

Internet-delivered Mindfulness-Based Cognitive Therapy for anxiety and depression in cancer survivors: Predictors of treatment response

Eva Rames Nissen^{a,*}, Robert Zachariae^{a,b}, Maja O'Connor^a, Viktor Kaldo^{c,d},
Carsten René Jørgensen^a, Inger Højris^b, Michael Borre^e, Mimi Mehlsen^a

^a Department of Psychology and Behavioral Sciences, Aarhus University, Aarhus, Denmark

^b Department of Oncology, Aarhus University Hospital, Aarhus, Denmark

^c Centre for Psychiatry Research, Department of Clinical Neuroscience, Karolinska Institutet & Stockholm Health Care Services, Region Stockholm, Sweden

^d Department of Psychology, Linnaeus University, Växjö, Sweden

^e Department of Urology, Aarhus University Hospital, Aarhus, Denmark

ARTICLE INFO

Keywords:

Internet-delivered therapy
Mindfulness-Based Cognitive Therapy
Anxiety
Depression
Breast cancer
Prostate cancer

ABSTRACT

Background: The present study investigates possible predictors of treatment response in an Internet-delivered Mindfulness-Based Cognitive Therapy (iMBCT) intervention with therapist support. This iMBCT program, a fully online delivered intervention with asynchronous therapist support, has previously been shown to be efficacious in reducing symptoms of anxiety and depression in women treated for breast cancer and men treated for prostate cancer.

Methods: Eighty-two breast- and prostate cancer survivors experiencing psychological distress received 8 weeks of therapist-guided iMBCT. Primary outcomes were improvement in anxiety and depression scores from baseline to post-treatment and from baseline to six-months follow-up. Clinical predictors included levels of depression and anxiety at the time of screening and at baseline, as well as time since diagnosis. Demographic predictors included age and educational level. Therapy-related predictors included working alliance, self-compassion, and five facets of mindfulness. Mixed Linear Models were employed to test the prediction effects over time.

Results: Higher levels of baseline depression were associated with increased treatment response in anxiety at post-treatment, and lower levels of self-compassion were associated with increased treatment response in depression at post-treatment. None of the proposed predictors significantly predicted treatment response at six-months follow-up.

Conclusion: The findings suggest that iMBCT can be provided for cancer survivors regardless of their age, educational level, and time since diagnosis (up to five years) and that therapeutic alliance is not crucial for treatment response. We did not identify characteristics predicting treatment response, although many factors were tested. Still, other characteristics may be predictors, and given the relatively small sample size and a large number of statistical tests, the results should be interpreted with caution.

1. Introduction

Breast- and prostate cancer are the most common cancer diseases among women and men, respectively, in Northern Europe. With 5-year

survival rates of 87% for both women with breast cancer and men with prostate cancer (from 2012 to 2016) (Engholm et al., 2010), a large proportion of people are living with physical and psychological late effects of cancer disease and cancer treatment. Psychological distress, i.

Abbreviations: MBCT, Mindfulness-Based Cognitive Therapy; iMBCT, Internet-delivered Mindfulness-Based Cognitive Therapy; MBI, Mindfulness-Based Intervention; iMBI, Internet-delivered Mindfulness-Based Intervention; MBSR, Mindfulness-Based Stress Reduction; RCT, randomized controlled trial; BDI-II, Beck Depression Inventory II; STAI-Y, State-Trait Anxiety Inventory, Y-Form; WAI-C, Working Alliance Inventory – Client Form; SCS-SF, Self-Compassion Scale – Short Form; FFMQ-SF, Five Facet Mindfulness Questionnaire – Short Form; FFMQ-SF-DS, FFMQ-SF subscale Describing; FFMQ-SF-NR, FFMQ-SF subscale Non-Reactivity to inner experience; FFMQ-SF-NJ, FFMQ-SF subscale Non-Judging of inner experience; FFMQ-SF-OB, FFMQ-SF subscale Observing; FFMQ-SF-AA, FFMQ-SF subscale Acting with Awareness.

* Corresponding author at: Department of Psychology and Behavioral Sciences, Aarhus University, Bartholins Allé 11, DK-8000 Aarhus C, Denmark.

E-mail address: enissen@psy.au.dk (E.R. Nissen).

<https://doi.org/10.1016/j.invent.2021.100365>

Received 22 July 2020; Received in revised form 2 January 2021; Accepted 5 January 2021

Available online 14 January 2021

2214-7829/© 2021 The Authors.

Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

e., symptoms of depression and anxiety, affects a substantial proportion of cancer patients, even after successful treatment (Honda and Goodwin, 2004; Mitchell et al., 2013; Dalton et al., 2009). Compared to the general population, mood disorders are 2 to 4 times more prevalent among cancer survivors (Mitchell et al., 2013; Mitchell et al., 2011), calling for research in efficacious therapies.

Mindfulness-Based Interventions (MBIs) have been found efficacious in treating psychological distress among cancer patients and –survivors (Piet et al., 2012; Cillessen et al., 2019). Recently, internet-delivered Mindfulness-Based Interventions (iMBIs) has also shown to be efficacious in treating psychological distress among cancer patients and –survivors (Nissen et al., 2020; Compen et al., 2018; Zernicke et al., 2014; Bruggemann-Everts et al., 2015; Matis et al., 2020), with a recent systematic review reporting a median effect size of Cohen's $d = 0.42$ for symptoms of anxiety and depression, when compared with control conditions (Matis et al., 2020). Internet-delivered interventions offer a flexible solution for patients and provide the possibility of disseminating the intervention broader, independently of geographical constraints and lack of educated therapists (Holm et al., 2012; Barak et al., 2008; Griffiths and Christensen, 2007; Stanton, 2006). Despite being shown efficacious, little is known about possible predictors of treatment response in iMBIs (Matis et al., 2020). Investigating possible predictors of treatment response could help to identify the patients who will benefit the most and suggest possible modifications of the program content and –procedures (Steketee and Chambless, 1992). Several potential candidates may affect intervention effectiveness.

First, it could be relevant to explore whether psychological distress levels at baseline predicts the efficacy of iMBIs for cancer patients and survivors. In contrast to a previous meta-analysis (Piet et al., 2012), a recent meta-analysis of MBIs for cancer, including Mindfulness-Based Cognitive Therapy (MBCT) and Mindfulness-Based Stress Reduction (MBSR), found no difference in effects on psychological distress between studies that had psychological distress as inclusion criterion compared to studies that did not (Cillessen et al., 2019). Only little is known about whether this also holds true for iMBIs. In a randomized controlled trial of internet-delivered MBCT (iMBCT), it was found that higher levels of distress at baseline predicted higher levels at follow-up, but it was not explored whether baseline distress levels predicted treatment effects (Cillessen et al., 2018). On the one hand, low baseline symptom levels may lead to floor effects making improvement less likely. On the other hand, given the high degree of self-help in iMBCTs, higher levels of baseline symptoms could perhaps lead to lower levels of adherence reducing the chance of a positive effect. Therefore, exploring whether baseline distress levels predict treatment response has an important clinical relevance.

A second predictor of the efficacy of iMBCT could be age. In the recent meta-analysis, older mean sample age was associated with smaller effects (Cillessen et al., 2019), which is also what was found in a previous study of an online Mindfulness-Based Cancer Recovery program, delivered in groups via video conference (Zernicke et al., 2016). A study investigating computer literacy and participation in online support groups for cancer patients found that older participants with lower levels of education had lower levels of digital literacy and experienced less improvement in psychological distress, compared with younger participants with higher levels of education (Lepore et al., 2019). Generally, older age has been found related to lower levels of psychological distress in cancer patients (Linden et al., 2012; Götze et al., 2020), and, due to floor effects, thus older age could also be associated with smaller effects. In a single previous study of iMBCT, however, neither age nor educational level emerged as predictors of treatment effect (Cillessen et al., 2018). Another study of iMBI did however find younger age as a predictor of treatment effect (Zernicke et al., 2016). Taken together, previous findings regarding age as a predictor of treatment response in both MBIs and internet-delivered interventions differ with a trend towards older age being associated with smaller treatment responses.

