

Making hard choices easier: a prospective, multicentre study to assess the efficacy of a fertility-related decision aid in young women with early-stage breast cancer

M Peate^{*,1,2}, B Meiser^{1,2}, BC Cheah³, C Saunders⁴, P Butow⁵, B Thewes⁵, R Hart⁶, K-A Phillips^{7,8}, M Hickey^{9,10} and M Friedlander^{1,2,10}

¹Prince of Wales Clinical School, University of NSW, Randwick, New South Wales, Australia; ²Department of Medical Oncology, Prince of Wales Hospital, Randwick, New South Wales, Australia; ³Neuroscience Research Australia, University of NSW, Randwick, New South Wales, Australia; ⁴School of Surgery, University of Western Australia, Crawley, Western Australia, Australia; ⁵Centre of Medical Psychology and Evidence Based Decision-Making, The University of Sydney, Sydney, New South Wales, Australia; ⁶School of Women's and Infants Health, The University of Western Australia, King Edward Memorial Hospital, Subiaco, Western Australia, Australia; ⁷Division of Cancer Medicine, Peter MacCallum Cancer Centre, East Melbourne, Victoria, Australia; ⁸Department of Medicine, St Vincent's Hospital, The University of Melbourne, Melbourne, Victoria, Australia; ⁹Department of Obstetrics and Gynaecology and the Royal Women's Hospital, The University of Melbourne, Parkville, Victoria, Australia

BACKGROUND: Fertility is a priority for many young women with breast cancer. Women need to be informed about interventions to retain fertility before chemotherapy so as to make good quality decisions. This study aimed to prospectively evaluate the efficacy of a fertility-related decision aid (DA).

METHODS: A total of 120 newly diagnosed early-stage breast cancer patients from 19 Australian oncology clinics, aged 18–40 years and desired future fertility, were assessed on decisional conflict, knowledge, decision regret, and satisfaction about fertility-related treatment decisions. These were measured at baseline, 1 and 12 months, and were examined using linear mixed effects models.

RESULTS: Compared with usual care, women who received the DA had reduced decisional conflict ($\beta = -1.51$; 95%CI: -2.54 to 0.48 ; $P = 0.004$) and improved knowledge ($\beta = 0.09$; 95%CI: 0.01 – 0.16 ; $P = 0.02$), after adjusting for education, desire for children and baseline uncertainty. The DA was associated with reduced decisional regret at 1 year ($\beta = -3.73$; 95%CI: -7.12 to -0.35 ; $P = 0.031$), after adjusting for education. Women who received the DA were more satisfied with the information received on the impact of cancer treatment on fertility ($P < 0.001$), fertility options ($P = 0.005$), and rated it more helpful ($P = 0.002$), than those who received standard care.

CONCLUSION: These findings support widespread use of this DA shortly after diagnosis (before chemotherapy) among younger breast cancer patients who have not completed their families.

British Journal of Cancer (2012) **106**, 1053–1061. doi:10.1038/bjc.2012.61 www.bjcancer.com
© 2012 Cancer Research UK

Keywords: breast cancer; fertility; decision-making; young women; decision aid

Approximately 3–7% of women with early-stage breast cancer are under 40 years of age at diagnosis (Australian Institute of Health and Welfare (AIHW) and Australasian Association of Cancer Registries (AACR), 2004; Bouchardy *et al*, 2007; Peate *et al*, 2009; American Cancer Society, 2011–2012). Most women receive adjuvant chemotherapy, which is often associated with diminished ovarian function (Bines *et al*, 1996; Goodwin *et al*, 1999; Minton and Munster, 2002). Fertility information is a priority for young women with breast cancer but provision of such information is often inadequate (Partridge *et al*, 2004; Peate *et al*, 2009).

Following diagnosis of early breast cancer, women need to make rapid decisions regarding fertility interventions before commencing chemotherapy. Decision making about fertility preservation is complex with many ill-defined risk factors, such as fertility-treatment-induced increases in ovarian sex steroid levels, which are contraindicated in women with breast cancer (Oktay *et al*, 2005; Lee *et al*, 2006; Partridge *et al*, 2007). Further, fertility decisions usually need to be made shortly after a new cancer diagnosis, concurrent with cancer treatment decisions. Therefore, it is vital that clear and current information about fertility is provided in a timely manner.

The American Society for Clinical Oncology has recommended that fertility preservation be discussed early in women's treatment trajectory (Lee *et al*, 2006). It has been previously reported that fertility-related issues are often inadequately addressed in clinical management (Biglia *et al*, 2003; Partridge *et al*, 2004; Duffy *et al*, 2005; Thewes *et al*, 2005). Recent data has indicated that rates of

*Correspondence: Dr M Peate; E-mail: michelle.peate@sydney.edu.au

¹⁰These authors share equal co-senior authorship.

Received 20 October 2011; revised 27 January 2012; accepted 6 February 2012

fertility referrals are increasing in the United States (Lee *et al*, 2011), yet another study reported that <25% of US oncologists report referring patients for fertility preservation, only 38% reported knowledge of the American Society of Clinical Oncology guidelines, and <25% reported distributing fertility-related materials (Quinn *et al*, 2009). Furthermore, a study among Irish cancer specialists has reported that awareness of ART success rates was poor and a barrier to referrals (Collins *et al*, 2011). In Australia, there are no clear guidelines for referral despite the existence of public and private fertility clinics, and fertility treatment is not available without cost. The complexity of discussing fertility-related issues, including current relationship status, plans for children, and the range of fertility-preserving options available further hinder timely and adequate exchange of information (Duffy *et al*, 2005; Quinn *et al*, 2007, 2008). It is not surprising that young early breast cancer patients have unmet fertility-related information needs (Knobf, 2001; Thewes *et al*, 2003, 2004, 2005; Partridge *et al*, 2004).

Decision aids (DAs) are educational materials designed to assist with treatment decision-making, addressing individual values and preferences (Janis and Mann, 1977). They increase knowledge and reduce decisional conflict without increasing anxiety (O'Connor *et al*, 2009). The efficacy of a DA has not previously been evaluated in the context of fertility and early breast cancer, in particular the impact the DA may have on distress (anxiety and depression) and on other decision-making outcomes (such as, decisional conflict and regret, and informed choice). Anxiety and depression were assessed to measure whether receiving detailed, potentially distressing information about fertility would lead to adverse emotional outcomes.

The DA is a C5-sized booklet that contains information about breast cancer and female fertility, and a discussion of the different fertility options available. It also includes a series of values clarification exercises that list the advantages and disadvantages of each treatment option to be rated by participants as an option that they are either 'leaning' towards or against. Development and pilot testing of the fertility DA has been previously reported (Peate *et al*, 2011b) and the DA can be found on the Cancer Council of Australia's website (Peate *et al*, 2011a).

