoc	old female, F carcinoma, cl	(PS score of 90% (able [1c, cN0, ER+, PR+, H	e to carry on n ler2neu—, no	ormal activity; minor s contraindications to bi	signs or sympton reast-conserving	ms of disease 3 therapy, no	e), right-sided breast can ) comorbidities	cer, one lesion of 1.7	cm in the up	oper outer qu	adrant,
	A 76-year-	old female (1A)				An 84-year-	-old female (1B)				
Question 1: What woul	ld be your tre	atment recommendatic	ion regarding .	resection of the tumour	i-						
	I would no I leave the	t give any advice, choice to the patient	Breast-cons followed by	erving surgery, radiotherapy	Mastectomy	I would not I leave the c	: give any advice, E :hoice to the patient for	reast-conserving surrighters	gery, M. apy	astectomy	
	n (%)		u (%)		n (%)	(%) u	Ē	(%)	u	(%)	þ
Total (n=167)	43 (26)		122 (73)		2 (1)	61 (37)	6	4 (56)	12	(/);	0.001
Surgical oncologists (n=104)	22 (21)		81 (78)		1 (1)	37 (36)	9	0 (58)	7(	(2)	0.003
Radiation oncologists (n=34)	17 (50)		17 (50)		0 (0)	16 (47)	-	8 (53)	0	(0)	0.81
Medical oncologists (n=29)	4 (14)		24 (83)		1 (3)	8 (28)	1	6 (55)	5 (	(17)	0.07
Question 2: Suppose th	e patient ind	licates that she would li	like to undergu	breast-conserving sur	gery, but <u>no</u> radi	otherapy. Wc	ould you accept this?				
	Yes, without question	Yes, but I would still convince her of the b of radiotherapy	l try to No, benefit her reco	I would recommend a mastectomy with onstruction	No	Yes, without question	Yes, but I would still try convince her of the ben of radiotherapy	to No, I would rev efit her a mastecto reconstruction	commend omy with	No	
	u (%)	n (%)	;) u	(%)	n (%)	n (%)	n (%)	n (%)		n (%)	р
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 (2	(1;	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
VDC - Variatelin Darfara	Century Century										

KPS = Karnotsky 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 r	ecommendation for adj	uvant systemic therap	y (scenario 2)		
A 77-year-old female, KPS score performed, pT2, pN1, grade 3, E	: of (90 or 50) %, right-sic R+, PR+, Her2neu–, no	led breast cancer, one les comorbidities	ion of 3.0 cm in the upper	outer quadrant, invasive	ductal adenocarcinoma, a	a modified radical mastec	omy was
	KPS score of 90% <sup>a</sup> (2A)			KPS score of $50\%^{b}$ (2B)			
What would be your treatment n	ecommendation?						
	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 (%)	b
Total (n=164) <sup>c</sup>	0 (0)	137 (86)	22 (14)	13 (8)	145 (92)	0 (0)	<0.001
Surgical oncologists (n=101) <sup>d</sup>	0 (0)	81 (83)	16 (17)	6 (6)	94 (94)	0 (0)	<0.001
Radiation oncologists (n=34) <sup>e</sup>	0 (0)	31 (91)	3 (9)	4 (13)	27 (87)	0 (0)	0.020
Medical oncologists (n=29) <sup>f</sup>	0 (0)	25 (89)	3 (11)	3 (11)	24 (89)	0 (0)	0.06
KPS = Karnofsky Performance Statu	S						

A p-value in bold means a significant difference in treatment recommendation between scenario 2A and 2B

<sup>b</sup>Requires considerable assistance and frequent ways and the defail care  $^{-1}$  Prequires considerable assistance and frequent medical care  $^{-2}$  Participants who filled in other for scenario 2A (n=5) or 2B (n=6) were excluded  $^{-2}$  Participants who filled in other for scenario 2A (n=4) or 2B (n=1) were excluded  $^{-1}$  Three participants who filled in other for scenario 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B (n=2) were excluded  $^{-2}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario 2A (n=4) or 2B were excluded  $^{-1}$  Participants who filled in other for scenario AA were excluded  $^{-1}$  Participants who filled in other for a for <sup>a</sup> Able to carry on normal activity; minor signs or symptoms of disease

