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ORIGINAL ARTICLE

Examining the preliminary efficacy of an intervention for fear of cancer recurrence in female cancer survivors: a randomized controlled clinical trial pilot study

Christina Tomei[1] · Sophie Lebel[1] · Christine Maheu[2] · Monique Lefebvre[3] · Cheryl Harris[3]

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Abstract

Purpose Among cancer survivors, fear of cancer recurrence (FCR) is the most frequently reported unmet need. Despite this, research on psychosocial interventions that target FCR is limited. To address this gap, an individual cognitive-existential psychotherapy intervention for FCR was pilot tested via small-scale RCT.

Methods Participants were recruited via study posters, healthcare professionals' referrals, and an electronic hospital database. Twenty-five female cancer survivors were randomized to experimental or wait-list control groups. Sessions included cognitive restructuring techniques, behavioral experiments, discussion of existential concerns, and relaxation exercises. Nineteen women completed the 6-week intervention and completed questionnaire packages at various time points. All participants completed self-administered questionnaires at pre-intervention (T1), post-intervention (T2), and at 3-month follow-up (T3). Participants in the control group also completed the same questionnaires, including at baseline (T0).

Results Statistically significant results of between-within ANOVAs included time by condition interactions in the primary outcome measure of FCR and, for the experimental group participants, time by condition interactions in the secondary outcome measures of cancer-specific distress and uncertainty in illness. Statistically significant results of repeated measures ANOVAs included reductions in FCR, cancer-specific distress, uncertainty in illness, reassurance seeking, cognitive avoidance, and intolerance of uncertainty, as well as improvements in positive reinterpretation and growth, emotional coping, and quality of life (improved mental health), when compared to the control group. Most changes were maintained at 3-month follow-up.

Conclusions This intervention responds to a need for evidence-based individual modality interventions targeting quality of life in cancer survivors. Our results demonstrate preliminary promising results in addressing FCR in female cancer survivors. Future research could seek to replicate results with a larger sample. Further research is needed to test this intervention with patients of mixed cancer sites.

Keywords Psychosocial oncology · Fear of cancer recurrence · Psychosocial interventions · Coping · Pilot study · Randomized controlled clinical trial

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✉ Christina Tomei
ctome085@uottawa.ca

[1] School of Psychology, University of Ottawa, 136 Jean-Jacques-Lussier Private, Vanier Hall, Ottawa, ON K1N 6N5, Canada

[2] Ingram School of Nursing, McGill University, Montreal, QC, Canada

[3] Psychology Department, The Ottawa Hospital, Ottawa, ON, Canada

Background

Cancer survivors have a variety of unmet needs, with fear of cancer recurrence (FCR) being the most frequent one [1–3]. FCR is defined as "fear, worry or concern relating to the possibility that cancer will come back or progress" [4]. Nearly 50% of cancer survivors experience moderate-to-high FCR [5], and some patients with FCR exhibit maladaptive coping behaviors, such as excessive bodily checking, reassurance seeking, and avoidance of feared outcomes [6–12]. FCR levels tend to remain stable over time, with high FCR at

baseline a strong predictor of higher long-term FCR [5, 12]. FCR is associated with psychological distress, anxiety, depression, lower quality of life, and stress-response symptoms [5, 13, 14]. Cancer patients endorsing high levels of FCR more often refuse transfer from a cancer centre to primary care and more often seek readmission to specialized care [15].

Despite evidence that cancer patients with higher FCR have poorer psychological adjustment and utilize healthcare resources excessively [7], few published psychosocial interventions address FCR. To address the needs of patients with moderate-to-high FCR, Lebel et al. [16] designed a cognitive-existential group intervention for treatment of FCR. The intervention is theoretically guided by Leventhal's common sense model [8], Mishel's uncertainty in illness [17], and cognitive models of worry [18, 19]. Lebel et al. [16] adapted components of Kissane et al.'s [20] group intervention, designed to address existential issues related to living with cancer. The intervention consists of six consecutive, 1.5-h weekly group therapy sessions. Participants complete several in-session tasks, including cognitive restructuring exercises, behavioral experiments, confrontation of specific fears, and relaxation techniques. Lebel et al. [16] piloted the group intervention with breast and ovarian cancer participants ($n = 54$), and results demonstrated significant patient improvement, with moderate time effects [16]. This intervention is currently being tested via multisite RCT [21].

While intervention research on FCR is emerging [12], it appears that few *individual* therapeutic FCR interventions exist. Humphris and Ozakinci [6] developed the Adjustment to the Fear, Threat, or Expectation of Recurrence (AFTER) intervention for head and neck cancer patients. Several FCR research studies have been or are being tested in RCTs. Lewis et al.'s [22] RCT for breast cancer patients involves randomization to 15 sessions of either a group FCR exposure or support group. Compared to patients attending the support group, patients in the FCR exposure group showed significantly greater reduction in FCR-related psychological distress [22]. Butow et al. [23] developed and pilot-tested the Conquer Fear Intervention—an individual therapy addressing FCR in breast and colorectal cancer patients. This intervention involves five sessions of 60–90 min each, where metacognitive and acceptance and commitment (ACT) techniques are applied. Results ($n = 8$) demonstrated clinically and statistically significant reductions in FCR and cancer-specific distress and clinically significant improvements in quality of life [10]. Butow et al. [23] are presently testing the Conquer Fear Intervention in a multicenter RCT, with patients randomized into an intervention group or relaxation-training group. Results are yet to be published. van de Wal et al. [11] compared a blended CBT (bCBT) individual intervention and treatment-as-usual (TAU) group in breast, prostate, and colorectal patients. The intervention combines online and face-to-face CBT delivered over nine sessions of 15 min (e-consultation or telephone session) to 90 min (face-to-face). Published results [11] indicate that bCBT participants reported experiencing significantly less FCR than TAU participants.

In addition to these FCR interventions, there is a need for further individualized FCR interventions that (a) address FCR as a primary outcome, (b) are grounded in evidence-based treatment, (c) are manualized to standardize delivery of therapeutic content, and (d) can be employed with patients with various cancer types. To address these elements, the present study was undertaken.