The current study prospectively evaluated the efficacy of this DA compared with usual care among young women diagnosed with early breast cancer. Specific aims were to:

- (i) Compare changes in decision-related outcomes, including decisional conflict about fertility treatment decisions (primary outcome) and knowledge, over time.
- (ii) Compare decision-related outcomes, including decisional regret about treatment decisions, and informed choice at 1 and 12 months post diagnosis.
- (iii) Examine potential changes in anxiety and depression as a result of the use of the DA compared to usual care.

METHODS

Participants

Participants were consecutive early breast cancer patients (stage I, II, and III, excluding ductal carcinoma *in situ* and metastatic disease) referred to 1 of 19 oncology clinics around Australia between 2006 and 2009. Approval was obtained from all institutional review boards, and all women provided written informed consent. Inclusion criteria were: 18–40 years of age; diagnosed with invasive early breast cancer (as defined above); proficient in English; pre-menopausal at time of diagnosis; not yet having commenced adjuvant therapy; and interest in having a child. Eligible women were invited to participate by breast care nurses (BCNs) at each site within a week of their diagnosis and before any medical oncologist or fertility specialist appointments.

Study design

The first 81 women recruited across all sites received a guide on early breast cancer developed for consumers, currently distributed to women at many clinics as part of usual care (National Breast Cancer Centre, 2003). This number was approached to account for attrition. The next 52 participants received the DA in addition to the consumer guide. A non-randomised trial design was undertaken to prevent participants sharing brochures.

Procedure

Women were identified and invited to participate, soon after diagnosis, by the breast care nurses at each site, who were trained in the recruitment process. After consenting to participate, participants were given a package containing an invitation letter, baseline questionnaire, reply-paid envelope, and a sealed envelope with instructions not to open it until the questionnaire was completed. Upon completing the questionnaire, participants were asked to read the consumer guide (usual care control) or DA, which included completing the values clarification exercises (intervention), supplied in the sealed envelope before their oncologist appointment, if possible. Follow-up questionnaires were posted 1 and 12 months later. Participants were asked to complete paper-based self-administered questionnaires.

Measures

Demographic, reproductive and disease-related data Age at diagnosis, relationship status, parity, desire for more children, and highest level of education attained were recorded at baseline.

Intended decision about fertility treatment Two items, measured at baseline and 1-month follow-up, asked 'At this point in time, are you leaning towards...' (a) 'waiting to see if fertility returns after treatment' and (b) 'in vitro fertilisation'. Participants could opt to include intended decisions for 'other' techniques (not included in analyses due to limited data).

The following outcome measures were administered at all three time points:

Decisional conflict scale (DCS): The 10-item low literacy version of this scale assessed decisional conflict regarding 'different fertility treatments' (O'Connor, 1995). Scores > 37.5 on the overall scale (range 0–100) indicate high decisional conflict, which is characterised by decision delay and/or uncertainty about decision implementation (O'Connor, 1995).

Knowledge of fertility-related information: The items were selected based on previous research exploring the unmet fertility-related needs of this population (Thewes *et al*, 2005). Ten true-false items measured knowledge of (i) assisted reproductive technologies; (ii) the impact of different therapy regimens on fertility; and (iii) the impact of pregnancy after breast cancer on prognosis. A total knowledge score was calculated (range, 0–10). The scale had satisfactory internal consistency with Cronbach's alpha of 0.63.

Hospital anxiety and depression scale: The 14-item Hospital Anxiety and Depression Scale was used to measure emotional disturbance (Zigmond and Snaith, 1983; Ibbotson *et al*, 1994). It has two subscales measuring anxiety and depression, with each subscale ranging 0–21 (Zigmond and Snaith, 1983; Ibbotson *et al*, 1994).

The following outcome measures were administered at the two follow-up assessments only:

Multidimensional measure of informed choice (MMIC): This assessed whether women made treatment decisions with adequate knowledge (based on the Knowledge of Fertility-Related Information Scale) in accordance with their values, assessed with an adaptation of the five-item scale to assess attitudes towards fertility treatment in regard to feeling 'beneficial'/'harmful',

'important'/'unimportant', 'a good thing'/'a bad thing', 'pleasant'/'unpleasant', and 'worthwhile'/'not worthwhile' (Michie *et al*, 2002). Response options ranged from 'very positive' (scored as 1) to 'very negative' (scored as 7). The MMIC was scored in accordance with the instructions provided by the developers – a total score was obtained by summing an individual's items (scores ranged from 5 to 35) (Michie *et al*, 2002). Two groups were classified as having made an informed choice: those who scored above the sample median on the knowledge of fertility-related information scale, had a positive attitude towards fertility treatments, and decided to undergo fertility treatments by the time of follow-up, and those who had a good knowledge score, a negative attitude towards fertility treatments, and did not undergo fertility treatments (Michie *et al*, 2002). All other women were categorised as having made an uninformed choice. The MMIC has good internal consistency (Cronbach's alpha of 0.66 and 0.81 for the knowledge and attitudes subscales, respectively, for this study) and excellent predictive and discriminant validity (Michie *et al*, 2002).

Decision regret scale (DRS) – fertility interventions This five-item scale was used as a quantifier of health care decision regret (Brehaut *et al*, 2003) about fertility treatment decisions, with higher total scores indicating more regret (range 0–100).

Use of materials: One item determined whether, and the extent to which, materials were read.

Satisfaction with, and helpfulness of, educational materials: Three items elicited satisfaction with, and perceived helpfulness of, the educational materials.

Actual decision: Participants were asked about whether they received adjuvant treatments and fertility-preserving interventions.

Partner's involvement: Four items assessed the use of the educational materials by, and impact on any partners. These included whether the educational materials were shared with the partner; the extent to which partners had read the materials; whether the materials stimulated discussion between partners; how useful the partners considered the booklet; and whether the partner contributed to the decision-making process about fertility-related issues.

Clinician discussion and referral: Four items assessed frequency of contact, thoroughness of fertility-related discussions, and extent to which discussion and fertility referrals were prompted by study materials.

The following outcome measure was administered at the last follow-up assessment only:

DRS – cancer treatments (Brehaut *et al*, 2003): This was used to assess regret about decisions made about cancer treatments. Higher total scores indicated greater regret (range 0–100).

Statistical analyses

An intention to treat analysis was undertaken. Linear mixed effects models (with random baseline measurements and slopes) were used to examine the effect of the DA on outcome variables assessed across three occasions (DCS, knowledge, anxiety, and depression), adjusting for potential confounders and for curvilinear change (time²). Confounders (education, relationship status, parity, and desire for more children) were incorporated into a statistical model if they were theoretically relevant and resulted in a >20% change in the treatment effect estimates. Confounders were also included if they were associated with substantial reduction in Akaike's Information Criterion and Schwarz's Bayesian Information Criterion. Depression scores were log-transformed, given their skewed distributions. For variables collected at 1 and 12 months only, raw scores were used for analyses. Linear regression was used to assess differences between groups for continuous variables (DRS), and logistic regression was used to assess group differences for binary outcome variables (MMIC).

