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Original article

Patient-reported outcomes with neoadjuvant vs adjuvant systemic therapy for operable breast cancer

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ABSTRACT

Background: Neoadjuvant systemic therapy (NAST) is used for large operable or highly proliferative breast cancers. It is not known whether psychological outcomes differ according to the treatment sequence (chemotherapy or surgery first) or tumour response.

Methods: This was a planned analysis of a multi-institutional single arm longitudinal study of patients considering NAST for operable breast cancer. Participants completed patient reported outcome questionnaires before and after the decision about NAST, between chemotherapy and surgery, and 12 months after diagnosis.

Results: Fifty-nine women enrolled. Fourteen of 51 (28%) who received NAST experienced pathological complete response (pCR). Patients who had surgery first ($n = 7$) had higher baseline anxiety, and a greater decrease in anxiety at 12 months follow up, compared with patients who received NAST ($n = 50$) (a decrease from baseline of 34 pts vs 17 points; $p = 0.033$). Distress declined at a similar rate in surgery first and NAST groups. Mean satisfaction with decision score post-decision was significantly lower in the adjuvant group compared with NAST (22 vs 26, $p = 0.02$). No differences were seen between patients with pCR vs residual cancer in: distress, anxiety, satisfaction with decision, fear of progression, and decision regret.

Conclusion: Most patients in this study proceeded with NAST when their surgeon offered it as an option. This exploratory analysis suggests that patients who chose surgery first tended to be more anxious, and had lower satisfaction with their decision, than those who had NAST. In patients who had NAST, lack of pCR does not appear to correlate with adverse psychological outcomes.

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Introduction

Neoadjuvant systemic therapy is increasingly used for women with large or highly proliferative operable breast cancer [1]. International guidelines indicate that neoadjuvant therapy is an option for any patient who is a candidate for chemotherapy, based on clinical staging and subtype [2–4]. The decision about whether to have neoadjuvant systemic therapy may be guided by preferences and values, leading individual patients with similar clinical

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circumstances to choose different options [5].

The neoadjuvant setting is a unique opportunity to test the chemo-sensitivity of early stage breast cancer in vivo. Decisions about neoadjuvant systemic therapy are based on an *a priori* probability of tumour regression. When neoadjuvant systemic therapy is offered by experienced multidisciplinary teams the rate of progression on neoadjuvant systemic therapy is <5% [6]. Consequent patient benefits of neoadjuvant systemic therapy include: reduction in the extent of breast cancer to allow breast conservation rather than mastectomy, axillary downstaging [7,8], better aesthetics in patients who are borderline candidates for breast conservation [9], and better oncologic clearance allowing consideration of immediate breast reconstruction in women still requiring mastectomy [10]. Neoadjuvant systemic therapy gives patients time to have testing for genes that predispose to breast cancer, and to consider and plan the optimal surgical approach [8,11]. Patients may value neoadjuvant trial opportunities [12]; or post-neoadjuvant trials with selection based on prior response to therapy (e.g. PenelopeB, NCT01864746). Importantly, disease-free and overall survival outcomes are equivalent, whether neoadjuvant systemic therapy or surgery is the first treatment modality, provided adequate local therapy is administered [14].

Despite equivalent cancer outcomes, patients who receive neoadjuvant systemic therapy may have different psychological outcomes to those who receive adjuvant therapy due to fears about delaying surgery, the potential for a poor response or progression during systemic therapy [6], and feeling marginalised by a less frequently used treatment [13]. Lack of tumour response or progression during neoadjuvant systemic therapy portends a worse prognosis compared with those who a have a complete or near complete pathological response [15]. For patients who experience a poor tumour response, knowledge of adverse prognostication has the potential to worsen psychological outcomes, including increased anxiety, distress [16], fear of progression during treatment [17] and fear of cancer recurrence following completion of treatment [18], compared with those whose cancer responds.

To our knowledge, there are no published data on psychological outcomes in the neoadjuvant operable breast cancer population. Thus, we aimed to explore the impact of (a) neoadjuvant vs adjuvant therapy; and (b) pathological response, on patient reported outcomes in patients who were offered neoadjuvant systemic therapy for operable breast cancer.