Third, it could be relevant to explore the role of time since diagnosis. Distress symptom levels generally appear to decrease over time within the first year after receiving a cancer diagnosis (Linden et al., 2012), which suggests that longer time since diagnosis could be associated with smaller effects. On the other hand, once patients have reached later phases of the survivorship trajectory, elevated levels of distress have been found equally prevalent when comparing survivors at five and ten years after diagnosis (Götze et al., 2020). Possibly, cancer survivors may therefore benefit from psychological interventions many years after their initial diagnosis, and it is relevant to evaluate whether the time since diagnosis predicts outcome response. The recent meta-analysis of MBIs found time since diagnosis unrelated to intervention gain (Cillessen et al., 2019). To our knowledge, no studies of iMBIs have explored this predictor.

Therapeutic alliance is a fourth potential predictor, defined as the cooperative and affective bond between therapist and patient (Horvath et al., 2011). Therapeutic alliance is acknowledged as an important facilitator of treatment effect across psychotherapeutic approaches (Horvath et al., 2011; Norcross and Lambert, 2011; Norcross and Lambert, 2018). Previous studies have provided evidence that a therapeutic alliance may be established successfully in fully internet-delivered therapy, even to degrees comparable to or even higher than in traditional face-to-face treatment (Pihlaja et al., 2018; Hadjistavropoulos et al., 2017; Cook and Doyle, 2002; Sucala et al., 2012; Andersson et al., 2012). Despite these findings, evidence is contradictory on whether therapeutic alliance may have less impact on the outcome of internet-delivered interventions (Pihlaja et al., 2018; Hadjistavropoulos et al., 2017; Bisseling et al., 2019a). In a recent study investigating the effects of both face-to-face group-based MBCT and iMBCT on distress in cancer patients, higher therapeutic alliance predicted treatment response in the face-to-face-delivered MBCT (Bisseling et al., 2019a), but not the iMBCT (Bisseling et al., 2019b). Investigating the predicting effect of therapeutic alliance is highly relevant for future attempts to optimize iMBIs.

Finally, it could be relevant to explore the predicting role of participants' baseline levels of mindfulness skills and self-compassion, two constructs proposed to be core working mechanisms in MBIs. Mindfulness, i.e., the ability to maintain a non-judgmental, moment-by-moment awareness of thoughts, feelings, bodily sensations, and the surrounding environment, is a core skill trained in MBIs (Hollis-walker and Colosimo, 2011), and, while the effect sizes are generally small, MBIs have been found to increase mindfulness (Cillessen et al., 2019). When considering the possibility of ceiling effects, it could be hypothesized that high baseline mindfulness levels would be associated with smaller treatment effects on psychological distress. This hypothesis has found support in a previous study reporting that baseline mindfulness levels were associated with lower levels of psychological distress after the iMBCT intervention (Cillessen et al., 2018). Self-compassion, described as kindness and understanding towards oneself and taking a balanced and gentle approach to one's thoughts and emotions (Neff et al., 2007), is linked to the construct of mindfulness and is proposed as a possible mechanism in mindfulness interventions (Hollis-walker and Colosimo, 2011). Again, it could be relevant to explore whether baseline levels of self-compassion is a potential predictor of the treatment response to iMBCT.

1.1. Aims and hypotheses

In the present paper, we aim to extend the previous results of a randomized controlled trial of iMBCT for psychological distress in breast and prostate cancer survivors, where statistically significant pre-post effects were found for both anxiety ($d = 0.45$) and depressive symptoms ($d = 0.42$), together with statistically significant pre-follow up effects for anxiety symptoms ($d = 0.40$), compared with treatment-as-usual waitlist controls (Nissen et al., 2020). In the present paper, we explore a range of possible predictors of the treatment response in the subgroup of participants randomized to active treatment. The predictors

included clinical factors, demographic factors, and therapy-related factors. The clinical predictors included levels of depression and anxiety at the time of screening for inclusion and at baseline, and time since cancer diagnosis. The demographic predictors included age and educational level. The therapy-related predictors included therapeutic alliance, self-compassion, and the five facets of mindfulness; describing (DS), non-reactivity to inner experience (NR), non-judging of inner experience (NJ), observing (OB), and acting with awareness (AA). Based on previous findings, we hypothesized that higher levels of therapeutic alliance would be associated with larger improvements, whereas longer time since diagnosis and older age would be associated with fewer improvements. Due to the limited existing research and contradictory findings, the analyses of baseline levels of psychological distress, i.e., depression and anxiety, self-compassion, mindfulness, and educational level, were considered exploratory.

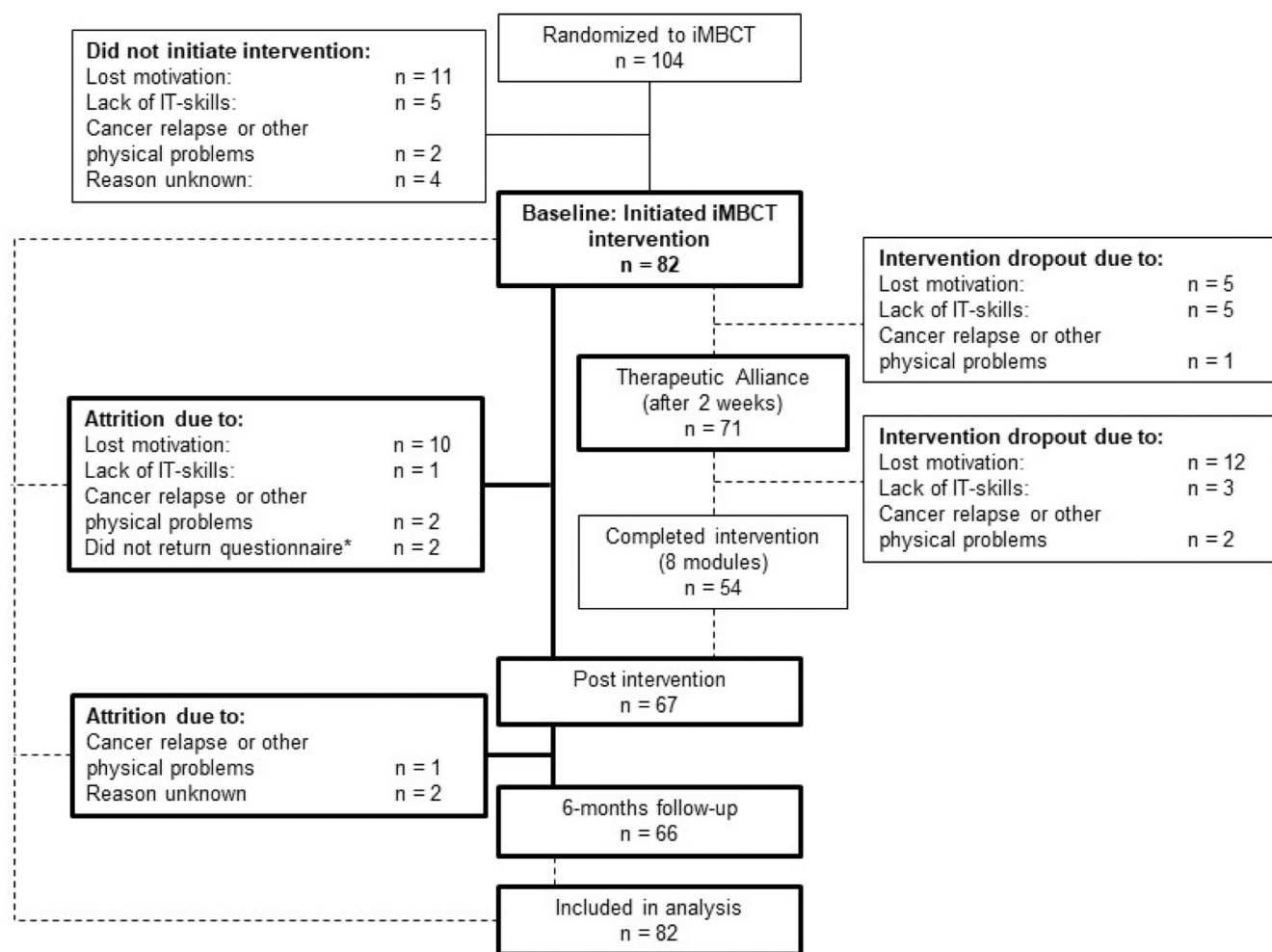
2. Materials and methods

2.1. Participants and recruitment

The study was conducted at the Unit for Psychooncology and Health Psychology, a research unit at the Department of Oncology, Aarhus University Hospital, and the Department of Psychology and Behavioral Sciences, Aarhus University, Denmark. Participants in the present study