The target sample size was 64 participants in each group. This would provide sufficient power (80%) to detect a difference of 0.5 between groups (i.e., a medium effect size; Cohen, 1988) in the primary outcome variable (DCS). This has been considered clinically important in a range of cancer-related scenarios (Frost, 2002).

RESULTS

Response rates

A total of 145 eligible women were invited to participate (Figure 1), of these 70 women in the control group and 44 in the intervention group returned the baseline questionnaire. The final questionnaire was returned by 96 women (60 usual care and 36 intervention participants). The target sample size was not achieved as a result of slower than anticipated recruitment, and the trial was stopped before the target sample size in the DA group was achieved. Participants who completed at least one questionnaire ($N=120$, 72 and 48 participants allocated to usual care and the DA, respectively) were included in the analysis. This represented 83.3% of eligible subjects and 90.2% of those agreeing to participate. Due to slower than anticipated recruitment rates, the study was closed before reaching the target sample size; however, the sample size was large enough to detect differences.

Participant characteristics

There were no significant differences in demographics between DA and usual care groups (Table 1). Most participants did not have children (69%, $N=79$). Of this group, 82% ($N=65$) reported that they planned to have children or that they were unsure whether they wished to have any children (18%, $N=14$). Of the 35 participants who already had children, 46% ($N=16$) definitely planned to have more children and the rest (54%, $N=19$) were unsure. Overall, most participants reported that they planned to have (more) children (71%, $N=81$).

Unadjusted mean scores and percentages are presented for all outcomes separately for the DA and usual care groups in Table 2.

The majority of participants (96%) who received the DA reported reading the materials, compared with 83% of participants allocated to usual care. The extent to which this was read is shown in Table 3.

Decisional conflict scale

Those who received the DA had a greater reduction in decisional conflict than those who received usual care over 12 months (Figure 2). Using a mixed effects model with random baseline measurements, the effect of the DA was significant after adjustment for education, desire for more children, and uncertainty at baseline (treatment group by time interaction: $\beta = -1.51$; 95%CI: -2.54 to 0.48 ; $P=0.004$), in a curvilinear manner ($\beta = 2.42$; 95%CI: 1.88 – 2.96 ; $P<0.001$). Adjusted results identified a negligible mean difference of 1.46 in DCS between groups at 1 month (s.e. = 3.66; 95%CI: 5.77 – 8.69 ; $P=1.00$). Decisional conflict scale scores were 15.30 units lower in the DA group at 12 months (s.e. = 5.52; 95%CI: -26.17 to 4.43 ; $P=0.02$).

Knowledge of fertility-related information

Figure 3 shows the change in correctly answered questions from baseline to 12 months in both study arms, and shows that across most items there was an increase in correct responses from baseline to final follow-up.

Use of the DA significantly improved fertility-related knowledge (Figure 4). Using a random baseline and slopes mixed effects model with adjustment for education, desire for more children and

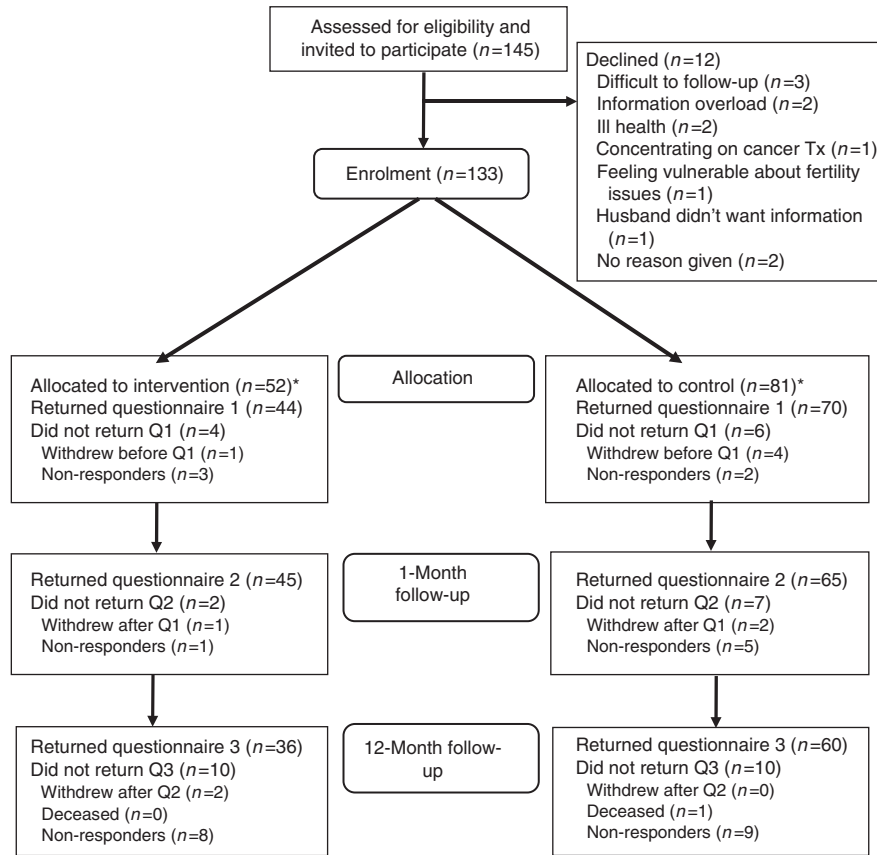


Figure 1 Participant flowchart. Q1, questionnaire one; Q2, questionnaire two; Tx, treatment; *four participants who were allocated to the intervention and five participants to the control did not respond to any questionnaires and have not been included in the statistical analyses.

Table 1 Demographic characteristics (N = 120)

Variable	Control		Intervention		Total	
	N	Mean (s.d.)	N	Mean (s.d.)	N	Mean (s.d.)
Age in years	72	33.8 (4.0)	48	32.3 (4.7)	120	33.23 (4.3)
Relationship length in years ^{a,b}	23	4.6 (3.9)	18	4.4 (3.3)	41	4.49 (3.6)
		%		%		%
Relationship status ^a						
Committed relationship	53	74.6	36	76.6	89	75.4
Not in a committed relationship	18	25.4	11	23.4	29	24.6
Parity						
No	46	63.8	36	75.0	79	69.3
Yes	26	36.1	12	25.0	35	30.7
Highest level of education						
High school only	13	18.3	5	10.6	18	15.3
Certificate/diploma	18	25.4	8	17.0	26	22.0
Undergraduate degree	27	38.0	20	42.6	47	39.8
Postgraduate degree	13	18.3	14	29.8	27	22.9
Medical or allied health training						
No	59	83.1	39	83.0	98	83.1
Yes	12	16.9	8	17.0	20	16.9
Stage						
Stage I	7	12.1	3	7.0	10	9.9
Stage II	18	31.0	15	34.9	33	32.7
Stage III	33	56.9	25	58.1	58	57.4

^aSeveral participants did not provide information for this item. ^bMedian = 3.0, inter-quartile range: 2.0–5.5 years.

uncertainty about the decision at baseline, a significant improvement in knowledge was noted (treatment group by time interaction: $\beta = 0.09$; 95%CI: 0.01–0.16; $P = 0.02$) in participants who received the DA, compared with the usual care group. Adjusted results identified a negligible mean difference of 0.01 in knowledge scores between groups at 1 month (s.e. = 0.032; 95%CI: –0.65 to 0.64; $P = 0.99$). Knowledge scores were 0.94 units lower in the DA group at 12-month follow-up (s.e. = 0.44; 95%CI: 0.08–1.81; $P = 0.03$).