Materials and methods

Design, patients and setting

This was a planned exploratory secondary analysis of a prospective, single arm, multicentre, longitudinal study to evaluate a decision aid for women considering neoadjuvant systemic therapy for operable breast cancer. Outcomes specific to the decision aid have been reported previously [19]. A detailed description of study design and methods has been published [20]. Participants were women aged 18 or over with a diagnosis of invasive breast cancer, operable at the time of diagnosis, attending outpatient oncology units, and considered candidates for neoadjuvant systemic therapy of 3 months' duration or longer. Exclusion criteria were: insufficient English language to complete study questionnaires; inflammatory, metastatic or inoperable breast cancer; lack of internet access and/or email address; or medical/psychiatric condition that would preclude informed consent or ongoing study participation. Participants were recruited by their breast surgeon or medical oncologist. All participants received a decision aid that describes neoadjuvant and adjuvant systemic therapy for breast cancer, including the probability of response according to subtype, and the prognostic implications of degree of response (Appendix A, available at www.breastcancertrials.org.au/brochures).

Outcomes

Online patient reported outcome measures (Appendix B, C) were completed by participants at baseline (assessment 1). After completion of assessment 1, the neoadjuvant systemic therapy decision aid was made available. Participants then attended one or more follow-up visits, at which time a decision was made about whether they would proceed with neoadjuvant systemic therapy, or surgery first, followed by assessment 2. Assessment 3 occurred after completion of systemic therapy and before surgery in neoadjuvant patients, and after surgery but before the start of chemotherapy in surgery-first patients. The final questionnaire (assessment 4) was 12 months after registration (Schema, Appendix D). Measures relevant to this analysis were: 6-item Spielberger State-Trait Anxiety Inventory [21]; Distress Thermometer [16]; Satisfaction With Decision Scale [22]; Fear of Cancer Progression Questionnaire [17]; Decision Regret Scale [23]; and Fear of Cancer Recurrence Inventory [24]. Distress is a broad construct, encompassing a broad continuum of psychological symptoms including anxiety and depression [16]. Anxiety is a more specific array of symptoms, requiring a more sensitive and specific assessment tool than the screening Distress Thermometer [25,26]. Demographic, clinical and treatment data were collected, including pathological response to neoadjuvant therapy.

Analysis

The parent study intended to recruit 50 participants who had completed assessment 2. Outcome measure scores were transformed using methods appropriate to each scale. Outcomes were compared according to whether neoadjuvant systemic therapy or adjuvant therapy was received, and whether a pathological complete response (pCR) or clinical response was observed in those who received neoadjuvant therapy. Linear mixed models were used to examine changes in distress and anxiety with fixed effects for final treatment choice and time (modelled as a categorical variable) and a subject level random intercept term. Fear of progression, satisfaction with decision, fear of cancer recurrence severity and decisional regret are reported using Student's t-test or test of proportions. A p-value of less than 0.05 was considered significant. Analyses were computed using STATA/IC version 13.1 (StataCorp, College Station, TX).

Ethical considerations

This study was designed and conducted according to the declaration of Helsinki, in accordance with the principles of the International Conference on Harmonisation Good Clinical Practice (ICH-GCP). All participants provided voluntary informed consent prior to participation. Registration: Australian New Zealand Clinical Trials Registry (www.anzctr.org.au/, ACTRN12614001267640).

Results

Between June 2015 and September 2016, 59 women completed the first questionnaire and accessed the decision aid (CONSORT diagram, Fig. 1). Participants characteristics are shown in Table 1 and tumour characteristics are shown in Table 2. There was no difference in mean age between neoadjuvant and adjuvant patients (51 vs 53 years, respectively). At assessment 1, 38 preferred neoadjuvant therapy, 2 preferred surgery and 18 were unsure (1 missing). Of the 18 who were unsure at assessment 1, 12 (67%) went

on to have neoadjuvant therapy and 6 (33%) had surgery; compared to the 40 who were sure, where 39 (98%) had neoadjuvant systemic therapy and 1 (2%) had surgery ($Chi^2 = 11.1$, $p = 0.001$). One patient who initially preferred surgery received neoadjuvant therapy. Of the 51 neoadjuvant patients, 14 (28%) had a pCR in the breast and lymph nodes, and a further 10 (20%) had minimal residual cancer burden (RCB 1). All patients with a pCR noted a reduction in the size of their breast tumour. Fifty-four percent had a mastectomy, 85% had radiotherapy.

A trend to higher mean baseline anxiety scores was seen in the adjuvant group (65.7), compared with 54.7 in the neoadjuvant group ($p = 0.056$). Mean baseline distress scores were no different (adjuvant 6.6 vs neoadjuvant 5.9, $p = 0.562$). Mean (SD) scores on the severity scale of the fear of cancer recurrence inventory at assessments 3 and 4 were 15.5 (7.7) and 14.4 (6.0), respectively. A score of 12 or more in this subscale indicates significant fear of cancer recurrence.

Table 1
Participant characteristics.