included 82 breast- and prostate cancer survivors who received an iMBCT intervention as participants in a randomized controlled trial (Nissen et al., 2020). In this RCT, a total of 1282 breast- and prostate cancer survivors were screened for psychological distress during routine control visits at the clinical departments, resulting in 389 eligible survivors. Of these, 237 patients received further information about the project, and 150 consented to participate and returned a baseline questionnaire. A 2:1 randomization allocated 104 survivors to the intervention and 46 to the waitlist control condition. Of the 104 participants allocated to the intervention, 82 individuals initiated the intervention program and were hence subjects to analysis in the present study. See study flowchart in Fig. 1.

Inclusion criteria were: a) a score of ≥ 3 (0- to 10-point numeric rating scale) on at least one of two screening items of symptoms of anxiety or depression, b) ≥ 3 months and ≤ 5 years after completed primary treatment for primary breast or prostate cancer, c) age ≥ 18 years, d) ability to understand and read Danish, e) internet access, and f) mobile phone ownership. Exclusion criteria were: a) recurrent cancer or active cancer treatment (except adjuvant endocrine treatment), b) qualitatively assessed insufficient IT skills, and c) self-reported severe mental illness. The study was approved by the local Ethics Committee of Central Denmark Region (registration no.: 1-10-72-16-16), registered at [ClinicalTrials.gov](https://www.clinicaltrials.gov) (registration no.: NCT03100981), and registered at the Danish Data Protection Agency. A detailed description of the RCT



*) 'Did not return questionnaire' refers to participants who failed to return the current questionnaire but did return the following questionnaire

Fig. 1. Study flowchart.

and its main effects has been published elsewhere (Nissen et al., 2020).

2.2. Measures

2.2.1. Primary outcome measures

The primary outcomes, symptoms of anxiety and depression, were assessed at baseline, 10 weeks later at post-treatment (post), and at six months follow-up (FU).

2.2.1.1. Depression. Depressive symptoms were assessed with the Beck Depression Inventory (BDI-II), a 21-item self-report scale scored on a 4-point Likert-scale (0–3). The scale is designed to measure symptoms of depression within the past two weeks (Beck et al., 1996). In the present sample, internal consistency (Cronbach's α) was 0.856.

2.2.1.2. Anxiety. Symptoms of anxiety was measured with the State-Trait Anxiety Inventory Y-Form (STAI-Y) (Spielberger et al., 1983), a 20 item self-report scale scored on a 4-point Likert-scale (Engholm et al., 2010; Honda and Goodwin, 2004; Mitchell et al., 2013; Dalton et al., 2009). Only the state-measure was used as it is considered sensitive to change. The scale measures the current state of anxiety. In the present study, we discovered a typing error in item 2. The question was supposed to be "I feel secure" and be a reversed item. The phrase in the present case was in the Danish translation corresponding to "I feel insecure" and hence the item was not reversed in the scoring calculations. However, internal consistency based on baseline data was still high (Cronbach's $\alpha = 0.931$).

2.2.2. Predictors

Clinical, demographic, and therapy-related predictors were all measured at baseline, with the exception of therapeutic alliance, which was assessed at the beginning of intervention week three.

2.2.2.1. Clinical predictors. Screening for symptoms of anxiety and depression was conducted during routine control visits at Department of Oncology for breast cancer patients and Department of Urology for prostate cancer patients. Screening measures included an item of depression ("Within the past week, how burdened of feeling depressed and sad have you been?") and one item of anxiety ("Within the past week, how burdened of being worried and restless have you been?"). The two items were answered on an 11-point Likert-scale (0 = not at all – 10 = extremely much). Baseline levels of anxiety and depression were measured with BDI-II and STAI-Y, described above. Predictor analyses including the same variable as predictor and outcome (BDI-II and STAI-Y, respectively) were omitted to prevent overlap. Time since diagnosis was calculated in months, based on the self-reported month of diagnosis and date of completing the baseline questionnaire.

2.2.2.2. Demographic predictors. Participants provided sociodemographic information at baseline including date of birth and educational level. Educational level was recoded into three categories: Short (primary school or similar, high school, apprenticeship, and short (1–2 years) further education), Medium (2–4 years of further education), and Long (5 years or more further education). Age (years) was based on the self-reported date of birth and date of completing the questionnaire.

2.2.2.3. Therapy-related predictors. Therapeutic alliance was assessed online with the Working Alliance Inventory – Client Form (WAI-C) (Horvath and Greenberg, 1989) at the beginning of intervention week three. WAI-C is a 12 item self-report scale scored on a 1–7-point Likert scale. The WAI-C scale is designed to measure therapeutic alliance from the client's perspective and is based on Bordin's pantheoretical tripartite conceptualization of the therapeutic alliance, including bonds, goals, and tasks of the therapy (Horvath and Symonds, 1991). Although originally developed to measure alliance in face-to-face therapy, the scale is

widely used by others to assess the therapeutic alliance in internet-delivered interventions (Pihlaja et al., 2018; Socala et al., 2012; Biseling et al., 2019b). Internal consistency (Cronbach's α) was 0.915 in the present sample. Mindfulness was measured with the Five-Facet Mindfulness Questionnaire – Short Form (FFMQ-SF), a 24 item self-report scale scored on a 1–5-point Likert scale. The FFMQ-SF includes five aspects of mindfulness, including "Describing" (DS), "Non-Reactivity to inner experience" (NR), "Non-judging of inner experience" (NJ), "Observing" (OB), and "Acting with Awareness" (AA) (Baer et al., 2008). Internal consistencies of the five subscales were 0.837 (DS), NR: $\alpha = 0.700$ (NR), NJ: $\alpha = 0.646$, OB: $\alpha = 0.763$, AA: $\alpha = 0.829$. Self-Compassion was measured with the Self-Compassion Scale – Short Form (SCS-SF). SCS-SF is a 12 item self-report scale scored on a 5-point Likert scale (Engholm et al., 2010; Honda and Goodwin, 2004; Mitchell et al., 2013; Dalton et al., 2009; Mitchell et al., 2011). The SCS-SF is designed to measure self-compassion, including self-kindness, self-judgment, common humanity, isolation, mindfulness, and over-identification (Raes et al., 2011). Baseline data from the present study revealed an internal consistency of Cronbach's $\alpha = 0.803$.