Prior to the present study, CT and SL adapted Lebel et al.'s [16] existing FCR group intervention to an individual format. This individual intervention was pilot tested ($n = 3$) for feasibility, acceptability, and patient satisfaction [24]. Quantitative results suggested that the intervention was preliminarily helpful in decreasing FCR and cancer-specific distress, and qualitative findings indicated that participants found the intervention both acceptable and satisfactory. By offering this individual FCR intervention, we could respond to cancer survivors' therapeutic needs and preferences, including patients who may prefer individual services and patients with cancers that are too rare to address in a group setting. It is preferable for cancer survivors to receive the treatment modality of their choice, as data suggest a link to better therapeutic outcomes [25, 26]. Indeed, individually based interventions for cancer patients have been found to be more effective than group-based interventions [27], supporting the development of individualized protocols. Given that the individual therapy format is still the most commonly used psychotherapeutic modality, and given that group-based interventions for FCR are not always feasible, our results could help guide usual practice. Thus, based on the successful results from Lebel et al.'s [16] cognitive-existential group intervention, the authors turned to examining the efficacy of the individual intervention via pilot RCT with women of mixed cancer sites. Developing and testing this individual FCR intervention was necessary to continue examining the impact of this highly debilitating concern among cancer survivors.

Method

Procedure

The pilot study consisted of a small-scale RCT. Female patients of mixed cancer sites (breast, gynecological and ocular melanoma) were recruited from The Ottawa Hospital (TOH) in Canada. Approval was obtained from the Institutional Research Ethics Boards of all affiliated investigators. This RCT was registered on http://www.clinicaltrials.gov (Identifier: NCT02382315). The authors utilized the CONSORT checklist and flow diagram. Inclusion criteria were as follows: (a) women diagnosed with cancer (stages I-

III), (b) fluency in English, (c) 18 years of age or older, (d) clinical level of FCR (13 or higher on the severity subscale of the Fear of Cancer Recurrence Inventory (FCRI; [28]), (e) clinical level of distress (24 or higher on the Impact of Events Scale (IES; [29]), and (f) completion of cancer treatment (e.g., chemotherapy, radiation, and/or surgery). Patients using hormonal therapy were eligible to participate. Exclusion criteria were as follows: (a) refusal to provide informed consent, (b) stage IV cancer, (c) previous cancer recurrence, (d) enrollment in group or individual psychotherapy for cancer issues during FCR treatment, and (e) evidence of unmanaged mental health disorder that could interfere with treatment for FCR (i.e., symptoms consistent with any DSM-IV diagnosis outlined in the Mini-International Neuropsychiatric Interview (MINI, [30]), if any impairment from said diagnosis would affect treatment for FCR). One participant endorsed symptoms of substance dependence and was referred to appropriate services.

Sample size

G*Power 3.1.5 was used to calculate the necessary sample size for a repeated measures analysis of variance (ANOVA), between-within factors, with two groups (intervention group and wait-list control group), and three measurement time points (pre-, post-, and 3-month follow-up). Taking into account the effect size found in Lebel et al.'s [16] pilot study (0.73 ($\phi = 0.80, p < .05$), it was determined that 14 participants would be required across the two groups to detect significant pre-vs. post-treatment time effects. While 14 participants were the minimum number necessary to detect significant pre- vs. post-treatment time effects, a total of 25 participants were recruited to account for attrition.

Participants were recruited via posters ($n = 9$), healthcare professionals' referrals ($n = 10$), and TOH's electronic patient database ($n = 10$), which searches for patients who have consented to be contacted for research purposes. Over a period of 6 months, $n = 29$ individuals expressed interest and were assessed for eligibility. Of these, $n = 4$ did not meet eligibility criteria. Thus, $n = 25$ individuals were enrolled. Of the 25 participants randomized, $n = 1$ could not be contacted, and $n = 2$ were deemed unsuitable and directed to other psychological services. During the study, $n = 1$ dropped out due to time restraints, and $n = 2$ experienced recurrences, for a final sample of $n = 19$ participants completing the intervention. For ethical reasons, the FCR intervention was provided to patients who experienced cancer recurrences. All data were kept and analyzed (i.e., that of all participants randomized and initially enrolled; $n = 25$). Please see CONSORT diagram in Fig. 1.

Random assignment of participants to groups was implemented by an individual outside the research team, through an online random number generator. Randomization outcomes were placed in sealed envelopes and revealed only at the time of the pre-therapy meeting with each participant. Due to unexpected study timeline restrictions, wait-list times for the control group varied from 2 to 6 weeks. While it was intended that all control group participants wait 6 weeks before the intervention, timelines had to be reduced when a study member's TOH position was made redundant.

All enrolled participants were randomly assigned (1:1 ratio) to one of two conditions: The intervention arm ($n = 11$), where they received the six-week FCR intervention immediately, or the control arm ($n = 14$), where they received standard medical care and were waitlisted to receive the FCR intervention 2–6 weeks later. Randomization was conducted after participants were found to be eligible for the study.

A pre-therapy meeting was conducted with each participant to document consent, assess psychotherapy readiness, and assess for any axis I psychiatric concerns using the MINI [30]. Participants were assigned a unique study number for identification purposes. The three therapists, including the first author, were clinical psychology doctoral students. All therapists received training through a 1-day workshop. All therapy sessions were video-recorded, and SL randomly reviewed 2/6 sessions per therapist, per participant to assess treatment integrity and fidelity. A systematic fidelity checklist was created to ensure adherence to protocol. Sample items on the fidelity checklist included the following: "therapist refers back to theoretical framework", "therapist initiated problem-solving skills," etc. Of the 48 sessions viewed and rated, all but one had an adherence rate above 80%, suggesting that the intervention was delivered systematically to all participants. Additional supervision was provided to the therapist whose session rated below 80%. SL and ML provided weekly clinical supervision.

The FCR intervention

Cognitive components of the intervention include psychoeducation on the CBT model, cognitive restructuring, behavioral activation strategies, imaginal exposure, and structured homework. The existential elements include discussion of specific fears identified through individual worst-case scenarios (e.g., death anxiety), addressing demoralization, and finding meaning in life post-diagnosis. Changes from the group format included session duration (from 120 to 60–90 min) to reflect the typical individual psychotherapy session and greater opportunity to process existential concerns emerging from worst-case scenarios [24]. Homework was assigned weekly. For further session content, please see [24].