Variable		N = 59
Age, years [mean (SD)]		52 (8.9)
Marital status	Married/De facto	48 (81.4%)
	Single	11 (18.6%)
Highest education level	Postgraduate	17 (28.8%)
	Undergraduate	13 (22.0%)
	Vocational	13 (22.0%)
	High school	15 (25.4%)
	Missing	1 (1.7%)
Private health insurance	Yes	51 (86.4%)
	No	8 (13.6%)
Health Professional	Yes	10 (17.0%)
	No	49 (83.0%)
English as first language	Yes	56 (94.9%)
	No	3 (5.1%)

Patient-reported outcomes according to treatment received

Anxiety and distress (Table 3) decreased at each follow up in a comparable way for patients who had surgery first compared with neoadjuvant systemic therapy but by 12 months follow-up the adjuvant group had a significantly greater decrease in anxiety ($p = 0.033$) (see Fig. 2). There was no difference in distress between surgery first and neoadjuvant systemic therapy, with both groups' scores decreasing over time. Mean satisfaction with decision score post-DA was significantly lower in the adjuvant group compared with neoadjuvant systemic therapy (22.0 vs 25.9, $p = 0.02$).

Patient-reported outcomes according to response

In patients who received neoadjuvant therapy, a comparison of those with pCR to those who had residual cancer in breast and/or lymph nodes showed: changes in baseline distress and anxiety were not significantly different immediately after completing chemotherapy and at 12 months (Table 3); satisfaction with decision and fear of progression during chemotherapy were not significantly different (Table 4); and decision regret was

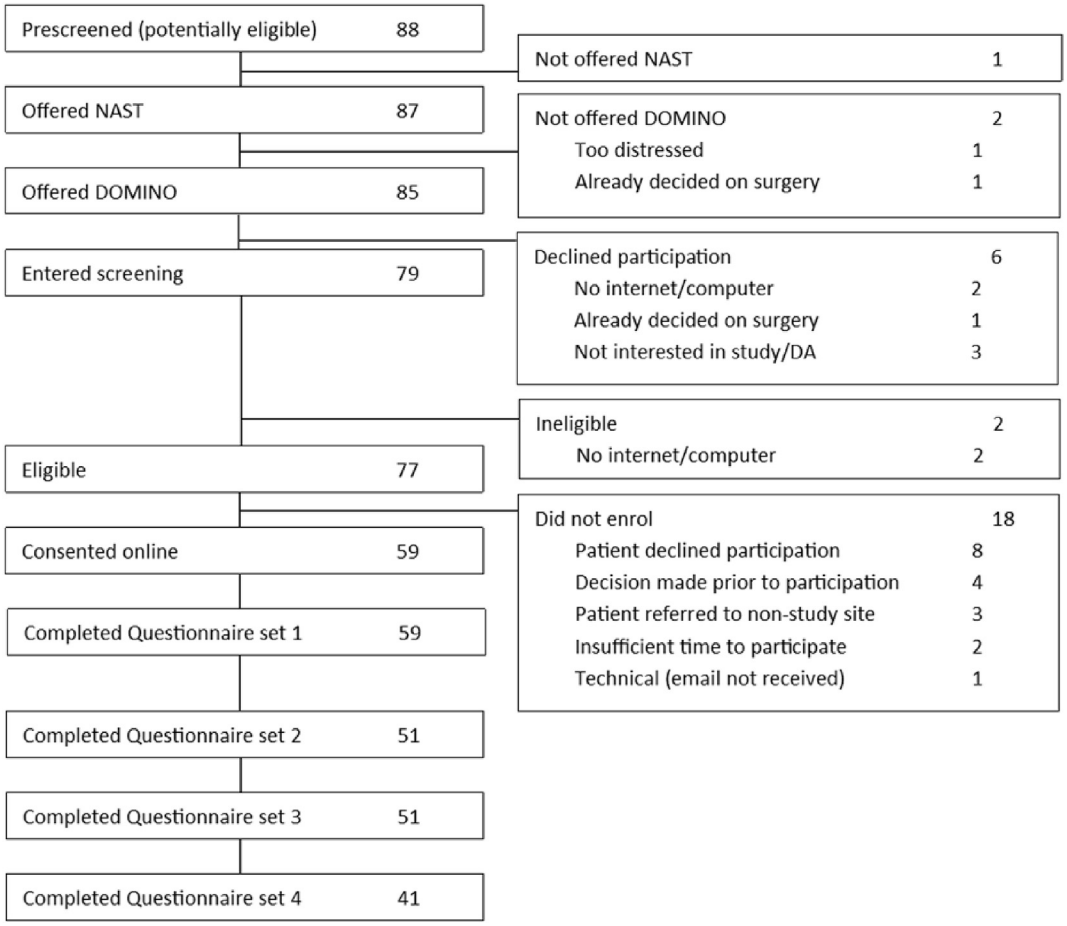

Fig. 1. CONSORT diagram.