2.3. Intervention

The iMBCT program was adapted from the original face-to-face MBCT manual (Segal et al., 2013) by clinical psychologists (M.O.C. and E.R.N.), both trained at Oxford Mindfulness Centre and with previous experience with MBCT with cancer survivors (Johannsen et al., 2016). Each of the eight one-week modules included written material, cancer-specific case examples, videos with patients and experts, audio exercises, and written reflective and cognitive tasks. After allocation to the intervention, participants received an introductory phone call from their therapist. The remaining planned contact between participant and therapist was in writing via the program platform. If participants did not adhere to the intervention tasks for one week or indicated suicidal thoughts in their weekly questionnaire, the therapist called them by phone. Participants completed a weekly training diary that was visible to their therapist, who gave written, asynchronous feedback on a pre-arranged day of the week. Participants were given access to the next module after submitting the tasks of the week. The program included an optional one-week break, which gave participants a total of nine weeks with therapist support, to complete the eight modules. For a detailed overview of the intervention content, please see Supplementary materials (S-i). After completing the program, participants had access to treatment materials for 6 months. The secure and encrypted intervention platform was provided by the Department of Internet Psychiatry, Karolinska Institutet, Stockholm, Sweden (Titov et al., 2018). For an example of the graphical user interface, see Supplementary materials, S-ii. A smartphone-compliant website with login provided access to daily audio exercises. Nine therapists, including eight Master's level psychology students trained in MBCT (Farver-Vestergaard et al., 2016) and one experienced psychologist trained in MBCT (E.R.N.) provided the therapist feedback. The student therapists, supervised by two authors (M.O.C., E.R.N.), based their written feedback to participants on a manual-based guide developed for the present study. The program content of iMBCT, including the incorporation of cancer-specific adjustments, and procedures in the overall research project, was carried out in collaboration with cancer survivor representatives. For further details on this process, see (Nissen et al., 2018). In the RCT of the overall efficacy of iMBCT, statistically significant effects ($p < .05$) of iMBCT were found for anxiety from baseline to post-intervention (Cohen's $d = 0.45$) and from baseline to six months follow-up ($d = 0.40$), as well as for depression from baseline to post-intervention ($d = 0.42$) when compared with a treatment-as-usual waitlist control condition (Nissen et al., 2020).

2.4. Statistical analysis

IBM SPSS Statistics v. 26 (IBM, Chicago, IL) was used for all statistical analyses. The main effect of iMBCT on symptoms of depression and anxiety within the breast- and prostate cancer survivor population has previously been established using mixed linear models (MLM) (Nissen et al., 2020). Associations between baseline outcome measures and predictor variables were first explored with Pearson's r. MLMs were then employed to test the effects of the predictor over time (predictor × time) on changes in depressive symptoms (BDI-II) and anxiety (STAI-Y). Each of the proposed predictors was explored in separate, linear models for each primary outcome (anxiety and depression) for each time point (baseline to post-treatment and baseline to six months follow-up). Data were hierarchically arranged in two levels with time at level 1, nested within individuals at level 2. MLMs tolerate missing values, and hence missing values were not imputed, which is a recommended procedure (Chakraborty and Gu, 2009). Effect sizes (Cohen's d) were derived from the Predictor × Time F test and calculated as $d = 2 * \sqrt{\frac{F}{df}}$ (Verbeke and Molenberghs, 2000), with magnitudes of 0.2, 0.5, and 0.8 considered small, medium, and large, respectively. A variable was considered a predictor if the two-way interaction term reached statistical significance.

3. Results

3.1. Study flow and sample characteristics

The study flow is shown in Fig. 1. Of the 82 participants, five were included based on their depression screening alone, 14 based on their anxiety screening alone, and 63 based on their scores on both items. Reasons for study dropout during the intervention period were lack of motivation, lack of IT-skills, cancer relapse, other physical problems, and unknown reasons. Sample characteristics are summarized in Table 1.

Table 1
Sample characteristics.

	Value M (SD)/N (%)
Clinical predictors [N = 82]	
Depression symptoms, screening (0–10 Likert scale)	4.65 (2.12)
Anxiety symptoms, screening (0–10 Likert scale)	5.54 (2.00)
Baseline depression (BDI-II)	15.06 (7.33)
Baseline anxiety (STAI-Y)	40.88 (9.82)
Time since diagnosis (months)	54.47 (10.10)
Demographics [N = 82]	
Cancer type and gender	
Breast cancer/women	75 (91.5%)
Prostate cancer/men	7 (8.5%)
Age (years)	54.47 (10.10)
Educational level	
Short	35 (42.7%)
Medium	32 (39.0%)
Long	15 (18.3%)
Therapy-related predictors	
WAI-C, A1 [N = 71]	57.87 (15.40)
SCS-SF	37.38 (7.56)
FFMQ - subscales	
DS	17.11 (3.75)
NR	13.57 (3.09)
NJ	16.12 (3.16)
OB	14.34 (3.19)
AA	16.65 (3.62)

Note: BDI-II: Beck Depression Inventory-II; STAI-Y: State-Trait Anxiety Inventory, Y-Form; WAI-C: Working Alliance Inventory – Client Form; SCS-SF: Self-Compassion Scale – Short Form; FFMQ-SF: Five Facet Mindfulness Scale – Short Form; DS: describing; NR: Non-Reactivity to inner experience; NJ: Non-Judging of inner experience; OB: Observing; AA: Acting with Awareness.

3.2. Predictor analyses

Results of correlation analyses of associations between potential predictors and baseline symptoms are summarized in Table 2. Results of analyses of data from baseline to post-treatment are summarized in Table 3. Results of analyses from baseline to follow-up are summarized in Supplementary material S-iii.

3.2.1. Associations between predictors and outcomes

Pearson's correlation analyses revealed that higher levels of baseline depression (BDI-II) were associated with higher levels of depression screening, baseline anxiety (STAI-Y), and younger age, Self-Compassion (SCS-SF), and the FFMQ-SF subscales DS, NJ, and AA. Higher levels of baseline anxiety (STAI-Y) were associated with higher levels of depression screening, baseline BDI-II, and lower levels of SCS-SF, and FFMQ-SF subscales DS, NJ, and AA. The predictor analyses explored whether the suggested variables could predict changes in the outcome variables over time.

3.2.2. Clinical predictors

As seen in Fig. 2, higher levels of depressive symptoms (BDI-II) at baseline were statistically significantly associated with larger improvement in anxiety symptoms (STAI-Y) at post-treatment ($d = 0.36$, $p = .036$), but did not reach statistical significance at follow-up ($d = 0.33$, $p = .064$). The levels of depressive symptoms and anxiety at the time of screening did not predict the effect on depressive symptoms (BDI-II) or anxiety symptoms (STAI-Y) at either post-intervention or follow-up ($d \leq 0.14$, $p > .05$). Baseline STAI-Y scores did not predict effects on BDI-II scores at any time point ($d = 0.23$, $p > .163$). Furthermore, time since diagnosis did not predict the effects on any of the primary outcome variables at any time point ($d = 0.01$ to 0.17 , $p > .308$).

Table 2
Baseline outcome scores associations with baseline predictor variables.

	Pearson's correlations r (p)	
	BDI-II	STAI-Y
Clinical predictors [N = 82]		
Depression symptoms, screening (0–10 Likert scale)	0.349 (0.001)	0.218 (0.049)
Anxiety symptoms, screening (0–10 Likert scale)	0.160 (0.150)	0.108 (0.336)
Baseline depression (BDI-II)	–	0.683 (<0.001)
Baseline anxiety (STAI-Y)	0.683 (<0.001)	–
Time since diagnosis (months)	0.074 (0.511)	–0.116 (0.298)
Demographics [N = 82]		
Age (years)	–0.341 (0.002)	–0.095 (0.398)
Educational level	–0.083 (0.458)	–0.159 (0.153)
Therapy-related predictors		
WAI-C, A1 [N = 71]	–0.044 (0.718)	–0.029 (0.808)
SCS-SF	–0.541 (<0.001)	–0.471 (<0.001)
FFMQ - subscales		
DS	–0.326 (0.003)	–0.413 (<0.001)
NR	–0.146 (0.190)	–0.136 (0.223)
NJ	–0.330 (0.002)	–0.385 (<0.001)
OB	–0.215 (0.052)	–0.121 (0.279)
AA	–0.457 (<0.001)	–0.409 (<0.001)

Note: BDI-II: Beck Depression Inventory-II; STAI-Y: State-Trait Anxiety Inventory, Y-Form; WAI-C: Working Alliance Inventory – Client Form; SCS-SF: Self-Compassion Scale – Short Form; FFMQ-SF: Five Facet Mindfulness Scale – Short Form; DS: Describing; NR: Non-Reactivity to inner experience; NJ: Non-Judging of inner experience; OB: Observing; AA: Acting with Awareness. Text in bold indicate significant results at $p \leq .05$.