Multidimensional measure for informed choice

There were no significant differences in the proportions of participants who made an informed vs an uninformed choice about fertility based on group allocation at 1 month (OR = 2.12; 95%CI: 0.32–2.26; $P = 0.75$), and at 12-month follow-up (OR = 4.41; 95%CI: 0.59–3.75; $P = 0.10$), after adjusting for relationship status, education, parity, and desire for more children.

Hospital anxiety and depression scale

There was no significant difference in anxiety between treatment groups after adjusting for education, parity, and desire for more children (treatment group by time interaction: $\beta = 0.02$; s.e., 0.06; 95%CI: –0.10 to 0.14; $P = 0.73$) or depression (treatment group by time interaction: $\beta = 0.09$; 95%CI: –0.03 to 0.21; $P = 0.14$, adjustment unnecessary).

Decisional regret scale

At 1 month, DRS scores regarding fertility-related decisions were not significantly different between groups ($\beta = 4.75$; 95%CI: –2.7

Table 2 Dependent variable mean scores and proportions on the DCS, HADS, DRS, and multidimensional measure of informed choice scale

	Control		Intervention		Unadjusted analysis ^a	
	N	Mean (s.d.)	N	Mean (s.d.)	β	P-value
Knowledge score						
T0	69	5.2 (2.13)	44	5.0 (2.61)	0.08	0.03
T1	65	6.3 (2.28)	44	7.0 (2.16)		
T2	59	5.9 (1.92)	33	6.9 (2.01)		
DCS						
T0	70	47.2 (30.98)	44	51.6 (32.76)	1.43	0.007
T1	64	23.1 (30.56)	45	16.6 (26.48)		
T2	58	29.3 (30.96)	34	14.7 (23.74)		
HADS: depression scale						
T0	70	5.1 (3.71)	44	4.6 (4.72)	0.02	0.15
T1	65	5.0 (3.38)	45	5.3 (4.68)		
T2	59	3.2 (3.18)	33	4.0 (4.94)		
HADS: anxiety scale						
T0	70	8.9 (4.32)	44	8.5 (4.40)	0.04	0.56
T1	65	7.8 (3.71)	45	7.3 (4.92)		
T2	59	7.0 (4.52)	33	7.1 (4.27)		
DRS: fertility						
T1	61	19.7 (18.86)	43	24.4 (19.00)	4.75	0.21
T2	57	49.1 (8.24)	32	45.8 (8.97)	3.34	0.047
DRS: cancer						
T2	58	47.8 (7.79)	34	46.5 (7.23)	-0.08	0.43
Proportional data for dichotomous variables (%)					OR	
Multidimensional measure of informed choice						
T1	37	60.7% Informed	22	64.3% Informed	3.22	0.071 ^b
T2	29	51.8% Informed	20	64.5% Informed	5.44	0.25 ^b
					χ^2	
Actual fertility treatment^a						
<i>In vitro fertilisation</i>						
T2	53	24.5%	33	30.3%	0.63	0.43
<i>'Wait and see'</i>						
T2	57	61.4%	33	66.6%	0.78	0.38
Actual cancer treatment						
<i>Radiotherapy</i>						
T2	59	78.0%	35	77.1%	0.33	0.87
<i>Chemotherapy</i>						
T2	59	84.7%	35	82.9%	0.15	0.70
<i>Endocrine therapy</i>						
T2	59	66.1%	34	70.6%	0.58	0.45

Abbreviations: DCS = decisional conflict scale; DRS = decisional regret scale; HADS = hospital anxiety and depression scale; s.d. = standard deviation; T0 = baseline; T1 = 1 month; T2 = 12 months. ^aUsing a mixed effects model with random baseline measurements, this value represents treatment group by time interaction, unadjusted for confounders. ^bUsing a linear or logistic regression models, unadjusted for confounders.

Table 3 Extent to which information materials given as part of this study were read

	Control (%)	DA (%)
Not at all	17	5
Yes, briefly	8	14
Yes, just the parts I felt were relevant	22	25
Yes, quite thoroughly	34	27
Yes, from cover to cover	19	29

Abbreviation: DA = decision aid.

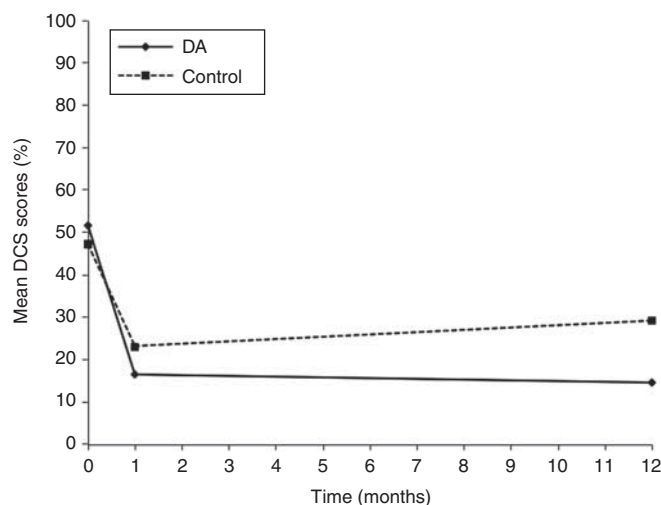


Figure 2 Mean DCS scores over the three data collection points.