Outcome measures

All participants completed a series of validated questionnaires before the intervention (T1), after the intervention (T2), and at 3-month follow-up (T3). Control group participants

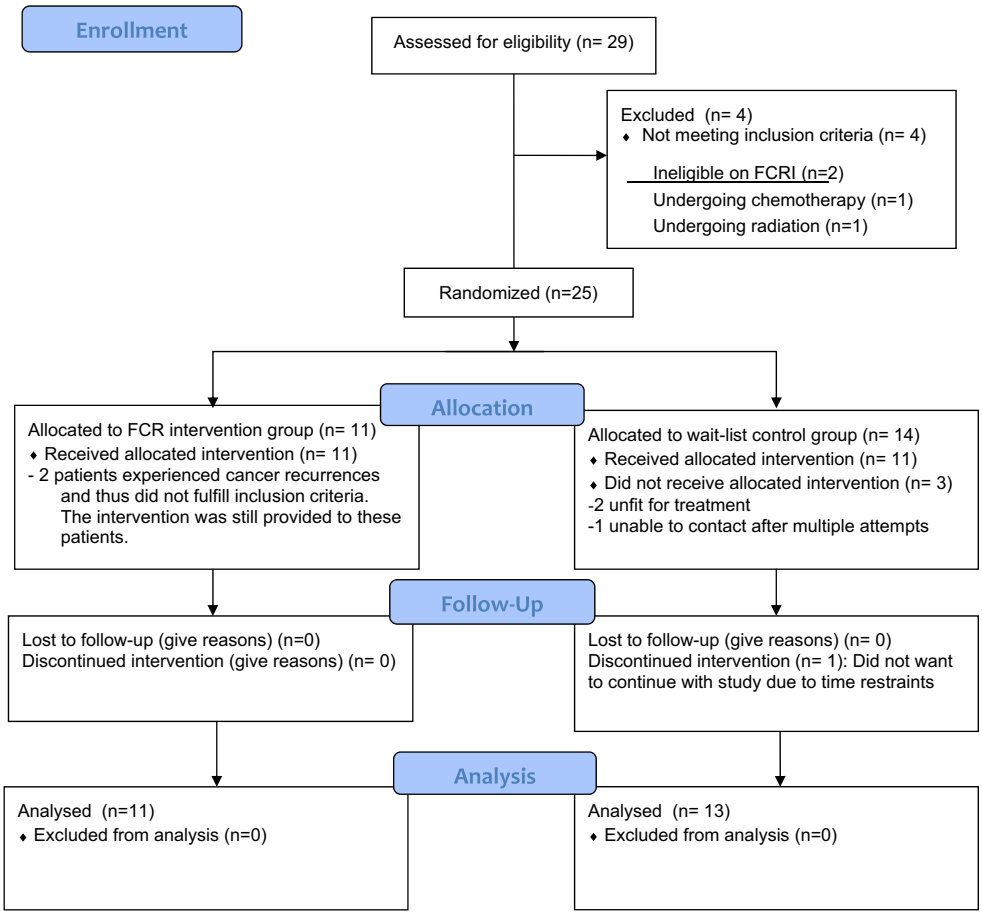

Fig. 1 CONSORT flow diagram

completed a baseline period assessment (T0), before the intervention (T1), after the intervention (T2), and at 3-month follow-up (T3). Please see Fig. 2 for a representation of study time points. All participants completed a demographic information form.

Primary outcome measure The primary outcome was change in FCR from pre-treatment to 3-month follow-up, which was measured using *The Fear of Cancer Recurrence Inventory* (FCRI; [28]), a 42-item instrument used to examine FCR in previous studies [31, 32]. Higher scores indicate higher FCR.

Secondary outcome measures *The Impact of Events Scale* (IES; [29]) was used to measure cancer-specific distress. Higher scores indicate higher distress. Quality of life was

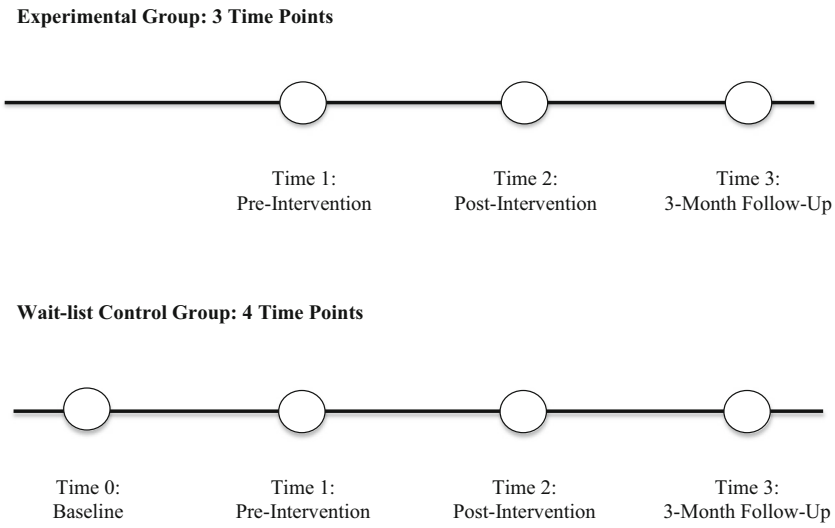

Fig. 2 Summary of time points across experimental group and control group

Table 1 Participant characteristics, $N = 24$

	Pooled		Experimental		Control			
Variable	*M*	SD	*M*	SD	*M*	SD	*t* value	*p* value
Age (years; range 34–74)	55.0	10.76	53.90	13.46	56.00	8.30	.466	.65
Time since diagnosis (years; range 0–6)	1.54	1.53	1.91	1.30	1.23	1.23	1.08	.29
	n	%	*n*	%	*n*	%	X^2	*p* value
Primary ethnic background								
Caucasian	23	95.8	11	100%	12	92.3		
Asian	1	4.2	–	–	1	7.7		
Civil status								
Married/cohabiting	19	79.2	9	81.8	10	76.9		
Divorced/separated	2	8.3	1	9.1	1	7.7		
Widowed	3	12.5	1	9.1	2	15.4	0.22	.89
Education								
High school or less	3	12.5	1	9.1	2	15.4		
College or more	21	87.5	10	90.9	11	84.6	0.22	.64
Occupation								
Employed full-time	10	41.7	6	54.5	4	30.8		
Employed part-time	2	8.4	–	–	2	15.4		
Unemployed	1	4.2	–	–	1	7.7		
Unemployed due to illness	5	20.8	2	18.2	3	23.1		
Retired	6	25.0	3	27.3	3	23.1	3.45	.63
Income (per year)								
0–20,000 CAD	3	12.5	–	–	3	23.1		
21–40,000 CAD	2	8.3	2	18.2	–	–		
41–60,000 CAD	1	4.2	–	–	1	7.7		
61–80,000 CAD	4	16.7	1	9.1	3	23.1		
81–100,000 CAD	5	20.8	4	36.4	1	7.7		
Over 100,000 CAD	9	37.5	4	36.4	5	38.5	8.81	.12
Cancer stage								
Stage I	9	37.5	3	27.3	6	46.2		
Stage II	2	8.3	1	9.1	1	7.7		
Stage III	10	41.7	7	63.6	3	23.1		
Not aware/missing	3	12.5	–	–	2	7.7	3.60	.31
Primary cancer site								
Breast	18	75.0	10	90.9	8	61.5		
Gynecological	5	20.8	1	9.1	4	30.8		
Other (ocular melanoma)	1	4.2	–	–	1	7.7	2.88	.24
Treatment regimen								
Surgery	4	16.7	1	9.1	3	23.1		
Chemotherapy	1	4.2	–	–	1	7.7		
Radiation therapy	1	4.2	1	9.1	–	–		
Chemotherapy and radiation	1	4.2	–	–	1	7.7		
Chemotherapy and surgery	2	8.3	1	9.1	1	7.7		
Radiation and surgery	4	16.7	2	18.2	2	15.4		
Chemotherapy, radiation, and surgery	11	45.8	6	54.5	5	38.5	3.95	.68