Table 3
Results from predictor analyses in mixed linear models.

	BDI-II			STAI-Y		
	Post			Post		
	F	p	d	F	p	d
	M = 10.33, SD = 6.42			M = 37.04, SD = 8.83		
<i>Clinical predictors</i>						
Depression, screening	0.03	.854	0.03	0.12	.733	0.06
Anxiety, screening	<0.01	.957	0.01	0.38	.541	0.10
Baseline depression (BDI-II)	–	–	–	4.48	.036	0.36
Baseline anxiety (STAI-Y)	1.96	.163	0.23	–	–	–
Time since diagnosis (months)	1.05	.308	0.17	<0.01	.978	0.01
<i>Demographic predictors</i>						
Age (years)	0.01	.930	0.01	0.31	.579	0.09
Educational level	0.50	.480	0.12	2.52	.114	0.26
<i>Therapy-related predictors</i>						
WAI-C	0.08	.774	0.05	0.08	.781	0.05
SCS-SF	5.13	.025	0.38	3.23	.074	0.30
FFMQ-SF DS	1.48	.225	0.20	2.31	.130	0.26
FFMQ-SF NR	0.04	.836	0.03	0.21	.650	0.08
FFMQ-SF NJ	0.43	.514	0.11	1.29	.257	0.19
FFMQ-SF OB	0.54	.462	0.12	0.05	.828	0.04
FFMQ-SF AA	2.05	.154	0.24	1.25	.266	0.18

BDI-II: Beck Depression Inventory – II; STAI-Y: State-Trait Anxiety Inventory – Y-Form; WAI-C: Working Alliance Inventory – Client Form; SCS-SF: Self-Compassion Scale – Short Form; FFMQ-SF: Five Facet Mindfulness Scale – Short Form; DS: Describing; NR: Non-Reactivity to inner experience; NJ: Non-Judging of inner experience; OB: Observing; AA: Acting with Awareness. Text in bold indicate significant results at $p \leq .05$.

3.2.3. Demographic predictors

Neither age ($d \leq 0.1, p \geq .542$) nor educational level ($d \leq 0.26, p \geq .114$) predicted any outcome at any time point.

3.2.4. Therapy-related predictors

Self-compassion (SCS-SF) at baseline predicted levels of depression at post-assessment ($d = 0.38, p = .025$), but not at follow-up ($d = 0.29, p = .096$). As depicted in Fig. 3, higher levels of self-compassion were associated with less improvement in depression at post-treatment

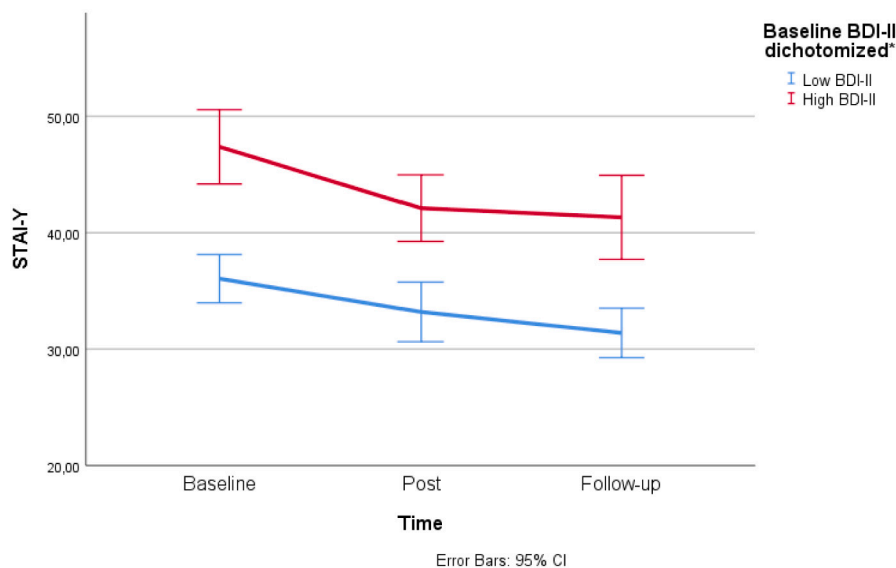
compared to lower levels of self-compassion. Mindfulness skills at baseline did not predict depression nor anxiety at any time point ($d \leq 0.24, p \geq .130$). Therapeutic alliance (WAI-C) measured at the beginning of intervention week three did not predict either depression or anxiety at any time point ($d \leq 0.16, p \geq .349$).

4. Discussion

The present study explored demographic-, clinical-, and therapy-related predictors of treatment response in a trial of iMBCT for women treated for breast cancer and men treated for prostate cancer, experiencing psychological distress. We found that only baseline level of depression and self-compassion were predictors of treatment response, other differences between participants were not associated with their outcome after iMBCT.

It is important to know if the program is suitable for cancer survivors with both lighter and more severe levels of distress, therefore we explored if baseline level of symptoms predicted treatment response. Baseline levels of depressive symptoms were positively associated with anxiety at baseline and emerged as a statistically significant predictor with higher levels of baseline depression predicting larger improvement in anxiety symptoms at post-treatment. This finding could indicate a higher potential gain for patients with elevated depressive symptoms at baseline, which is consistent with the findings of others, who found that higher baseline severity benefitted more from MBI treatment (Lengacher et al., 2016). It could also indicate a floor effect in the overall sample, given the relatively low baseline scores of both anxiety and depression. The mean depression score for the entire sample fell within the range for mild depressive symptoms on the BDI-II, and the mean anxiety scores for the entire sample just exceeded the cut-off for clinically significant anxiety assessed with the STAI-Y scale. The relatively low mean distress scores of the included patients could indicate either that this group of cancer survivors did not experience psychological distress to the same degree as previously reported (Linden et al., 2012; Christensen et al., 2009; Riba et al., 2019), or that the patients consenting to participate had lower levels of distress than those who declined. Nevertheless, we did not find any contraindications for including patients with more severe distress.

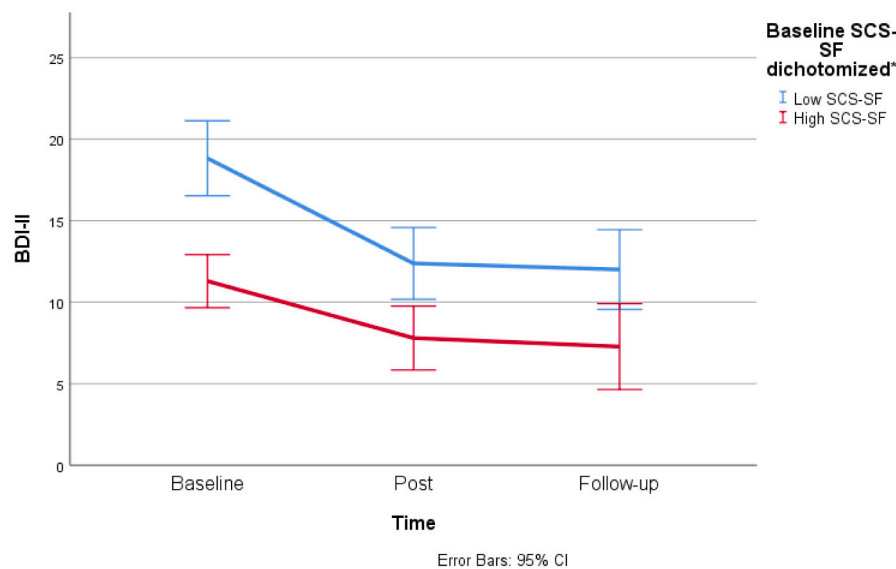
Another question was whether the results of an initial screening could identify survivors who benefit more from the program. Positive



*Low versus high BDI-II scores were based on the median (median = 14.0)

Fig. 2. STAI-Y over time by baseline BDI-II.