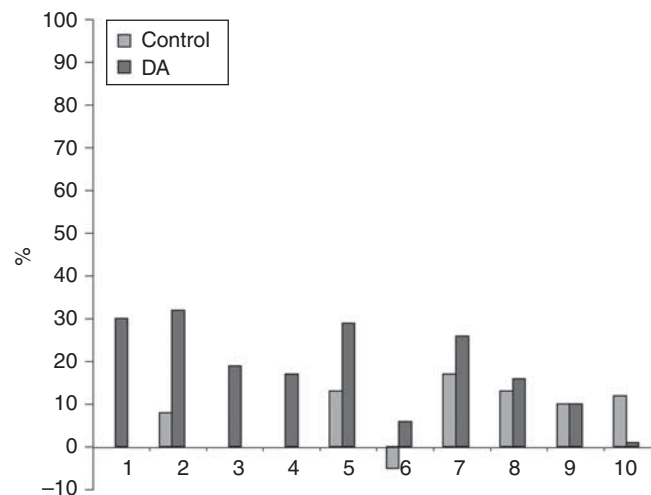


Figure 3 Change in the percentage of correct answers in the knowledge scale from baseline to 12 months, shown in order of the greatest difference between groups. Key: (1) IVF (*in vitro* fertilisation) has highest success rate of fertility options (True); (2) some fertility procedures are still experimental and not widely available (true); (3) pregnancy after breast cancer treatment is safe for mother and baby (true); (4) impact of chemotherapy on fertility is not dependent on age (false); (5) IVF will not delay cancer treatment (false); (6) pregnancy after breast cancer treatment will increase chance of recurrence (false); (7) hormonal therapy will not cause infertility except for time spent on treatment (true); (8) many breast cancers depend on hormones to grow – thus some fertility drugs are not recommended (true); (9) fertility treatment can be costly (true); (10) chemotherapy impacts on fertility by depleting eggs in the ovaries (true).

to 12.22; $P=0.21$), or after adjusting for education ($\beta=5.40$; 95%CI: -2.19 to 12.99; $P=0.16$). After adjusting for education, participants who received the DA had significantly lower decisional regret at 12 months ($\beta=-3.73$; 95%CI: -7.12 to -0.35; $P=0.031$).

Satisfaction with information

Sixty-seven percent of participants receiving usual care and 70.5% of participants allocated the DA were satisfied with the information provided on the impact of breast cancer treatment on fertility. Similarly, 54.4% and 77.3% were satisfied with the information given on the impact of treatment and fertility options, respectively. Compared with participants who received usual care, participants

Clinical Studies

allocated the DA were significantly more satisfied with the materials they received on the impact of breast cancer treatment on fertility ($\chi^2=15.49$; $P<0.001$) and on the different fertility options available ($\chi^2=10.66$; $P=0.005$). Participants were also significantly more likely to score the DA more highly on a helpfulness scale in terms of making fertility-related decisions ($\chi^2=0.61$; $P=0.002$).

Partner's involvement

The impact of the DA on partner's involvement in reading and discussing the educational materials and contributing to fertility-related decision making is shown in Table 4. Partner's involvement did not significantly differ between groups. Partners were considered to be 'very' or 'extremely' involved in the decision-making process (77.6%) with most participants rating the DA as 'somewhat' or 'very' useful to partners (74.2%).

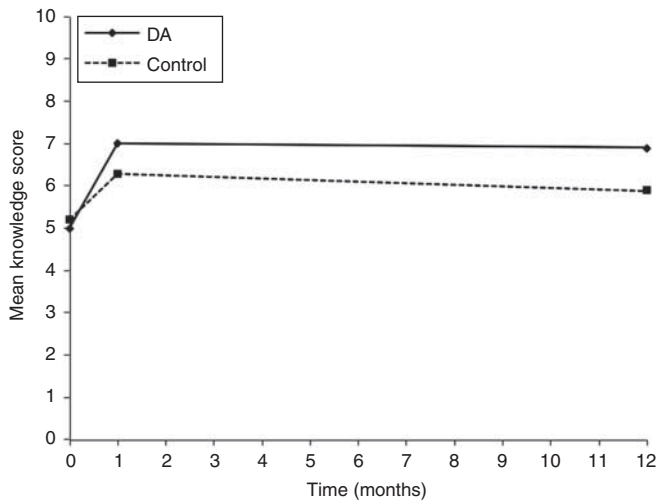


Figure 4 Mean knowledge scale scores over the three data collection points.

Table 4 Partner involvement in sharing of materials, discussion, and decision making

Item	Responses	Control		Intervention		χ^2	P-value
		N	%	N	%		
Materials read by partners	Yes	33	67.3	17	51.2	2.08	0.15
	No	16	32.7	16	48.5		
Thoroughness in which partner read the information ^a	Briefly	9	29.4	6	33.3	0.91	0.34
	Just relevant parts	8	23.5	6	33.3		
	Quite thoroughly	13	38.2	6	33.3		
	Cover to cover	3	8.8	0	0.0		
Discussions stimulated by the materials	Yes	17	36.2	12	38.7	0.052	0.82
	No	30	63.8	19	61.3		
Perceived usefulness of the material for the partner ^b	Not at all	2	5.3	3	10.7	0.48	0.49
	Not very	9	23.7	3	10.7		
	Somewhat	16	42.1	14	50.0		
	Very useful	11	28.9	8	28.6		
Partner contribution to fertility-related decision making ^c	Yes	43	87.8	30	93.8	—	—
	No	6	12.2	2	6.2		
Perceived level of partner involvement in fertility-related treatment decisions ^d	Not at all	0	0.0	0	0.0	0.042	0.84
	A little	4	9.3	4	13.3		
	Quite	4	9.3	5	16.7		
	Very	13	30.2	7	23.3		
	Extremely	22	51.2	14	46.7		

^aDue to small cell sizes, for χ^2 analyses responses were grouped into 'briefly and just relevant parts' and 'quite thoroughly and cover to cover'. ^bDue to small cell sizes, for χ^2 analyses responses were grouped into 'not at all and not very' and 'somewhat and very useful'. ^cDue to small cell sizes statistical tests could not be conducted. ^dDue to small cell sizes, for χ^2 analyses responses were grouped into 'not at all, a little and quite' and 'very and extremely'.

Fertility-related discussions with oncologists

Perceived thoroughness of discussions with oncologists and the extent to which the discussions were prompted by the educational materials are reported in Table 5. Most women had discussed fertility to some extent with their medical oncologists (92.5% of controls and 97.7% of women who received the DA, $\chi^2=1.50$; $P=0.47$).

Referrals to fertility specialists

Sixty-two percent of participants who received the DA and 55.6% allocated to usual care were referred to a fertility specialist ($\chi^2=0.48$; $P=0.49$). One participant in each group sought a fertility specialist, although these patients were not referred by their oncologists. Of those who received a referral to a fertility specialist, 91.4% of controls consulted or were planning to see a fertility specialist, compared with 97.7% participants who received the DA ($\chi^2=0.71$; $P=0.40$).

Intended decisions and fertility treatment uptake

Leaning towards the 'wait and see' option did not change significantly from baseline to 1 month between groups ($P=0.31$). Additionally, no differences in change scores were observed for intention to undergo IVF between groups ($P=0.42$). For the total patient sample, 79.7% of controls reported having made a decision about fertility treatment at 1 month compared with 91.1% of participants who were allocated the DA ($\chi^2=2.62$; $P=0.11$). At 12 months, 71.2% of participants allocated to usual care and 76.5% of participants allocated to the DA had made a decision about fertility preserving options ($\chi^2=0.84$; $P=0.36$).