Table 2
Tumour and treatment data. ER, oestrogen receptor; HER2, human epidermal growth factor 2; N/A, not applicable; PR, progesterone receptor; SE, standard error. *Data missing for one participant who withdrew consent after assessment 1.

Variable	Neoadjuvant (n = 51)*	Adjuvant (n = 7)
Baseline tumour diameter [mean (SE)]	31.4 (6.3)	37.3 (2.7)
Baseline node positive [n (%)]	21 (41.2%)	6 (85.7%)
HER2 positive	21 (41.2%)	1 (14.3%)
Triple negative	11 (21.6%)	0 (0%)
ER/PR positive	31 (60.8%)	7 (100%)
Pathological complete response	14 (27.5%)	N/A
Residual cancer burden class 1	10 (19.6%)	N/A
Residual cancer burden class 2/3	17 (33.3%)	N/A
Residual cancer burden unknown	10 (19.6%)	N/A
Mastectomy	26 (51.0%)	6 (85.7%)
Lumpectomy	25 (49.0%)	1 (14.3%)
Radiotherapy	45 (88.2%)	5 (71.4%)

Table 3
Mean anxiety and distress scores according to response and treatment received. pCR, pathological complete response; n, number. P-values reported as the difference between groups estimated from the linear mixed regression model.

Outcome	Assessment	Response			Treatment received		
		pCR	Non-pCR	p-value	Neoadjuvant	Adjuvant	p-value
Anxiety score [mean (n)]	Baseline (1)	–	–	–	54.9 (50)	65.7 (7)	
	Post-decision (2)	54.1 (12)	46.9 (35)		48.1 (46)	62.9 (5)	.479
	Between chemotherapy and surgery (3)	41.6 (12)	40.5 (34)	.112	39.7 (46)	46.2 (3)	.512
	12 months (4)	38.4 (10)	37.9(28)	.146	37.1 (39)	31.4 (2)	.033
Distress score [mean (n)]	Baseline (1)	–	–	–	5.9 (51)	6.6 (7)	
	Post-decision (2)	5.3 (12)	4.7 (35)		4.8 (46)	6.6 (5)	.380
	Between chemotherapy and surgery (3)	3.8 (13)	3.1 (35)	.856	3.2 (48)	3.6 (3)	.847
	12 months (4)	1.8 (10)	1.9 (28)	.584	1.8 (39)	0.7 (2)	.307