$N = 24$ (11 experimental, 13 control)

*$p < .05$

measured using the *SF-8* [33]. Higher scores indicate higher quality of life. Uncertainty was measured using Mishel's [17] *Uncertainty in Illness Scale* (MUIS-C). Higher scores indicate higher uncertainty in illness. Uncertainty was also measured using the *Intolerance of Uncertainty Scale* (IUS; [34]). Higher scores indicate higher intolerance for uncertainty. Perceived benefits of worrying was measured using the *Why do people Worry about Health (WW-H)* questionnaire [35]. Higher scores indicate higher positive beliefs about worry.

Coping was measured using the *Cognitive Avoidance Questionnaire* (CAQ; [36, 37]. Higher scores indicate greater cognitive avoidance. The *Reassurance Questionnaire* (RQ; [38]) was also used to measure coping. Higher scores indicate a higher need for reassurance. Coping was also measured using three subscales of the Brief COPE questionnaire [39]: (1) Positive reinterpretation and growth, (2) use of emotional support, and (3) acceptance. Higher scores indicate higher positive reinterpretation and growth, higher use of emotional support, and higher acceptance.

Statistical analyses

Statistical analyses were performed using SPSS version 23. Participant demographic characteristics are presented in

Table 2 Mixed between-within ANOVA analyses comparing the experimental group's T1 (pre-intervention) and T2 (post-intervention) with the wait-list control groups T0 (baseline period) and T1 (pre-intervention)

Outcome variable	Main effect for group *F* values, *p* values, and r^2 values	Main effect for time *F* values, *p* values, and r^2 values	Interaction effect (RCT group × time) *F* values, *p* values, and r^2 values	Simple main effects *p* values	Estimated marginal means Time
FCRI Fear of cancer recurrence (range 0–168)	F (1, 21.50) = .027, p = .871, r^2 = 0.92	F (1, 15.18) = 8.04, p = .012*, r^2 = 0.12	F (1, 15.18) = 4.57, p = .049*, r^2 = 0.12	p = .003*	Experimental group: T1 (116), T2 (91) Wait-list control group: T0 (104), T1 (100)
IES Cancer-specific distress (range 0–75)	F (1, 20.96) =20.96 p = .332, r^2 = 0.03	F (1, 14.63) = 3.33, p = .089, r^2 = 0.01	F (1, 14.63) = 6.05, p = .027*, r^2 = 0.03	p = .016*	Experimental group: T1 (41), T2 (30) Wait-list control group: T0 (40), T1 (42)
SF-8: Physical Health Quality of life (range 9–69)	F (1, 22.47) =3.30, p = .082, r^2 = 0.156	F (1, 14.61) = .380, p = .547, r^2 = 0.026	F (1, 14.61) =2.13, p = .166, r^2 = 0.174	–	Experimental group: T1 (42), T2 (40) Wait-list control group: T0: (46), T1 (50)
SF-8: Mental Health Quality of life (range 5–72)	F (1, 21.16) = .139, p = .713, r^2 = 0.000	F (1, 17.02) = 1.31, p = .268, r^2 = 0.016	F (1, 17.02) = 2.63, p = .123, r^2 = 0.002	–	Experimental group: T1 (34), T2 (41) Wait-list control group: T0: (37), T1 (36)
MUIS Uncertainty in Illness (range 1–165)	F (1, 22.50) =1.50, p = .234, r^2 = 0.03	F (1, 13.71) = 6.38, p = .025*, r^2 = 0.04	F (1, 13.71) = 14.91, p = .002*, r^2 = 0.08	p = .001*	Experimental group: T1 (93), T2 (80) Wait-list control group: T0: (91), T1 (94)
IUS Intolerance of uncertainty (range 1–135)	F (1, 20.82) = .030, p = .864, r^2 = 0.002	F (1, 11.49) = .910, p = .360, r^2 = 0.001	F (1, 11.49) = .736, p = .409, r^2 = 0.002	–	Experimental group: T1 (86), T2 (79) Wait-list control group: T0: (84), T1 (84)
WW-H Worry (range 1–65)	F (1, 20.76) = .494, p = .490, r^2 = 0.013	F (1, 16.81) =1.21, p = .288, r^2 = 0.002	F (1, 16.81) = .159, p = .695, r^2 = 0.029	–	Experimental group: T1 (27), T2 (26) Wait-list control group: T0:(26), T1 (24)
CAQ Cognitive avoidance (range 1–125)	F (1, 18.70) = .000, p = .997, r^2 = 0.001	F (1, 12.24) = .1.92, p = .191, r^2 = 0.036	F (1, 12.24 = .401, p = .538, r^2 = 0.036	–	Experimental group: T1 (72), T2 (63) Wait-list control group: T0: (69), T1 (66)
RQ Reassurance seeking (range 1–40)	F (1, 18.87) = .029, p = .867, r^2 = 0.000	F (1, 13.74) = .108, p = .747, r^2 = 0.004	F (1, 13.74) = .103, p = .753, r^2 = 0.000	–	Experimental group: T1 (26), T2 (26) Wait-list control group: T0: (25), T1 (26)
BRIEF COPE: Positive Reinterpretation Coping	F (1, 22.08) =2.12, p = .159, r^2 = 0.057	F (1, 19.09) = .016, p = .899, r^2 = 0.000	F (1, 19.09) =2.65, p = .120, r^2 = 0.055	–	Experimental group: T1 (5), T2 (6)