DISCUSSION

This study is the first to report the impact of a fertility DA on decisional conflict, decision regret, and fertility choices in young breast cancer patients. The DA reduced decisional conflict about fertility-related treatment options and reduced decisional regret about fertility treatments compared with usual care over

Table 5 Reported details about discussions with medical oncologists about fertility related issues

Item	Responses	Control		Intervention		χ^2	P-value
		N	%	N	%		
Thoroughness of fertility-related discussions with oncologist ^a	Not at all	4	6.2	1	2.3	1.50	0.47
	Briefly	18	27.7	19	43.2		
	Moderately	22	33.8	12	27.3		
	Quite a bit	13	20.0	9	20.5		
	Extensively	8	12.3	3	6.8		
Who was the discussion initiated by? ^b	Patient	25	38.5	16	37.2	<0.001	1.00
	Clinician	36	55.4	23	53.5		
	Not discussed	4	6.2	4	9.3		
Extent to which discussion was prompted by educational materials ^a	Not at all	28	43.1	12	26.7	1.28	0.53
	A little bit	12	18.5	11	24.4		
	Moderately	16	24.6	15	33.3		
	Quite a bit	7	10.8	4	8.9		
	Very much	2	3.1	3	6.7		

^aDue to small cell sizes, for χ^2 analyses responses were grouped into 'not at all and briefly', 'moderately', and 'quite a bit and extensively'. ^b χ^2 analyses excluded those in which fertility was not discussed.

12 months. The DA also improved fertility-related knowledge. The reduction in decisional conflict and improvements in knowledge may be considered clinically important (Ringash *et al*, 2007). It is likely that the DA achieved these outcomes by providing more comprehensive information about fertility options and by facilitating timely and personalised decision making (O'Connor *et al*, 1998). Lower decisional regret indicates reduced distress or remorse after a decision (Brehaut *et al*, 2003). Ultimately, these outcomes indicate that access to the DA increased satisfaction with choices made and enabled women to feel more informed about their options and clearer regarding their personal values (O'Connor *et al*, 2009).

Access to the DA did not impact on uptake of fertility-preserving interventions. Uptake of fertility interventions is not only dependent on information, but also on personal circumstances (such as having a male partner), availability and cost of interventions, previous fertility as well as religious and personal beliefs (Lee *et al*, 2006; Dutney, 2007; Jukkala, 2009; Ata and Seli, 2010; Eisenberg *et al*, 2010; Hershberger and Pierce, 2010). In addition, uptake of interventions is likely to be influenced by clinician recommendations (Young, 1996a,b; Cyrus-David and Strom, 2001; Bober *et al*, 2004; Taylor and Taguchi, 2005; McGregor *et al*, 2007). Little is known about how and why women and their partners make decisions about fertility interventions following a cancer diagnosis, or how clinicians decide who to refer to a fertility specialist. In particular, the relative influence of patient wishes and clinical recommendation is poorly understood. It is likely that patients are highly influenced by clinical recommendations regarding fertility interventions, particularly from their medical oncologist (Silvestri *et al*, 2003; Lam *et al*, 2005). Thus, it is important to provide cancer clinicians with accurate information about fertility options so that patients are advised and referred appropriately. Improved understanding of how oncologists make decisions about fertility specialist referral is needed.

Reported discussions with oncologists and referrals to specialists did not differ, with or without the DA. Our findings suggested that most medical oncologists discussed fertility with breast cancer patients of reproductive age. These statistics are higher than the rate of ~70% reported in previous studies (Partridge *et al*, 2004; Thewes *et al*, 2005), and may reflect selection bias in clinicians who participated in our study. A national survey of American oncologists reported that those with favourable attitudes towards fertility preservation were nearly twice as likely to discuss the issue, compared with those who had unfavourable attitudes, with male oncologists approximately half as likely to refer patients as their female colleagues (Quinn *et al*, 2009).

Compared with participants who received usual care, those with access to the DA reported higher rates of satisfaction with the fertility information received (>70%), which is above the 51% previously reported as having their concerns addressed adequately (Partridge *et al*, 2004). Limited discussion may be the result of women or their clinicians feeling uncomfortable about the topic, particularly as the primary concern for most is the cancer diagnosis and treatment. Younger breast cancer patients may expect that their health care providers, as the experts, will discuss all that is relevant without prompting, in which case the opinion of the oncologist regarding fertility may be crucial. Fertility treatments are rapidly evolving. The level of current knowledge of oncologists about potential fertility preserving options remains unknown. All participants in this study were considering pregnancy in the future, but only half were referred to a fertility specialist, who could offer fertility-preservation techniques. This is greater than the reported rate of >25% referrals to fertility specialists reported in a 2009 study of a random sample of oncologists in the United States (Quinn *et al*, 2009). Again, this may reflect either a selection bias of participating oncologists, or a genuine increase in fertility awareness among oncologists. The same study reported that <25% of clinicians distributed fertility preservation materials (Quinn *et al*, 2009). In comparison, all participants in our study were given fertility information, either the control booklet or DA, which may have been the impetus for a higher referral rate. Though clinic staff was trained in recruitment procedure to minimise variation across sites, we acknowledge that there is the potential that different clinicians' attitudes may influence decision making. The numbers recruited at each site for this study were limited; thus, we lacked the capacity to compare individual effects. More information is needed about how breast cancer specialists approach fertility issues and how the latest information about fertility can be effectively provided to oncologists, and subsequently delivered to patients (including involving patients in research).

In addition to the limitations discussed above, the non-randomised design of the study may lead to bias. However, studies in similar populations using this study design have not shown bias as a result of time (Goodwin *et al*, 1999). Additionally, the target sample size was not achieved most likely a result of slower than anticipated recruitment as a consequence of strict eligibility criteria (age, desire for future fertility, and not yet started adjuvant treatment). It was possible that some women who were eligible for study participation were not recruited in the short time between diagnosis and commencing treatment. There is also the potential that low numbers were a result of the fact that women were

approached at a highly stressful time. An increased sample may have improved the power to detect a difference where trends were seen (MMIC). Nevertheless, the sample size obtained appeared large enough to detect a statistically significant result in the primary outcome variable, DCS. This may have been because the actual treatment effect was greater than originally anticipated.

Our results raise some interesting questions that may need further exploration. Most of our participants reported that their partners were involved in the fertility treatment decision-making process, yet very little is known about how partners perceive their role despite fertility-related decisions being a decision for both parties. Understanding the mechanisms of fertility-related decision making should incorporate this factor.

Within individual items of our knowledge scale there were improvements of varying extent. Further exploration of the specific informational domains would assist in improving the information delivered and improve the DA. Other considerations include that the DA will require regular updating as reproductive technologies advance, bringing ongoing costs. Online resources may facilitate updating and reduce costs. Also, the DA is currently available only in English and is not appropriate for culturally and linguistically diverse populations. Further research into these issues would further advance support this body of work.