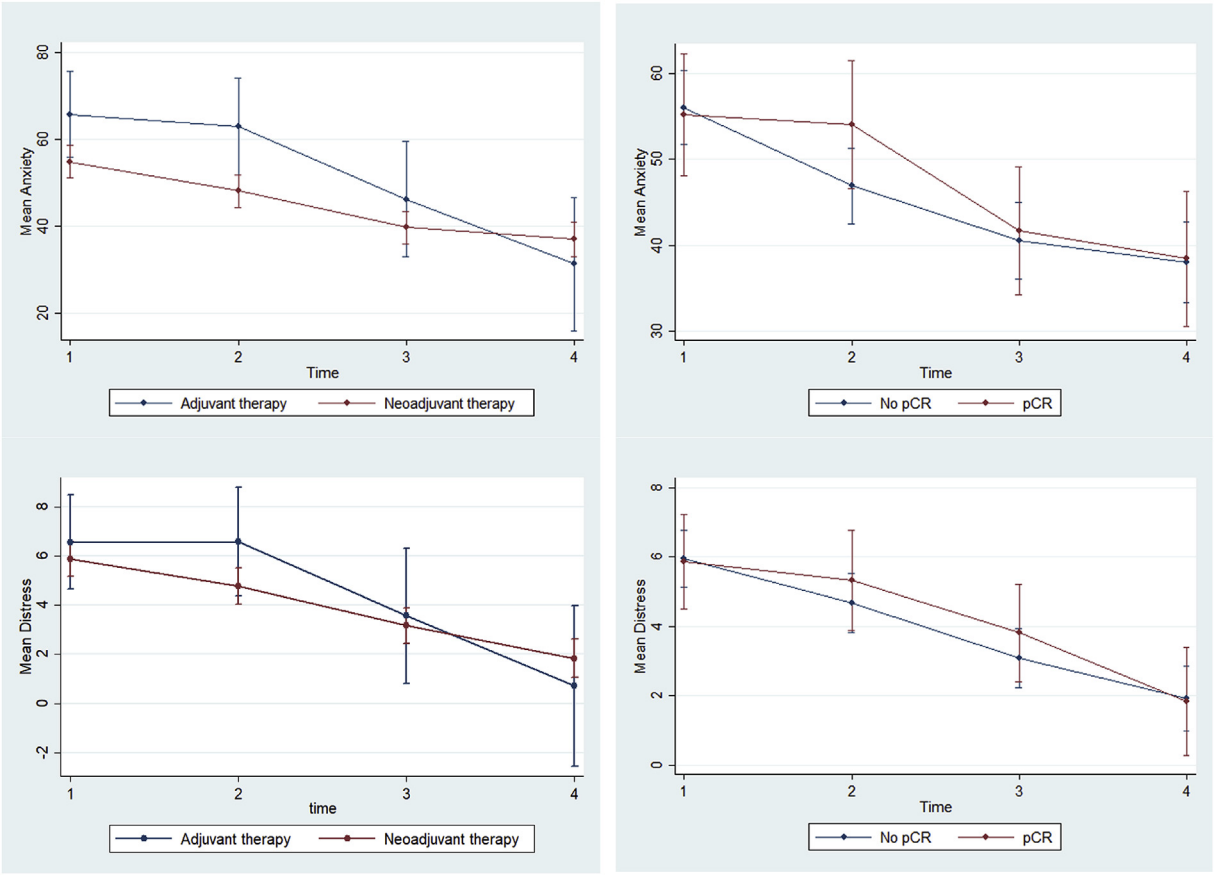

Fig. 2. Outcomes according to treatment and response at assessments 1–4. A, B: Anxiety and distress according to treatment received. C,D: Anxiety and distress according to response. Whiskers indicate 95% confidence intervals.

Table 4
Patient-reported outcome measure scores according to tumour response and treatment received. N, number; pCR, pathological complete response.

Outcome	Assessment	Response			Treatment received		
		pCR	Non-pCR	p-value	Neoadjuvant	Adjuvant	p-value
Satisfaction with decision score [mean(n)]	2	–	–	–	25.9 (46)	22.0 (5)	0.022
Low fear of cancer progression [%(n)]	2	–	–	–	76.1% (35/46)	80.0% (4/5)	0.845
	3	84.6% (11/13)	89.2% (33/37)	0.663	89.6% (43/48)	66.7% (2/3)	0.238
Decisional regret score [mean (n)]	3	12.3 (13)	18.8 (35)	0.307	16.9 (48)	11.7 (3)	0.648
	4	4.0 (10)	15.5 (28)	0.060	12.2 (39)	20.0 (2)	0.516
Fear of cancer recurrence score, severity subscale [mean (n)]	3	16.5 (14)	15.4 (38)	0.662	15.6 (50)	14.7 (3)	0.847
	4	14.3 (10)	14.9 (30)	0.765	14.9 (39)	5.0 (2)	0.021

numerically (but not significantly) lower in the pCR group after chemotherapy (18.8 vs 12.3, $p = 0.307$) and at 12 months (15.5 vs 4.0, $p = 0.060$). Ninety-three percent of patients noted a reduction in tumour size prior to surgery. No differences in anxiety or distress were seen at assessment 3 according to patient-reported response.

Conclusions

This study provides hypothesis-generating data about psychological outcomes in a small sample of patients who received neoadjuvant versus adjuvant therapy. We were unable to conclude that patients who receive neoadjuvant systemic therapy and do not achieve a pathological complete response differ in their psychological outcomes compared to those who have a complete response. Nor could we conclude that outcomes differ in patients who receive adjuvant vs neoadjuvant therapy. Further research is required to investigate the psychological impact of (a): fear of progression during neoadjuvant therapy; and (b) the adverse prognosis associated with incomplete response to neoadjuvant chemotherapy.

All participants in this study had access to a decision aid developed according to international standards specifically for the decision about neoadjuvant systemic therapy for operable breast cancer [19]. Decision aid content ensured that patients were well informed about the implications of receiving neoadjuvant systemic therapy versus a surgery-first approach. One pictograph in the decision aid aimed to reduce unwarranted fear of progression by showing the small chance of progression during neoadjuvant systemic therapy, based on work by Caudle et al. [6]. Therefore, these patients may have had relatively low fear of cancer progression because they were well informed.