Table 2 (continued)

Outcome variable	Main effect for group	Main effect for time	Interaction effect (RCT group × time)	Simple main effects	Estimated marginal means
	F values, *p* values, and r^2 values	*F* values, *p* values, and r^2 values	*F* values, *p* values, and r^2 values	*p* values	Time
(range 1–8)					Wait-list control group: T0: (5), T1 (4)
BRIEF COPE: Use of Emotional Support Coping (range 1–8)	F (1, 20.82) = .001, p = .981, r^2 = 0.001	F (1, 20.69) = .298, p = .591, r^2 = 0.003	F (1, 20.69) = 1.74, p = .201, r^2 = 0.004	–	Experimental group: T1 (5), T2 (6) Wait-list control group: T0: (6), T1 (5)
BRIEF COPE: Acceptance Coping (range 1–8)	F (1, 19.89) =12.08 p = .002*, r^2 = 0.29	F (1, 17.62) = .206, p = .655, r^2 = 0.000	F (1, 17.62) = .458, p = .507, r^2 = 0.301	—–	Experimental group: T1 (7), T2 (6) Wait-list control group: T0: (5), T1 (5)

Effect sizes: r^2 = 0.02 (small); 0.15 (medium); 0.35 (large) [41]

*Significant differences at $p < 0.05$

Table 1. No statistically significant differences were found between the experimental and control groups at pre-intervention time points. Further, the wait-list control group did not spontaneously improve or worsen between T0 and T1. A mixed between-within-subject ANOVA and repeated measures ANOVAs were carried out within the linear mixed model component of SPSS. The linear mixed model approach allows for an unequal number of evaluations at each time point and, thus, preserves more values [40]. Linear mixed models handle missing values by estimating values using maximum likelihood estimation [40]. The between-within-subject ANOVA was conducted to compare the experimental group's T1 (pre-intervention) and T2 (post-intervention) with the wait-list control groups T0 (baseline period) and T1 (pre-intervention) and to assess for differences over time between both groups. Repeated measures ANOVAs were carried out to assess changes in the means across all participants over time (T1—pre-intervention; T2—post-intervention; and T3—3-month follow-up). Lastly, within linear mixed models, a mixed between-within-subject ANOVA design was also performed to identify any individual therapist differences across outcome measures over time.

Results

Participants

A total of 25 women were enrolled in the study. After accounting for attrition and ineligibility, n = 19 women completed the intervention (13 breast, 5 gynecological, 1 ocular melanoma). Most participants had stage III breast cancer and were diagnosed on average 1.5 years prior to participation. Mean age of participants was 55 years old (range 34–74 years). Most participants were university educated, employed full-time, and married/cohabiting.

Changes in outcome measures

Mixed between-within-subject ANOVAs Of the nine outcome measures in between-within analyses, three variables showed significant interactions: FCRI (fear of cancer recurrence), IES (cancer-specific distress), and MUIS (uncertainty in illness). A linear mixed model analysis was conducted to assess the impact of RCT group on FCRI scores across two time periods (experimental group: pre-intervention and post-intervention; wait-list control: baseline period (± 6 weeks) and pre-intervention). There was a significant interaction effect between RCT group and time, F (1, 15.18) = 4.57, p = .049, r^2 = 0.12. There was no main effect for RCT group, F (1, 21.50) = .027, p = .871, r^2 = 0.92. There was a main effect for time, F (1, 15.18) = 8.04, p = .012, r^2 = 0.12. Mean difference across time for the control group was not significant, p =.638. Tests of simple main effects revealed that the mean difference across time for the experimental group was significant at p = .003.

Table 3 Repeated measures ANOVA analyses examining psychological outcomes at baseline (T1), post-intervention (T2), and 3-month follow-up (T3): means, standard deviations, and effect size

Outcome Variable		Mean (SD)			F and p values	r^2 values
	N	T1	T2	T3	Time	
FCRI Fear of cancer recurrence (range 0–168)	19	108.68 (4.94)a	90.37 (5.24)b	82.03 (5.35)b	$F(2, 27.87) = 15.82$, $p < 0.001$*	0.28
IES Cancer-specific distress (range 0–75)	20	41.36 (3.09)a	28.91 (3.31)b	26.98 (3.31)b	$F(2, 28.68) = 10.58$, $p < 0.001$*	0.21
SF-8: Physical Health Quality of life (range 9–69)	20	47.45 (2.29)a	46.77 (2.61)a	46.89 (2.56)a	$F(2,27.93) = .052$, $p = .950$	0.00
SF-8: Mental Health (range 5–72)	20	35.63 (1.95)a	43.94 (2.32)b	43.78 (2.26)b	$F(2, 28.72) = 8.24$, $p < 0.001$*	0.18
MUIS Uncertainty in Illness (range 1–165)	21	93.048 (2.29)a	84.31 (2.58)b	76.65 (2.58)c	$F(2, 30.24) = 21.46$, $p < 0.001$*	0.34
IUS Intolerance of uncertainty (range 1–135)	20	83.93 (5.88)a	79.38 (6.05)ab	71.84 (5.99)b	$F(2,24.71) = 5.43$, $p = .011$*	0.04
WW-H Worry (range 1–65)	20	25.45 (1.55)a	24.24 (1.67)a	23.30 (1.67)a	$F(2,31.34) = 1.02$, $p = .371$	0.21
CAQ Cognitive avoidance (range 1–125)	20	67.86 (4.22)a	59.30 (4.54)ab	53.63 (4.54)b	$F(2, 29.01) = 6.22$, $p = .006$*	0.10
RQ Reassurance seeking (range 1–40)	20	26.49 (1.04)a	26.48 (1.12)a	23.57 (1.12))a	$F(2, 29.63) = 3.92$, $p = .031$*	0.10
BRIEF COPE: Positive Reinterpretation Coping (range 1–8)	21	4.71 (0.342)a	6.28 (0.376)b	5.79 (0.369)b	$F(2,32.71) = 9.93$, $p < 0.001$*	0.17
BRIEF COPE: Use of Emotional Support (range 1–8)	21	5.29 (0.354)a	6.13 (0.398)a	5.60 (0.388)a	$F(2, 32.92) = 1.82$, $p = .178$	0.04
BRIEF COPE: Acceptance (range 1–8)	21	5.86 (0.304)a	6.47 (0.338)ab	6.90 (0.330)b	$F(2,33.66) = 4.75$, $p = .015$*	0.09