*Low versus high BDI-II scores were based on the median (median = 14.0).



*Low versus high SCS-SF scores were based on the median (median = 36.5)

Fig. 3. BDI-II over time by Self-Compassion.

*Low versus high SCS-SF scores were based on the median (median = 36.5).

baseline associations between the depression screening item and depressive- (BDI-II) and anxiety (STAI-Y) symptoms were found, but neither of the screening items predicted outcome response over time. The small and insignificant effect sizes ($d = 0.1-0.14$) suggest that it could be beneficial for patients to engage in iMBCT, regardless of their screening levels. This finding is consistent with the recent meta-analysis of MBIs that did not find screening levels of psychological distress to predict outcome (Cillessen et al., 2019). Since we included only participants who screened positive for some degree of distress, we cannot evaluate whether screening for psychological distress among cancer survivors is at all relevant, it seems, however, unlikely that survivors who do not indicate any distress when screened will be motivated for and/or in need of an intervention. Referring to the association between depression screening and baseline levels of both depressive- and anxiety symptoms found in the present study, the screening could give clinicians a simple indication of which patients will be most in need of psychological treatment. Furthermore, the screening may have detected distressed patients in need, who would not themselves have requested help with managing their symptoms, which is consistent with a study of screening for psychological distress among cancer patients which revealed that screening increased the number of distressed patients who accepted psychological treatment when referred (Bauwens et al., 2014). An alternative to recruiting patients through systematic screening of psychological distress is self-referral, which has been employed in several previous studies of internet-delivered interventions (Hoffmann et al., 2019). Here, it has been found that patients who self-refer to treatment equally well meet inclusion criteria or even better than patients referred by clinicians (Hoffmann et al., 2019; van Scheppingen et al., 2014). A methodological advantage of self-referral could be higher levels of motivation of study participants, which, in turn, may reduce study attrition (Cavanagh, 2010; Schellekens et al., 2016; Thewes et al., 2018). How to best meet patients in need and reduce the risk of sampling bias should be considered when deciding recruitment procedures in future studies.

When considering future implementation it is also important to know if some groups would benefit more from the program. Therefore, we explored whether iMBCT for distress is still relevant for survivors years after their cancer diagnosis. Time since diagnosis, from three months to five years, did not significantly predict outcome response in neither depression nor anxiety, at any time point. With small and non-

significant effect sizes, this finding suggests that psychological distress in cancer survivors may be alleviated regardless of where they are in the survivorship trajectory (up to five years). This is a positive finding because it offers a potential treatment option for patients experiencing persistent psychological distress, which has been found to be equally prevalent among cancer survivors after 5 to 10 years (Götze et al., 2020).

Moreover, an internet-delivered intervention might not be equally suitable for both younger and older cancer survivors or could depend on their level of education. Our analyses did not find age or educational level to predict outcome response, which is corresponding to the previous findings in a study of iMBCT (Cillessen et al., 2018), but contradictory to another previous study of an iMBI finding younger age to predict larger effects (Zernicke et al., 2016). Our findings indicate that patients regardless of age and educational level may benefit from the treatment, which is a positive finding taking the existing disparities in health care into consideration. However, as noted in our main study (Nissen et al., 2020), higher age was associated with attrition. In addition to age and educational level, it could, therefore, in future studies be relevant to consider computer literacy, which has previously been found to be associated with both older age and lower educational level, as well as with treatment response (Lepore et al., 2019).

Furthermore, we explored whether patient characteristics of relevance to the content of the intervention might influence the treatment effect. Here we found that self-compassion was negatively associated with both baseline depressive- and anxiety symptoms and that higher level of self-compassion predicted less improvement in depressive symptoms at post-treatment. Self-compassion has previously been shown to be a mechanism of change in MBCT and to be inversely associated with depressive symptoms (Neff, 2009), which was also found in the present study. The findings of self-compassion as a predictor of outcome response could be an indication of a ceiling effect where participants with a certain level of self-compassion at baseline may have less room for improvement during the intervention and hence benefit less because they already master one of the main mechanisms.

In contrast to pre-treatment self-compassion, individual differences in survivors' mindfulness characteristics were not associated with treatment effects. Despite negative associations between depressive- and anxiety symptoms and baseline levels of the three facets of mindfulness: describing, non-judging of inner experience, and acting with awareness, none of the five facets of mindfulness predicted outcomes of depression

or anxiety at any time point. Thus, the program may be helpful for survivors with both high and low initial levels of mindfulness characteristics.

Finally, of particular relevance for this program that was adapted from a face-to-face intervention to an internet-delivered intervention, we tested the significance of therapeutic alliance for treatment effect. Therapeutic alliance was not found to predict outcome response, which was contradictory to our hypothesis and the findings of the other study of iMBCT for cancer patients (Bisseling et al., 2019b). It is, however, in concordance with the trend described by Bisseling et al. (2019b) where therapeutic alliance was less associated with outcome response in iMBCT compared to the face-to-face MBCT condition. A systematic review of guided internet therapy programs for depression and anxiety (Pihlaja et al., 2018) found associations between higher levels of therapeutic alliance and positive treatment responses in only three of six included studies, whereas the therapeutic alliance is generally found to be a predictor of treatment response in face-to-face-delivered individual psychotherapy (Horvath et al., 2011). A possible explanation for our finding could be that therapeutic alliance is a less important predictor in internet-delivered therapies in general (Andersson et al., 2012). It could also be that an essentially different type of therapeutic alliance is established in internet-delivered interventions with little or no unstructured interaction between patient and therapist, as in the present program. If this is the case, there is a need for reevaluating the understanding of the role of therapeutic alliance in internet-delivered therapy (Hadjistavropoulos et al., 2017). Others have found that the therapist support in internet-delivered therapy do increase outcome, but not as a direct, general effect, but by mediating patients' involvement and engagement in important therapeutic processes, which underlines a complexity in understanding the role of the therapist in these types of interventions (Kaldo et al., 2015). Another explanation of why therapeutic alliance did not predict outcomes in the present study could be that the mechanisms of change in MBIs, in general, are more dependent on the participants' thought processes and their acquisition of mindfulness-skills and not to the same degree depends on the interaction with a therapist (Snippe et al., 2015). Since positive effects were found both of the present intervention program and an equivalent Dutch iMBCT program (Compen et al., 2018; Cillessen et al., 2018; Bisseling et al., 2019a), mindfulness interventions may be effective despite little involvement of the therapeutic alliance, and it is possible that even more automatized versions of iMBCT with less or even no therapist involvement could be feasible (Snippe et al., 2015).

4.1. Limitations

The present study has several limitations that should be taken into consideration. First of all, the study was a derived study from the main efficacy study of iMBCT (Nissen et al., 2020) and was hence not a priori powered for the predictor analyses carried out in the present study. With respect to age as a predictor of outcome response, the results ($p \geq .542$, and $d \leq 0.1$) indicate that a larger sample would not likely result in neither statistical nor clinically significant results. Based on the relatively small sample size with non-significant effect sizes ranging from Cohen's d 0.01 to 0.33, the remaining potential predictors should be interpreted with caution before being rejected as potential predictors. Furthermore, our study includes 26 analyses and two time-points, and while we kept the statistical significance level at 0.05 to reduce the risk of type-II-errors, the two statistically significant results are close to what would be expected from random associations, and hence imply a high risk of type I-error. Our exploratory findings should therefore be considered preliminary, be interpreted with caution, and preferably be replicated in a priori powered prediction studies.