The decision aid also included information about the likelihood of a pathological complete response following neoadjuvant systemic therapy, with associated prognostic implications according to their breast cancer subtype. For example, approximately 85% of patients with triple negative breast cancer who have a pathological complete response are alive and disease-free at 5 years, compared with 50% of those who do not have a pathological complete response after neoadjuvant systemic therapy [15]. Informing patients without a complete response that their cancer is more likely than average to recur may cause or exacerbate fear of cancer recurrence, anxiety, and/or distress. However, worsening of these outcomes was not apparent in our data, with no differences in these outcomes after surgery. Fear of cancer recurrence severity was high at assessments 3 and 4 [27]. There are mixed data on fear of cancer recurrence in breast cancer patients, with some studies showing a correlation between higher stage and greater fear, and others showing no relationship [28]. Likewise, there are conflicting data on whether or not receiving more breast cancer treatment correlates with greater fear of cancer recurrence [28]. The patients in the present study all received chemotherapy, most received radiotherapy, and all but one (who elected not to undergo surgery, which would not be considered standard practice) had surgery. Fear of cancer recurrence tends to be higher in breast cancer compared with other cancer types [29].

Anxiety scores were similar to historical scores associated with being in a stressful situation, decreasing to approximate population norms by 12 months [21]. A trend toward lower baseline anxiety in the neoadjuvant group might be explained by patients' expectations of receiving neoadjuvant therapy if that was perceived to be the clinicians' preferred option, however this was based on a small sample size. Alternatively, the more anxious patients might have elected to have surgery first. Lower anxiety might also have been associated with seeing their tumour shrink, and with getting chemotherapy 'over and done with'. While patients who chose surgery first tended to be more anxious, causality cannot be claimed in this single-arm study. Because this study recruited patients who were offered neoadjuvant systemic therapy, those who chose surgery first may have been more anxious because they perceived that they were making that decision against the medical recommendation. Anxiety scores declined to a greater extent in the surgery-first group, perhaps because higher baseline scores gave a greater opportunity to regress to the mean.

These patients were treated in experienced cancer centres with a high volume of neoadjuvant patients. The clinical context is likely to influence the outcomes observed, for example the strength of clinical recommendation for neoadjuvant systemic therapy varies based on individual patient and tumour characteristics. Clinical equipoise was not expected for each patient about whether neoadjuvant systemic therapy or surgery was the best initial approach, and the clinicians' framing of options may have influenced patients' confidence in their chosen treatment option.

This study is limited by its small sample size and non-randomised design, which renders it underpowered for definitive conclusions about these outcomes. These data were secondary outcomes from a single arm study to evaluate the safety, feasibility and acceptability of a decision-aid. Despite email and phone reminders, not all patients completed all assessments. The study population was well educated, which may reduce generalisability of the results to a less educated group. As the parent study was a decision aid study, the population may have self-selected based on information seeking behavior. Patients were relatively young, consistent with the mean age of 53.6 years in the United States National Cancer Database neoadjuvant therapy analysis [1]. Studying other populations would be valuable, such as those of older age or with smaller tumours. Access to the decision aid may have impacted upon outcomes in a positive or negative direction. Strengths include the evidence-based, systematic development process and the use of validated patient reported outcome measures.

In conclusion, most patients who were given the option of neoadjuvant systemic therapy by their surgeon proceeded with neoadjuvant systemic therapy. An association was observed between patients who were more anxious, and receipt of surgery first. In patients who had neoadjuvant systemic therapy, pCR does not appear to correlate with anxiety, distress, fear of progression, fear of recurrence, satisfaction or regret.

Conflicts of interest

NZ: Travel: Eisai, Amgen; Honoraria: Eisai, Astra-Zeneca, Roche. All other authors do not have any competing interests to declare.

ICMJE authorship statement

Conception or design: NZ, PB, CD, FMB.
Acquisition of data: NZ, AS, KS, FMB.
Analysis or interpretation of data: NZ, PB, MJ, CO, CD, FMB.
Drafting and/or critical revision of the manuscript: All authors.
Final approval of the manuscript prior to submission: All authors.
Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: All authors.

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Appendix A

Neoadjuvant decision aid.

Appendix B

	Pre-DA Assessment	Post-Treatment Decision Assessment	Post-Chemo therapy (NAST) Assessment, or post-surgery (non-NAST)	Post-Treatment Assessment
Decision conflict scale	X	X		
STAI-6 Anxiety	X	X	X	X
DMPQ Preferred	X	X		
Actual		X		
Distress thermometer	X	X	X	X
Information and involvement preferences	X	X		
EQ-5D-5L (optional)	X	X	X	X
Knowledge of DA Information		X		
Decision Aid Feedback		X		
Satisfaction with decision scale		X		
Fear of progression (FOP 12)		X	X	
Decision regret scale			X	X
Fear of Cancer Recurrence Inventory			X	X