Within a row, values with different lowercase letters indicate significant differences at $p < 0.05$. Effect sizes: $r^2 = 0.02$ (small), 0.15 (medium), 0.35 (large) [41]

*Significant differences at $p < 0.05$

Scores on the IES revealed a significant interaction effect between RCT group and time, $F(1, 14.63) = 6.05$, $p = .027$, $r^2 = 0.03$. There was no main effect for RCT group, $F(1, 20.96) = 20.96$, $p = .332$, $r^2 = 0.03$. The main effect for time was not significant, $F(1, 14.63) = 3.33$, $p = .089$, $r^2 = 0.01$. The mean difference across time for the control group was not significant, $p = .611$. Tests of simple main effects revealed that mean difference across time for the experimental group was significant at $p = .016$.

Scores on the MUIS revealed that there was a significant interaction effect between RCT group and time, $F(1, 13.71) = 14.91$, $p = .002$, $r^2 = 0.08$. There was no main effect for RCT group, $F(1, 22.50) = 1.50$, $p = .234$, $r^2 = 0.03$. There was a main effect for time, $F(1, 13.71) = 6.38$, $p = .025$, $r^2 = 0.04$. Mean difference across time for the control group was not significant, $p = .323$. Tests of simple main effects revealed that the mean difference across time for the experimental group was significant at $p = .001$. Effect sizes of the observed changes on the aforementioned outcome measures are considered to be small effects [41]. No observed changes were found for the remaining outcome variables, with the exception of a significant group effect on the BRIEF COPE acceptance subscale, $F(1, 19.89) = 12.08$, $p = .002$*, $r^2 = 0.29$.

These findings indicate that the experimental group reported improvements in FCR, cancer-specific distress, and uncertainty in illness, while the control group did not report such change. Please see Table 2 for the between-within ANOVA results.

Repeated measures ANOVAs The repeated measures ANOVAs were conducted after the experimental and control groups were combined. The means and standard deviations of the primary and secondary outcome variables at baseline (T1), post-intervention (T2), and 3-month follow-up (T3) are displayed in Table 3. A linear mixed model analysis was conducted and revealed significant time effects and overall improvements in FCR, cancer-specific distress, uncertainty in illness, cognitive avoidance, reassurance seeking, intolerance of uncertainty, quality of life (improved mental health), and coping subscales of positive reinterpretation and growth and acceptance. The variables that improved from T1 to T2 include fear of cancer recurrence, cancer-specific distress, uncertainty in illness, positive reinterpretation and growth, and quality of life (mental health). Further, uncertainty in illness continued to show improvement from T2 to T3, while fear of cancer recurrence, cancer-specific distress, positive reinterpretation and growth, and quality of life (mental health) were maintained from T2 to T3. The variables that did not change from T1 to T2 include acceptance, cognitive avoidance, reassurance seeking, intolerance of uncertainty, worry, quality of life (physical health), and use of emotional support. These variables remain unchanged from T2 to T3. Repeated measures ANOVA results are found in Table 3. Effect sizes of the observed changes ranged from 0.04 to 0.34 (small to medium effects [41]).

Individual therapist differences A linear mixed model analysis was performed to evaluate any differences in outcome measures achieved by different therapists over time. There was one interaction effect between therapist and time on the BRIEF COPE acceptance subscale, F (4, 29.18) = 3.17, p = .028. This interaction suggests that patterns across therapists on the acceptance coping subscale changed as a function of time. No significant interactions between therapist and time emerged on the remaining outcome measures (p = .13–.88). These results suggest that as a whole, all three therapists were applying the same standard of treatment and seeing the same effect.

Discussion

Our goal was to test the preliminary effects of this individualized, manualized FCR intervention. Based on our results, it appears that the intervention may be helpful in decreasing FCR in female cancer survivors. Participants in the experimental group had lower scores on FCR (primary outcome) after treatment compared to the control group. Participants in the experimental group also had lower scores on cancer-specific distress and uncertainty in illness compared to the control group but did not show improvements on the remaining secondary outcome variables (e.g., worry, intolerance of uncertainty). It is possible that the protocol exercises were not specific enough to significantly reduce the aforementioned non-significant variables, given that this is a treatment targeting FCR, or, other outcome measures might have better captured these constructs. Future research could examine whether other validated instruments might be more appropriate for these variables.

For the repeated measures analyses, those variables that changed either maintained or improved at the 3-month follow-up. While these data are preliminary, the results suggest a need for further investigation in larger studies.

It appears that this intervention is feasible. We recruited our target number of 25 participants, with 19 participants successfully completing the intervention. Based on these numbers, it appears that the intervention appealed to the majority of our participants.

Limitations

This is a pilot RCT with a small sample size, and results should be interpreted with caution. Further, the study was not adequately powered to detect anything smaller than a medium effect size on our time-by-group interactions. Future studies could strive to recruit larger sample sizes to increase generalizability. Larger RCTs are also necessary to further establish intervention efficacy using a broader oncology population (e.g., male patients, different cancer types). The original study timeline was reduced due to a study member's position being made redundant at TOH. Thus, the original 6-week waitlist for the control group was reduced to a 2–6 week waitlist, compromising the initial study design. For those participants with a 2–3-week wait, it is unlikely that their FCR level had improved, underestimating the changes occurring through passage of time or natural remission. Therefore, the probability of finding significant differences between post-treatment assessment of the intervention group and post-waiting assessment of the control group was likely artificially inflated. It is worth noting that half of the control group participants waited the intended 6 weeks.

Another limitation is the absence of a control group at 3-month re-assessment. For ethical and practical reasons (i.e., retention, timely study completion), we limited comparisons to T1 and T2 only.

The efficacy of this intervention may be partially explained by participants having high levels of FCR and cancer-specific distress (i.e., it is possible that the time effects were due to a regression to the mean). It is unknown if the intervention would be as effective in reducing FCR in individuals with lower FCR and cancer-specific distress.