The main reasons reported for study attrition and intervention dropout were lack of motivation and IT-skills, which indicate a need for a more clear examination of participants' expectations before enrolling patients in the program. Furthermore, it would be relevant in future

studies to include a standardized measure of computer literacy to ascertain whether a certain level of computer literacy is needed for optimal effects or to prevent attrition.

The present results only concern patients treated for breast- or prostate cancer in the survivorship phase of their course of disease. This limits the generalizability of the results to other cancer diagnoses and other phases of the disease, i.e. during treatment and terminal phases. In addition to the predictors included in the present study, it could be relevant to investigate cancer type, gender, and treatment adherence as possible predictors. The results of these analyses were reported in the main study (Nissen et al., 2020), and no prediction effects were found.

5. Conclusion

Taken together, higher levels of depression at baseline appeared to predict higher levels of improvement in anxiety, and lower baseline levels of self-compassion predicted greater improvement in depression at post-treatment. None of the suggested predictors predicted treatment response for either outcome at the six months follow-up. The findings suggest that iMBCT can be administered to cancer survivors regardless of age, educational level, and time since diagnosis. Given a relatively low sample size and a large number of tests, the results need replication. To improve our understanding of predictors of treatment success, future studies should explore additional characteristics not included in the present study.

Declaration of competing interest

The authors declare no conflicting interests.

Acknowledgements

We wish to thank the participating patients in the study, the staff at the Department of Oncology and the Department of Urology at Aarhus University Hospital, the research assistants and the student therapists.

Funding

This work was supported by TrygFonden, Denmark [grant number: 7-12.0736]; and The Danish Cancer Society [grant number: R113-A7015-14-S34].

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.invent.2021.100365>.

References

- Andersson, G., Paxling, B., Wiwe, M., Vernmark, K., Felix, C.B., Lundborg, L., Furmark, T., Cuijpers, P., Carlbring, P., 2012. Therapeutic alliance in guided internet-delivered cognitive behavioural treatment of depression, generalized anxiety disorder and social anxiety disorder. *Behav. Res. Ther.* 50, 544–550.
- Baer, R.A., Smith, G.T., Lykins, E., Button, D., Krietemeyer, J., Sauer, S., Walsh, E., Duggan, D., Williams, J.M.G., 2008. Construct validity of the five facet mindfulness questionnaire in meditating and nonmeditating samples. *Assessment* 15, 329–342.
- Barak, A., Hen, L., Boniel-nissim, M., Shapira, N., 2008. A comprehensive review and a meta-analysis of the effectiveness of internet-based psychotherapeutic interventions a comprehensive review and a meta-analysis of the effectiveness of internet-based psychotherapeutic interventions. *J. Technol. Hum. Serv.* 26, 109–160.
- Bauwens, S., Baillon, C., Distelmans, W., Theuns, P., 2014. Systematic screening for distress in oncology practice using the Distress Barometer: the impact on referrals to psychosocial care. *Psychooncology* 23, 804–811.
- Beck, A. T., R. A. Steere, and G. K. Brown. 1996. Manual for the Beck Depression Inventory-II. The Psychological Corporation, San Antonio. TX.
- Bisseling, E.M., Schellekens, M.P.J., Spinhoven, P., Compen, F.R., Speckens, A.E.M., van der Lee, M., 2019a. Therapeutic alliance-not therapist competence or group cohesion-contributes to reduction of psychological distress in group-based Mindfulness-Based Cognitive Therapy for cancer patients. *Clin. Psychol. Psychother.* Epub ahead.