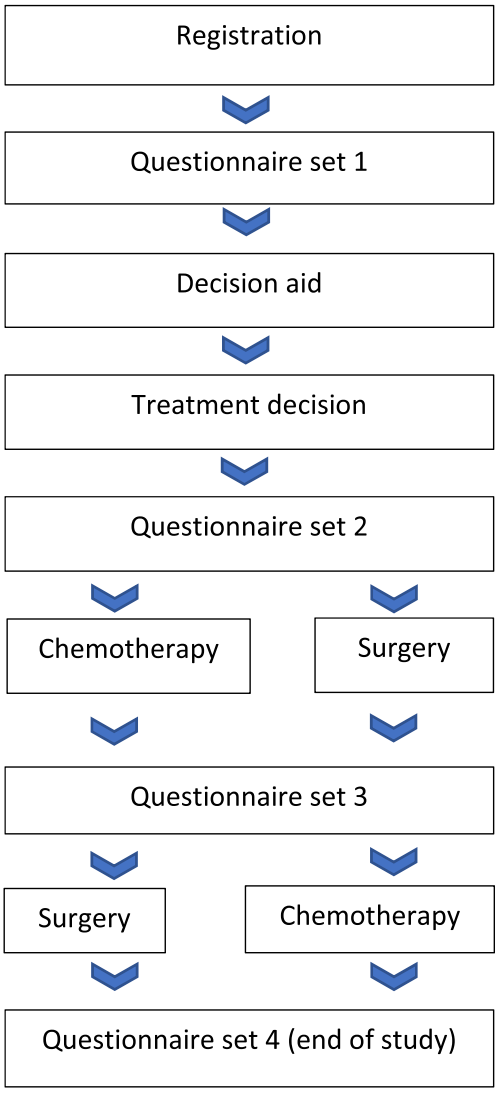
Schedule of assessments. DA: decision aid; DMPQ: Decision Making Preference Questionnaire; NAST: neoadjuvant systemic therapy.

Appendix C

Patient reported outcome measure descriptions

Scale	Items	Notes
Spielberger State-Trait Anxiety Inventory [21]	6	Higher score indicates greater anxiety.
Distress Thermometer [16]	1 (0–10 visual analogue)	Higher score indicates greater distress.
Satisfaction with Decision [22]	6	Perceived quality of a decision prior to its consequences. Higher score indicates greater satisfaction.
Fear of Cancer Progression [17]	12	Concern about progression of cancer. Higher score indicates greater fear.
Decision Regret [23]	5	Regret after consequences of a decision. Higher score indicates greater regret.
Fear of Cancer Recurrence [24]	42	Worry about cancer recurrence after definitive treatment. Higher score indicates greater fear; >12 on the severity subscale indicates significant impact.

Appendix D



Study Schema.

Appendix E. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2019.04.003.