Future directions

These results suggest that it is possible to help cancer survivors manage FCR. The steady recruitment pace and low drop-out rate suggest that participants felt interested and motivated to complete the intervention. The recruitment and dropout rates for this study (6 months and 4% drop-out for the individual intervention) are different from those in Lebel et al.'s [16] group-based pilot study where recruitment of 56 participants took 2 years, and the dropout rate was 21%. This raises the question of whether the individual intervention was perceived differently or considered relatively more acceptable than the group version. Clinical experience suggests that female patients often do decline group therapy for fear of being too distressed by others' anguish. It is possible that the differences in recruitment and attrition rates across the group and individual interventions may in part be due to scheduling factors (e.g., 50% of dropouts in Lebel et al.'s [16] study cited scheduling conflicts). A future study could compare the feasibility, acceptability, and efficacy of the group intervention vs. the individual intervention to determine if treatments are comparably effective and for whom.

Medium to large effect sizes were found for our quality of life and coping subscales in our between-within analyses. The SF-8 Physical Health subscale was not statistically significant but yielded medium effect sizes ($r^2 = 0.16$ for group effect; $r^2 = 0.17$ for the interaction effect), and the BRIEF COPE: Acceptance subscale yielded medium to large effect sizes ($r^2 = 0.29$ for the group effect, $r^2 = 0.30$ for the interaction effect), despite the absence of statistically significant differences. In the repeated measures analyses, our worry outcome variable (WW-H) yielded a medium effect size ($r^2 = 0.21$), despite not being statistically significant. These effect sizes are intriguing and may warrant further investigation by other researchers in the near future. Given that these variables yielded medium to large effect sizes in the absence of statistical significance, there certainly could be value and worth in pursuing future research on these specific variables.

While our results show that the FCR intervention was effective in reducing FCR, it was not effective in reducing some of our secondary variables. These findings illustrate the need for future study of specific therapeutic elements most effective for treatment of FCR. Lastly, this is the first FCR-related intervention with two validated treatment modalities. As both group and individual modalities appear to be preliminarily effective, this could encourage further research using both interventions.

Clinical implications

This individual intervention may preliminarily help cancer survivors reduce FCR through gentle confrontation of fear, regaining meaning, and increased use of adaptive coping strategies. It may help participants replace existing maladaptive coping behaviors with authentic connection and helpful, realistic tools. As oncology-related specialists refer only 21% of patients with high FCR for psychosocial services [42], the need for a standard method for screening patients with FCR within onco-medical settings would be beneficial. Emerging interventions for FCR, such as the present individual intervention, have potential benefit to the healthcare system, as well as to patients and loved ones.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Baker F, Denniston M, Smith T, West MM (2005) Adult cancer survivors: how are they faring? Cancer 104:2565–2576. https://doi.org/10.1002/cncr.21488
2. Lebel S, Rosberger Z, Edgar L, Devins GM (2007) Comparison of four common stressors across the breast cancer trajectory. J Psychosom Res 63:225–232. https://doi.org/10.1016/j.jpsychores.2007.02.002
3. Armes J, Crowe M, Colbourne L, Morgan H, Murrells T, Oakley C, Palmer N, Ream E, Young A, Richardson A (2009) Patients' supportive care needs beyond the end of cancer treatment: a prospective, longitudinal survey. J Clin Oncol 27:6172–6179. https://doi.org/10.1200/JCO.2009.22.5151
4. Lebel S, Ozakinci G, Humphris G et al (2016) From normal response to clinical problem: definition and clinical features of fear of cancer recurrence. Support Care Cancer 24:3272–3275. https://doi.org/10.1007/s00520-016-3272-5
5. Simard S, Thewes B, Humphris G, Dixon M, Hayden C, Mireskandari S, Ozakinci G (2013) Fear of cancer recurrence in adult cancer survivors: a systematic review of quantitative studies. J Cancer Surviv 7:300–322. https://doi.org/10.1007/s11764-013-0272-z
6. Humphris G, Ozakinci G (2008) The AFTER intervention: a structured psychological approach to reduce fears of recurrence in