CONCLUSION

We have shown that this fertility DA reduced decisional conflict and regret about fertility-related treatment options in young breast cancer patients. Lower decisional conflict and regret indicate increased satisfaction with choices with respect to personal values. The DA also improved fertility-related knowledge, which is an important aspect of informed decision making. The DA also improved satisfaction with information received and was considered helpful by patients. These findings suggest that this DA should be widely distributed to young breast cancer patients considering future pregnancies before chemotherapy.

REFERENCES

- American Cancer Society (2011–2012) *Breast Cancer Facts and Figures 2011–2012*. American Cancer Society: Atlanta, GA
- Ata B, Seli E (2010) Economics of assisted reproductive technologies. *Curr Opin Obstet Gynecol* 22(3): 183–188
- Australian Institute of Health and Welfare (AIHW), Australasian Association of Cancer Registries (AACR) (2004) *Cancer in Australia 2001*. Australian Institute of Health and Welfare: Canberra
- Biglia N, Cozzarella M, Cacciari F, Ponzzone R, Roagna R, Maggiorotto F, Sismondi P (2003) Menopause after breast cancer: a survey on breast cancer survivors. *Maturitas* 45(1): 29–38
- Bines J, Oleske DM, Cobleigh MA (1996) Ovarian function in premenopausal women treated with adjuvant chemotherapy for breast cancer. *J Clin Oncol* 14(5): 1718–1729
- Bober SL, Hoke LA, Duda RB, Regan MM, Tung NM (2004) Decision-making about tamoxifen in women at high risk for breast cancer: clinical and psychological factors. *J Clin Oncol* 22(24): 4951–4957
- Bouchardy C, Fioretta G, Verkooyen HM, Vlastos G, Schaefer P, Delaloye J-F, Neyroud-Caspar I, Balmer Majno S, Wespi Y, Forni M, Chappuis P, Sappino A-P, Rapiti E (2007) Recent increase of breast cancer incidence among women under the age of forty. *Br J Cancer* 96: 1743–1746
- Brehaut JC, O'Connor AM, Wood TJ, Hack TF, Siminoff L, Gordon E, Feldman-Stewart D (2003) Validation of a decision regret scale. *Med Decis Making* 23(4): 281–292
- Cohen J (1988) *Statistical Power Analysis for the Behavioural Sciences*, 2nd edn, Academic Press: New York
- Collins IM, Fay L, Kennedy MJ (2011) Strategies for fertility preservation after chemotherapy: awareness among Irish cancer specialists. *Ir Med J* 104(1): 6–9
- Cyrus-David M, Strom S (2001) Chemoprevention of breast cancer with selective estrogen receptor modulators: views from broadly diverse focus groups of women with elevated risk for breast cancer. *Psychooncology* 10(6): 521–533
- Duffy CM, Allen SM, Clark MA (2005) Discussions regarding reproductive health for young women with breast cancer undergoing chemotherapy. *J Clin Oncol* 23(4): 766–773
- Dutney A (2007) Religion, infertility and assisted reproductive technology. *Best Pract Res Clin Obstet Gynaecol* 21(1): 169–180
- Eisenberg ML, Smith JF, Millstein SG, Nachtigall RD, Adler NE, Pasch LA, Katz PP, Infertility Outcomes Program Project G (2010) Predictors of not pursuing infertility treatment after an infertility diagnosis: examination of a prospective US cohort. *Fertil Steril* 94(6): 2369–2371
- Frost M (2002) Symposium on clinical significance of quality of life measures in cancer patients. *Mayo Proc* 77: 488–494
- Goodwin PJ, Ennis M, Pritchard KI, Trudeau M, Hood N (1999) Risk of menopause during the first year after breast cancer diagnosis. *J Clin Oncol* 17(8): 2365–2370
- Hershberger PE, Pierce PF (2010) Conceptualizing couples' decision making in PGD: emerging cognitive, emotional, and moral dimensions. *Patient Educ Couns* 81(1): 53–62
- Ibbotson T, Maguire P, Selby P, Priestman T, Wallace L (1994) Screening for anxiety and depression in cancer patients: the effects of disease and treatment. *Eur J Cancer* 30A(1): 37–40
- Janis IL, Mann L (1977) Emergency decision-making – theoretical-analysis of responses to disaster warnings. *J Hum Stress* 3(2): 35
- Jukkala A (2009) Breast cancer survivors and fertility preservation: ethical and religious considerations. *Semin Oncol Nurs* 25(4): 278–283

ACKNOWLEDGEMENTS

We would like to thank the all the women who participated in this study and the oncology clinic staff at each study site for their assistance with participant recruitment. Furthermore, we would like to acknowledge the Australian Fertility Decision Aid Collaborative Group for their contribution to the study. The additional members of the Australian Fertility Decision Aid Collaborative Group are (in alphabetical order of institute): Calvary Health Care ACT (B Holley, J McGuiggan, M McNair); Concord Hospital (K Kerin-Ayres, H Wiese); Goulburn Valley Health (K Patford); Liverpool Hospital (AM Griffin); Mount Medical Centre (C Griffiths); Peter MacCallum Cancer Institute (T Griffiths, J McGirr, S Pratt); Prince of Wales Hospital (G Neil, S Rovelli, C Wakefield); Royal Adelaide Hospital (J Iasiello); Royal Brisbane and Women's Hospital (W Pritchard); Royal North Shore Hospital (M Arvin, T Cosgrove); Royal Perth Hospital (L Kydd, S Reid); Royal Prince Alfred Hospital (A Carrigy, K Robinson, R Wicks); Sir Charles Gairdner (S Boyle, L O'Brien, K O'Driscoll, L Wilson); St George Hospital (E Carrusca, R Hannan, A Szwajcer); St Vincent's Hospital (K Aylward, S Stewart, S Turley); St Vincent's Hospital (D Maguire); Shoalhaven Hospital (M Brien); Strathfield Breast Centre (R Martin); The Mater Hospital (F Boyle, C John, K Watts); University of Western Australia (J Fallon-Ferguson); Westmead Hospital (L Black, J Cooper, M Sweeny, R Winter); Wollongong Hospital (J Hollis, L Horning, R Mickleus, V Millwood, G Swift); and Young Breast Cancer Action Group (R Martinello, K Parkinson). The study was funded by The Cancer Council, New South Wales (Project Grant RG 06-13). Bettina Meiser is supported by a Career Development Award from the National Health and Medical Research Council of Australia (NHMRC; ID 350989 and 1003921) and a Cancer institute NSW Career Development Fellowship. Kelly-Anne Phillips is the Cancer Council Victoria Colebatch Clinical Research Fellow. Martha Hickey holds a NHMRC Clinical Career Development Award from the NHMRC (404094). This trial was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12605000402640).