### Neo-adjuvant hormonal therapy (scenario 3)

For an otherwise healthy 75-year-old woman who was not initially a candidate for breastconserving 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 re	ecommendation?			
	l would not give any advice, l leave the choice to the patient	Mastectomy	Neo-adjuvant hormonal therapy, followed by breast-conserving surgery	
	n (%)	n (%)	n (%)	р
Total (n=164) <sup>a</sup>	36 (23)	80 (50)	43 (27)	-
Surgical oncologists (n=101) <sup>b</sup>	21 (21)	51 (52)	26 (27)	0.12
Radiation oncologists (n=34) <sup>c</sup>	12 (37)	14 (44)	6 (19)	
Medical oncologists (n=29)	3 (10)	15 (52)	11 (38)	

KPS = Karnofsky Performance Status

<sup>a</sup> Five participants who filled in 'other' were excluded from the analyses

<sup>b</sup>Three participants who filled in 'other' were excluded from the analyses

<sup>c</sup> 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) <sup>b</sup>	13 (14)	39 (41)	43 (45)	0.30
Radiation oncologists (n=34) <sup>c</sup>	8 (25)	7 (22)	17 (53)	
Medical oncologists (n=29)	6 (21)	11 (38)	12 (41)	

KPS = Karnofsky performance status

<sup>a</sup> Eight participants who filled in 'other' were excluded from the analyses

<sup>b</sup> Six participants who filled in 'other' were excluded from the analyses

<sup>c</sup>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.<sup>19</sup> 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.<sup>12,13,15</sup>

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.<sup>20,21</sup> Since the absolute recurrence risk was low, these results suggested that

radiotherapy omission can be considered for selected groups of older, hormone receptorpositive 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.<sup>6</sup> 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.<sup>22</sup> 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.<sup>23</sup> As radiotherapy is generally well-tolerated by most older women,<sup>24</sup> 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%<sup>22</sup>), and use of neo-adjuvant hormonal therapy for a clinically large hormone receptor-positive tumour (27% versus 6%<sup>22</sup>) 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.<sup>6</sup> Another difference was found between the recommendation of use of adjuvant chemotherapy for triple-negative BC and actual practice (83% versus 27%<sup>22</sup>). The proportion considering adjuvant chemotherapy in this scenario is in accordance to the guidelines.<sup>6</sup>

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.<sup>25,26</sup> 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<sup>27</sup> 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  $\geq 60$  years).<sup>28</sup> 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.

...... / ...... / ...... (day/month/year) Fill in date: 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)
  - $\Box$  < 2 years
  - 2-5 years
  - □ 6-10 years
  - $\square$  >10 years
- 8. Approximately how many new breast cancer patients do you see <u>per month</u>, 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
- Approximately how many new breast cancer patients of <u>70 years of age or older</u> do you see <u>per</u> <u>month</u>, where initially the treatment intent is curative? (please choose one answer)

0 🗆

- □ 1-2 patients
- □ 3-5 patients
- □ 6-10 patients
- □ 11-15 patients
- $\square$  >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
- Suppose the patient indicates that she would like to undergo breast-conserving surgery, but <u>no</u> radiotherapy. Would you accept this? (please choose one answer)
  - $\Box$  Yes, without question
  - □ Yes, but I would still try to convince her of the benefit of radiotherapy
  - $\square$  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
  - $\Box$  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 <u>no</u> radiotherapy. Would you accept this? (*please choose one answer*)
  - $\Box$  Yes, without question
  - $\Box$  Yes, but I would still try to convince her of the benefit of radiotherapy
  - $\Box$  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
- $\Box$  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

<ul> <li>A 75-</li> </ul>	year-old	female
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- 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:

.....