patients with head and neck cancer. Br J Health Psychol 13:223–230. https://doi.org/10.1348/135910708X283751
7. Lebel S, Tomei C, Feldstain A, Beattie S, McCallum M (2013) Does fear of cancer recurrence predict cancer survivors' health care use? Support Care Cancer 21:901–906. https://doi.org/10.1007/s00520-012-1685-3
8. Lee-Jones C, Humphris G, Dixon R, Hatcher MB (1997) Fear of cancer recurrence—a literature review and proposed cognitive formulation to explain exacerbation of recurrence fears. Psycho-Oncology 6:95–105. https://doi.org/10.1002/(SICI)1099-1611(199706)6:2<95::AID-PON250>3.0.CO;2-B
9. Simard S, Savard J, Ivers H (2010) Fear of cancer recurrence: specific profiles and nature of intrusive thoughts. J Cancer Surviv 4:361–371. https://doi.org/10.1007/s11764-010-0136-8
10. Smith AB, Thewes B, Turner J et al (2015) Pilot of a theoretically grounded psychologist-delivered intervention for fear of cancer recurrence (Conquer Fear). Psychooncology 24(8):967–970. https://doi.org/10.3322/caac.21261
11. van de Wal M, Thewes B, Gielissen M, Speckens A, Prins J (2017) Efficacy of blended cognitive behavior therapy for high fear of recurrence in breast, prostate, and colorectal cancer survivors: the SWORD study, a randomized controlled trial. J Clin Oncol 35(19):2173–2183. https://doi.org/10.1200/JCO.2016.70.5301
12. Thewes B, Butow P, Bell ML et al (2012) Fear of cancer recurrence in young women with a history of early-stage breast cancer: a cross-sectional study of prevalence and association with health behaviours. Support Care Cancer 20:2651–2659. https://doi.org/10.1007/s00520-011-1371-x
13. Crist JV, Grunfeld EA (2013) Factors reported to influence fear of recurrence in cancer patients: a systematic review. Psycho-Oncology 22:978–986. https://doi.org/10.1002/pon.3114
14. Vickberg S (2003) The concerns about recurrence scale (CARS): a systematic measure of women's fears about the possibility of breast cancer recurrence. Ann Behav Med 25:16–24. https://doi.org/10.1207/S15324796ABM2501_03
15. Glynne-Jones R, Chait I, Thomas SF (1997) When and how to discharge cancer survivors in long term remission from follow-up: the effectiveness of a contract. R Coll Radiol 9:25–29. https://doi.org/10.1016/S0936-6555(97)80055-6
16. Lebel S, Maheu C, Lefebvre M, Secord S, Courbasson C, Singh M, Jolicoeur L, Benea A, Harris C, Fung MFK, Rosberger Z, Catton P (2014) Addressing fear of cancer recurrence among women with cancer: a feasibility and preliminary outcome study. J Cancer Surviv 8:485–496. https://doi.org/10.1007/s11764-014-0357-3
17. Mishel MH (1981) The measurement of uncertainty in illness. Nurs Res 30(5):258–263
18. Ladouceur R, Dugas MJ, Freeston MH, Léger E, Gagnon F, Thibodeau N (2000) Efficacy of a cognitive-behavioral treatment for generalized anxiety disorder: evaluation in a controlled clinical trial. J Consult Clin Psychol 68:957–964. https://doi.org/10.1037/0022-006X.68.6.957
19. Langlois F, Ladouceur R, Patrick G, Freeston MH (2004) Characteristics of illness intrusions in a non-clinical sample. Behav Res Ther 42:683–696. https://doi.org/10.1016/S0005-7967(03)00191-8
20. Kissane DW, Bloch S, Miach P, Smith GC, Seddon A, Keks N (1997) Cognitive-existential group therapy for patients with primary breast cancer: techniques and themes. Psycho-Oncology 6:25–33. https://doi.org/10.1002/(SICI)1099-1611(199703)6:1<25::AID-PON240>3.0.CO;2-N
21. Maheu C, Lebel S, Courbasson C, Lefebvre M, Singh M, Bernstein LJ, Muraca L, Benea A, Jolicoeur L, Harris C, Ramanakumar AV, Ferguson S, Sidani S (2016) Protocol of a randomized controlled trial of the fear of recurrence therapy (FORT) intervention for women with breast or gynecological cancer. BMC Cancer 16:291. https://doi.org/10.1186/s12885-016-2326-x
22. Lewis F, Merckaert I, Caillier M et al (2013) Reducing breast cancer patients' psychological distress related to fear of recurrence: a randomized study comparing the efficacy of a therapy group and a support group [Abstract]. Psycho-Oncology 22:74
23. Butow P, Bell M, Smith AB et al (2013) Conquer fear: protocol of a randomized controlled trial of a psychological intervention to reduce fear of cancer recurrence. BMC Cancer 13:201. https://doi.org/10.1186/1471-2407-13-201
24. Tomei C, Lebel S, Maheu C, Mutsaers B (2016) Addressing fear of recurrence: improving psychological care in cancer survivors. Support Care Cancer:1–4. https://doi.org/10.1007/s00520-016-3103-8
25. Carlson L, Tamagawa R, Stephen J et al (2014) Tailoring mind-body therapies to individual needs: patients' program preference and psychological traits as moderators of the effects of mindfulness-based cancer recovery and supportive-expressive therapy in distressed breast cancer survivors. J Natl Cancer Inst Monogr 50:308–314. https://doi.org/10.1093/jncimonographs/lgu034
26. Wu S, Brothers BM, Farrar W, Anderson BL (2014) Individual counselling is the preferred treatment for depression in breast cancer survivors. J Psychos Oncol 32:637–646. https://doi.org/10.1080/07347332.2014.955239
27. Osborn R, Demoncada A, Feuerstein M (2006) Psychosocial interventions for depression, anxiety, and quality of life in cancer survivors: meta-analyses. Int J Psychiatry Med 36(1):13–34. https://doi.org/10.2190/EUFN-RV1K-Y3TR-FK0L
28. Simard S, Savard J (2009) Fear of cancer recurrence inventory: development and initial validation of a multidimensional measure of fear of recurrence. Support Care Cancer 17:241–251. https://doi.org/10.1007/s00520-008-0444-y
29. Horowitz M, Wilner N, Alvarez W (1979) Impact of events scale: a measure of subjective stress. Psychosom Med 41:209–218
30. Sheehan D, Lecrubier Y, Sheehan KH, et al. (2006) Mini-international neuropsychiatric interview (MINI). 5.0. 0. c. Swedish version
31. Savard J, Ivers H (2013) The evolution of fear of cancer recurrence during the cancer care trajectory and its relationship with cancer characteristics. J Psychosom Res 74:354–360. https://doi.org/10.1016/j.jpsychores.2012.12.013
32. Thewes B, Butow P, Zachariae R, Christensen S, Simard S, Gotay C (2012) Fear of cancer recurrence: a systematic literature review of self-report measures. Psycho-Oncology 21:571–587. https://doi.org/10.1002/pon.2070
33. Ware JE, Kosinski M, Dewey JE, Gandek B (2001) How to score and interpret single-item health status measures: a manual for users of the of the SF-8 health survey. Lincoln, RI. QualityMetric, Inc., Boston
34. Buhr K, Dugas MJ (2002) The intolerance of uncertainty scale: psychometric properties of the English version. Behav Res Ther 40:931–945. https://doi.org/10.1016/S0005-7967(01)00092-4
35. Freeston MH, Rhéaume J, Letarte H, Dugas MJ, Ladouceur R (1994) Why do people worry? Pers Individ Diff 17:791–802. https://doi.org/10.1016/0191-8869(94)90048-5
36. Pelletier O, Gosselin P, Langlois F et al (2002) Le questionnaire d'évitement cognitif (QEC): développement et validation auprès d'adultes et d'adolescents. [The Cognitive Avoidance Questionnaire (CAQ): development and validation among adult and adolescent samples.] J Ther Comport Cogn 12:24–37
37. Sexton KA, Dugas MJ (2008) The cognitive avoidance questionnaire: validation of the English translation. J Anxiety Disord 22:355–370. https://doi.org/10.1016/j.janxdis.2007.04.005

38. Speckens AEM, Spinhoven P et al (2000) The Reassurance Questionnaire (RQ): psychometric properties of a self-report questionnaire to assess reassurability. Psychol Med 30:841–847
39. Carver CS (1997) You want to measure coping but your protocol's too long: consider the BRIEF COPE. Int J Behav Med 4:92–100. https://doi.org/10.1207/s15327558ijbm0401_6
40. Garson GD (2012) Hierarchical linear modeling: guide and applications. Sage Publications Inc., Thousand Oaks
41. Cohen J (1992) A power primer. Psychol Bull 112:155–159. https://doi.org/10.1037/0033-2909.112.1.155
42. Thewes B, Brebach R, Dzidowska M, Rhodes P, Sharpe L, Butow P (2014) Current approaches to managing fear of cancer recurrence; a descriptive survey of psychosocial and clinical health professionals. Psycho-Oncology 23:390–396. https://doi.org/10.1002/pon.3423