- Knobf MT (2001) The menopausal symptom experience in young mid-life women with breast cancer. *Cancer Nurs* 24(3): 201–210; quiz 210–211
- Lam W, Fielding R, Ho E, Chan M, Or A (2005) Surgeon's recommendation, perceived operative efficacy and age dictate treatment choice by Chinese women facing breast cancer surgery. *Psychooncology* 14: 585–593
- Lee S, Heytens E, Moy F, Ozkavukcu S, Oktay K (2011) Determinants of access to fertility preservation in women with breast cancer. *Fertil Steril* 95(6): 1932–1936
- Lee SJ, Schover LR, Partridge AH, Patrizio P, Wallace WH, Hagerty K, Beck LN, Brennan LV, Oktay K, American Society of Clinical Oncology (2006) American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. *J Clin Oncol* 24(18): 2917–2931
- McGregor SE, Hilsden RJ, Li FX, Bryant HE, Murray A (2007) Low uptake of colorectal cancer screening 3 years after release of national recommendations for screening. *Am J Gastroenterol* 102(8): 1727–1735
- Michie S, Dormandy E, Marteau TM (2002) The multi-dimensional measure of informed choice: a validation study. *Patient Edu Couns* 48(1): 87–91
- Minton SE, Munster PN (2002) Chemotherapy-induced amenorrhea and fertility in women undergoing adjuvant treatment for breast cancer. *Cancer Control* 9(6): 466–472
- National Breast Cancer Centre (2003) *A Guide for Women with Early Breast Cancer*. Camperdown. <http://canceraustralia.nbcc.org.au/view-document-details/ebc-guide-for-women-with-early-breast-cancer>
- O'Connor AM (1995) Validation of a decisional conflict scale. *Med Decis Making* 15: 25–30
- O'Connor AM, Bennett CL, Stacey D, Barry M, Col NF, Eden KB, Entwistle VA, Fiset V, Holmes-Rovner M, Khangura S, Llewellyn-Thomas H, Rovner D (2009) Decision aids for people facing health treatment or screening decisions (update of Cochrane Database Syst Rev. 2003; (2): CD001431; PMID: 11686990). *Cochrane Database Syst Rev*, (3): CD001431
- O'Connor AM, Tugwell P, Wells GA, Elmslie T, Jolly E, Hollingworth G, McPherson R, Drake E, Hopman W, Mackenzie T (1998) Randomized trial of a portable, self-administered decision aid for postmenopausal women considering long-term preventive hormone therapy. *Med Decis Making* 18(3): 295–303
- Oktay K, Buyuk E, Libertella N, Akar M, Rosenwaks Z (2005) Fertility preservation in breast cancer patients: a prospective controlled comparison of ovarian stimulation with tamoxifen and letrozole for embryo cryopreservation. *J Clin Oncol* 23(19): 4347–4353
- Partridge A, Gelber S, Gelber RD, Castiglione-Gertsch M, Goldhirsch A, Winer E (2007) Age of menopause among women who remain premenopausal following treatment for early breast cancer: long-term results from International Breast Cancer Study Group Trials V and VI. *Eur J Cancer* 43(11): 1646–1653
- Partridge AH, Gelber S, Peppercorn J, Sampson E, Knudsen K, Laufer M, Rosenberg R, Przyppyszny M, Rein A, Winer EP (2004) Web-based survey of fertility issues in young women with breast cancer. *J Clin Oncol* 22(20): 4174–4183
- Peate M, Butow P, Fallon Ferguson J, Friedlander M, Hart R, Hickey M, Irle J, Ives A, Martinello R, Meiser B, Parkinson K, Rovelli S, Saunders C, Thewes B, Wakefield CE, Zorbas H (2011a) Fertility-related choices: a decision aid for younger women with early breast cancer. http://www.bcna.org.au/sites/default/files/fertility_decision_aid_20120117.pdf
- Peate M, Meiser B, Friedlander M, Saunders C, Martinello R, Wakefield CE, Hickey M (2011b) Development and pilot testing of a fertility decision aid for young women diagnosed with early breast cancer. *Breast J* 17(1): 112–114
- Peate M, Meiser B, Hickey M, Friedlander M (2009) The fertility-related concerns, needs and preferences of younger women with breast cancer: a systematic review. *Breast Cancer Res Treat* 116(2): 215–223
- Quinn GP, Vadaparampil ST, Bell-Ellison BA, Gwede CK, Albrecht TL (2008) Patient-physician communication barriers regarding fertility preservation among newly diagnosed cancer patients. *Soc Sci Med* 66(3): 784–789
- Quinn GP, Vadaparampil ST, Gwede CK, Miree C, King LM, Clayton HB, Wilson C, Munster P (2007) Discussion of fertility preservation with newly diagnosed patients: oncologists' views. *J Cancer Survivorship* 1(2): 146–155
- Quinn GP, Vadaparampil ST, Jacobson P, Lee J, Lancaster J, Bepler G, Keefe DL, Albrecht TL (2009) National survey of physicians practice patterns: fertility preservation and cancer patients. *J Clin Oncol* 27: 18S (suppl; abstr CRA9508)
- Ringash J, O'Sullivan B, Bezjak A, Redelmeier DA (2007) Interpreting clinically significant changes in patient-reported outcomes. *Cancer* 110(1): 196–202
- Silvestri G, Knittig S, Zoller J, Nietert P (2003) Importance of faith on medical decisions regarding cancer care. *J Clin Oncol* 21(7): 1379–1382
- Taylor R, Taguchi K (2005) Tamoxifen for breast cancer chemoprevention: low uptake by high-risk women after evaluation of a breast lump. *Ann Fam Med* 3(3): 242–247
- Thewes B, Butow P, Girgis A, Pendlebury S (2004) The psychological needs of breast cancer survivors; a qualitative study of the shared and unique needs of younger vs older survivors. *Psycho-Oncology* 13: 177–189
- Thewes B, Meiser B, Rickard J, Friedlander M (2003) The fertility- and menopause-related information needs of younger women with a diagnosis of breast cancer: a qualitative study. *Psycho-Oncology* 12(5): 500–511
- Thewes B, Meiser B, Taylor A, Phillips KA, Pendlebury S, Capp A, Dalley D, Goldstein D, Baber R, Friedlander ML (2005) Fertility- and menopause-related information needs of younger women with a diagnosis of early breast cancer. *J Clin Oncol* 23(22): 5155–5165
- Young KS (1996a) Internet addiction: the emergence of a new clinical disorder. *CyberPsychology Behavior* 1(3): 237–244
- Young KS (1996b) Psychology of computer use: XL. Addictive use of the internet a case that breaks the stereotype. *Psychol Rep* 79: 899–902
- Zigmond AS, Snaith RP (1983) The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica* 67: 361–370

This work is published under the standard license to publish agreement. After 12 months the work will become freely available and the license terms will switch to a Creative Commons Attribution-NonCommercial-Share Alike 3.0 Unported License.