References

[1] Mougalian SS, Soulos PR, Killelea BK, Lannin DR, Abu-Khalaf MM, DiGiovanna MP, et al. Use of neoadjuvant chemotherapy for patients with stage I to III breast cancer in the United States. Cancer 2015;121(15):2544–52.
[2] Curigliano G, Burstein HJ, Winer EP, Gnant M, Dubsky P, Loibl S, et al. De-escalating and escalating treatments for early-stage breast cancer: the St. Gallen international expert consensus conference on the primary therapy of early breast cancer 2017. Ann Oncol 2017;28(8):1700–12.
[3] National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology. Breast Cancer; 2017. accessed, . [Accessed 21 September 2017].
[4] Onkologie Arbeitsgemeinschaft. Diagnosis and treatment of patients with primary and metastatic breast cancer. 2017. accessed, . [Accessed 1 January 2015].
[5] Llewellyn-Thomas HA, Crump RT. Decision support for patients: values clarification and preference elicitation. Med Care Res Rev 2013;70(1 suppl):50S–79S.
[6] Caudle AS, Gonzalez-Angulo AM, Hunt KK, Pusztai L, Kuerer HM, Mittendorf EA, et al. Impact of progression during neoadjuvant chemotherapy on surgical management of breast cancer. Ann Surg Oncol 2011;18(4):932–8.
[7] Shin HC, Han W, Moon HG, Im SA, Moon WK, Park IA, et al. Breast-conserving surgery after tumor downstaging by neoadjuvant chemotherapy is oncologically safe for stage III breast cancer patients. Ann Surg Oncol 2013;20(8):2582–9.
[8] Read RL, Flitcroft K, Snook KL, Boyle FM, Spillane AJ. Utility of neoadjuvant chemotherapy in the treatment of operable breast cancer. ANZ J Surg 2015;85(5):315–20.
[9] Killelea BK, Yang VQ, Mougalian S, Horowitz NR, Pusztai L, Chagpar AB, et al. Neoadjuvant chemotherapy for breast cancer increases the rate of breast conservation: results from the National Cancer Database. J Am Coll Surg 2015;220(6):1063–9.
[10] Wengler CA, Valente SA, Al-Hilli Z, Woody NM, Muntean JH, Abraham J, et al. Determinants of short and long term outcomes in patients undergoing immediate breast reconstruction following neoadjuvant chemotherapy. J Surg Oncol 2017;116(7):797–802.
[11] Monrigal E, Dauplat J, Gimbergues P, Le Bouedec G, Peyronie M, Achard JL, et al. Mastectomy with immediate breast reconstruction after neoadjuvant chemotherapy and radiation therapy. A new option for patients with operable invasive breast cancer. Results of a 20 years single institution study. Eur J Surg Oncol 2011;37(10):864–70.
[12] DeMichele A, Yee D, Berry DA, Albain KS, Benz CC, Boughey J, et al. The neoadjuvant model is still the future for drug development in breast cancer. Clin Cancer Res 2015;21(13):2911–5.
[13] Zdenkowski N, Butow P, Fewster S, Beckmore C, Wells K, Forbes JF, et al. Exploring decision making about neoadjuvant chemotherapy for breast cancer. Breast J 2016;22(1):133–4.
[14] Mauri D, Pavlidis N, Ioannidis JP. Neoadjuvant versus adjuvant systemic treatment in breast cancer: a meta-analysis. J Natl Cancer Inst 2005;97(3):188–94.
[15] Cortazar P, Zhang L, Untch M, Mehta K, Costantino JP, Wolmark N, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet 2014;384(9938):164–72.
[16] Hegel MT, Collins ED, Kearing S, Gillock KL, Moore CP, Ahles TA. Sensitivity and specificity of the Distress Thermometer for depression in newly diagnosed breast cancer patients. Psycho Oncol 2008;17(6):556–60.
[17] Mehnert A, Berg P, Henrich G, Herschbach P. Fear of cancer progression and cancer-related intrusive cognitions in breast cancer survivors. Psycho Oncol 2009;18(12):1273–80.
[18] Lee-Jones C, Humphris G, Dixon R, Bebbington Hatcher M. Fear of cancer recurrence — a literature review and proposed cognitive formulation to explain exacerbation of recurrence fears. Psycho Oncol 1997;6(2):95–105.
[19] Zdenkowski N, Butow P, Spillane A, Douglas C, Snook K, Jones M, et al. Single-arm longitudinal study to evaluate a decision aid for women offered neoadjuvant systemic therapy for operable breast cancer. J Natl Compr Cancer Netw 2018;16(4):378–85.
[20] Zdenkowski N, Butow P, Hutchings E, Douglas C, Coll JR, Boyle FM. A decision aid for women considering neoadjuvant systemic therapy for operable invasive breast cancer: development and protocol of a phase II evaluation study (ANZ1301 DOMINO). JMIR Res Protoc 2016;5(2):e88.
[21] Marteau TM, Bekker H. The development of a six-item short-form of the state scale of the Spielberger State—trait Anxiety Inventory (STAI). Br J Clin Psychol 1992;31(3):301–6.
[22] Holmes-Rovner M, Kroll J, Schmitt N, Rovner DR, Breer ML, Rothert ML, et al. Patient satisfaction with health care decisions: the satisfaction with decision scale. Med Decis Making 1996;16(1):58–64.
[23] Brehaut JC, O'Connor AM, Wood TJ, Hack TF, Siminoff L, Gordon E, et al. Validation of a decision regret scale. Med Decis Making 2003;23(4):281–92.
[24] Simard S, Savard J. Fear of Cancer Recurrence Inventory: development and initial validation of a multidimensional measure of fear of cancer recurrence. Support Care Canc 2009;17(3):241–51.
[25] Mitchell AJ. Pooled results from 38 analyses of the accuracy of distress thermometer and other ultra-short methods of detecting cancer-related mood disorders. J Clin Oncol 2007;25(29):4670–81.
[26] Luckett T, Butow PN, King MT, Oguchi M, Heading G, Hackl NA, et al. A review and recommendations for optimal outcome measures of anxiety, depression and general distress in studies evaluating psychosocial interventions for English-speaking adults with heterogeneous cancer diagnoses. Support Care Canc 2010;18(10):1241–62.
[27] Simard S, Savard J. Screening and comorbidity of clinical levels of fear of cancer recurrence. J Canc Survivorship : Res Pract 2015;9(3):481–91.
[28] Crist JV, Grunfeld EA. Factors reported to influence fear of recurrence in cancer patients: a systematic review. Psycho Oncol 2013;22(5):978–86.
[29] Tan SY, Turner J, Kerin-Ayres K, Butler S, Deguchi C, Khatri S, et al. Health concerns of cancer survivors after primary anti-cancer treatment. Support Care Canc 2019 [e-pub 2/3/2019].