- Bisseling, E., Cillessen, L., Spinhoven, P., Schellekens, M., 2019b. Development of the therapeutic alliance and its association with internet-based mindfulness-based cognitive therapy for distressed cancer patients: secondary analysis of a multicenter corresponding author: *J. Med. Internet Res.* 21, e14065.
- Bruggemann-Everts, F.Z., van der Lee, M.L., de J. Meezenbroek, E., 2015. Web-based individual Mindfulness-Based Cognitive Therapy for cancer-related fatigue — a pilot study. *Internet Interv.* 2, 200–213.
- Cavanagh, K., 2010. Turn on, tune in and (don't) drop out: engagement, adherence, attrition, and alliance with internet-based interventions. In: *Oxford Guide to Low Intensity CBT Interventions*. Oxford Guides in Cognitive Behavioural Therapy. Oxford University Press, New York, NY, pp. 227–233.
- Chakraborty, H., Gu, H., 2009. A Mixed Model Approach for Intent-to-treat Analysis in Longitudinal Clinical Trials With Missing Values.
- Christensen, S., Zachariae, R., Jensen, A.B., Vaeth, M., Møller, S., Ravnsbaek, J., von der Maase, H., 2009. Prevalence and risk of depressive symptoms 3–4 months post-surgery in a nationwide cohort study of Danish women treated for early stage breast-cancer. *Breast Cancer Res. Treat.* 113, 339–355.
- Cillessen, L., Schellekens, M., Van de Ven, M., Donders, A., Compen, F., Bisseling, E.M., Van der Lee, M.L., Speckens, A.E.M., 2018. Consolidation and prediction of long-term treatment effect of group and online mindfulness-based cognitive therapy for distressed cancer patients. *Acta Oncol. (Madr)*. 57, 1293–1302.
- Cillessen, L., Johannsen, M., Speckens, A.E.M., Zachariae, R., 2019. Mindfulness-based interventions for psychological and physical health outcomes in cancer patients and survivors: a systematic review and meta-analysis of randomized controlled trials. *Psychooncology*. 28, 2257–2269.
- Compen, F., Bisseling, E., Schellekens, M., Donders, R., Carlson, L., van der Lee, M., Speckens, A., 2018. Face-to-face and internet-based mindfulness-based cognitive therapy compared with treatment as usual in reducing psychological distress in patients with cancer: a multicenter randomized controlled trial. *J. Clin. Oncol.* 36, 2413–2421.
- Cook, J.E., Doyle, C., 2002. Working alliance in online therapy as compared to face-to-face therapy: preliminary results. *Cyber Psychol. Behav.* 5.
- Dalton, S.O., Laursen, T.M., Ross, L., Mortensen, P.B., Johansen, C., 2009. Risk for hospitalization with depression after a cancer diagnosis: a nationwide, population-based study of cancer patients in Denmark from 1973 to 2003. *J. Clin. Oncol.* 27, 1440–1445.
- Engholm, G., J. Ferlay, N. Christensen, F. Bray, L. Gjerstorff, Å. Klint, J. E. Køtlum, E. Ólafsdóttir, E. Pukkala, H. H. Storm, G. Engholm, J. Ferlay, N. Christensen, F. Bray, L. Marianne, Å. Klint, J. E. Køtlum, E. Ólafsdóttir, E. Pukkala, and H. H. Storm. 2010. NORDCAN – a Nordic tool for cancer information, planning, quality control and research. *Acta Oncol. (Madr)*. 49: 725–736.
- Farver-Vestergaard, I., Johannsen, M., Nissen, E.R., O'Connor, M., 2016. Mindfulness-Baseret Kognitiv Terapi i en sundhedspsykologisk kontekst: Effektstudier og kliniske betragtninger fra Enhed for Psykoonkologi og Sundhedspsykologi. *Psyke & Logos* 37, 12–29.
- Götze, H., Friedric, M., Taubenheim, S., Dietz, A., Lordick, F., Mehnert, A., 2020. Depression and anxiety in long-term survivors 5 and 10 years after cancer diagnosis. *Support. Care Cancer* 28, 211–220.
- Griffiths, K.M., Christensen, H., 2007. Internet-based mental health programs: a powerful tool in the rural medical kit. *Aust. J. Rural Health* 15, 81–87.
- Hadjistavropoulos, H.D., Pugh, N.E., Hesser, H., Andersson, G., 2017. Therapeutic alliance in internet-delivered cognitive behaviour therapy for depression or generalized anxiety. *Clin. Psychol. Psychother.* 24, 451–461.
- Hoffmann, D., Rask, C.U., Hedman-Lagerlöf, E., Eilenberg, T., Frosthalm, L., 2019. Accuracy of self-referral in health anxiety: comparison of patients self-referring to internet-delivered treatment versus patients clinician-referred to face-to-face treatment. *BJPsych Open* 5, 1–9.
- Hollis-walker, L., and K. Colosimo. 2011. Mindfulness, self-compassion, and happiness in non-meditators: a theoretical and empirical examination. *Pers. Individ. Dif.* 50: 222–227.
- Holm, L.V., Hansen, D.G., Johansen, C., Vedsted, P., Larsen, P.V., Kragstrup, J., Søndergaard, J., 2012. Participation in cancer rehabilitation and unmet needs: a population-based cohort study. *Support. Care Cancer* 20, 2913–2924.
- Honda, K., Goodwin, R.D., 2004. Cancer and mental disorders in a national community sample: findings from the national comorbidity survey. *Psychother. Psychosom.* 73, 235–242.
- Horvath, A.O., Greenberg, L.S., 1989. Development and validation of the Working Alliance Inventory. *J. Couns. Psychol.* 36, 223–233.
- Horvath, A.O., Symonds, B.D., 1991. Relation between working alliance and outcome in psychotherapy: a meta-analysis. *J. Couns. Psychol.* 38, 139–149.
- Horvath, A. O., A. C. Del Re, C. Flückiger, and D. Symonds. 2011. Alliance in individual psychotherapy. *Psychotherapy* 48: 9–16.
- Johannsen, M., M. O'Connor, M. S. O'Toole, A. B. Jensen, I. H??jris, and R. Zachariae. 2016. Efficacy of mindfulness-based cognitive therapy on late post-treatment pain in women treated for primary breast cancer: a randomized controlled trial. *J. Clin. Oncol.* 34: 3390–3399.
- Kaldo, V., Ramnerö, J., Jernelöv, S., 2015. Involving clients in treatment methods: a neglected interaction in the therapeutic relationship. *J. Consult. Clin. Psychol.* 83, 1136–1141.
- Lengacher, C.A., Reich, R.R., Paterson, C.L., Ramesar, S., Park, J.Y., Alinat, C., Johnson-Mallard, V., Moscoso, M., Budhrani-Shani, P., Miladinovic, B., Jacobsen, P.B., Cox, C. E., Goodman, M., Kip, K.E., 2016. Examination of broad symptom improvement resulting from mindfulness-based stress reduction in breast cancer survivors: a randomized controlled trial. *J. Clin. Oncol.* 34, 2827–2834.
- Lepore, S.J., Rincon, M.A., Buzzaglio, J.S., Golant, M., Lieberman, M.A., Bauerle, S., Suzanne, B., 2019. Digital literacy linked to engagement and psychological benefits among breast cancer survivors in Internet-based peer support groups. *Eur. J. Cancer Care (Engl)* 28, e13134.
- Linden, W., Vodermaier, A., Mackenzie, R., Greig, D., 2012. Anxiety and depression after cancer diagnosis: prevalence rates by cancer type, gender, and age. *J. Affect. Disord.* 141, 343–351.
- Matis, J., Svetlak, M., Slezackova, A., Svoboda, M., Sumec, R., 2020. Mindfulness-based programs for cancer patients via eHealth and mHealth: a systematic review and synthesis of quantitative research (preprint). *J. Med. Internet Res.* 22, 1–21.
- Mitchell, A.J., Chan, M., Bhatti, H., Halton, M., Grassi, L., Johansen, C., Meader, N., 2011. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol.* 12, 160–174.
- Mitchell, A.J., Ferguson, D.W., Gill, J., Paul, J., Symonds, P., 2013. Depression and anxiety in long-term cancer survivors compared with spouses and healthy controls: a systematic review and meta-analysis. *Lancet Oncol.* 14, 721–732.
- Neff, K.D., 2009. The role of self-compassion in development: a healthier way to relate to oneself. *Hum. Dev.* 52, 211–214.
- Neff, K.D., Kirkpatrick, K.L., Rude, S.S., 2007. Self-compassion and adaptive psychological functioning. *J. Res. Pers.* 41, 139–154.
- Nissen, E.R., Bregnballe, V., Mehlsen, M.Y., Muldbjerg, A.K.Ø., O'Connor, M., Lomborg, K.E., 2018. Patient involvement in the development of a psychosocial cancer rehabilitation intervention: evaluation of a shared working group with patients and researchers. *Res. Invol. Engagem.* 4.
- Nissen, E.R., O'Connor, M., Kaldo, V., Højris, I., Borre, M., Zachariae, R., Mehlsen, M., 2020. Internet-delivered mindfulness-based cognitive therapy for anxiety and depression in cancer survivors: a randomized controlled trial. *Psychooncology*. 29, 68–75.
- Norcross, J.C., Lambert, M.J., 2011. Psychotherapy relationships that work II. *Psychotherapy* 48, 4–8.
- Norcross, J.C., Lambert, M.J., 2018. Psychotherapy relationships that work III. *Psychotherapy* 55, 303–315.
- Piet, J., Würtzen, H., Zachariae, R., 2012. The effect of mindfulness-based therapy on symptoms of anxiety and depression in adult cancer patients and survivors: a systematic review and Meta-analysis. *J. Consult. Clin. Psychol.* 80, 1007–1020.
- Pihlaja, S., Stenberg, J., Joutsenniemi, K., Mehik, H., Ritola, V., Joffe, G., 2018. Therapeutic alliance in guided internet therapy programs for depression and anxiety disorders – a systematic review. *Internet Interv.* 11, 1–10.
- Raes, F., Pommier, E., Neff, K.D., Van Gucht, D., 2011. Construction and factorial validation of a short form of the Self-Compassion Scale. *Clin. Psychol. Psychother.* 18, 250–255.
- Riba, M.B., Donovan, K.A., Andersen, B., Braun, I., Breitbart, W.S., Brewer, B.W., Buchmann, L.O., Clark, M.M., Collins, M., Corbett, C., Fleishman, S., Garcia, S., Greenberg, D.B., Handzo, R.G.F., Hoofring, L., Huang, C., Lally, R., Martin, S., McGuffey, L., Mitchell, W., Morrison, L.J., Paillet, M., Palesh, O., Parnes, F., Pazar, J. P., Ralston, L., Salman, J., Shannon-Dudley, M.M., Valentine, A.D., McMillian, N.R., Darlow, S.D., 2019. Distress management, version 3.2019. *J. Natl. Compr. Cancer Netw.* 17, 1229–1249.
- Schellekens, M.P.J., Thewes, B., Speckens, A.E.M., 2016. Comments on 'Psychological intervention targeting distress for cancer patients: a meta-analytic study investigating uptake and adherence' by Brebach and colleagues (2016). *Psychooncology*. 997, 4178.
- van Scheppingen, C., Schroevers, M.J., Pool, G., Smink, A., Mul, V.E., Coyne, J.C., Sanderman, R., 2014. Is implementing screening for distress an efficient means to recruit patients to a psychological intervention trial? *Psychooncology*. 23, 516–523.
- Segal, Z.V., Williams, J.M.G., Teasdale, J.D., 2013. *Mindfulness-based Cognitive Therapy for Depression*, 2nd ed. The Guilford Press, New York.
- Snippe, E., Flee, J., Tovote, K.A., Sanderman, R., Emmelkamp, P.M.G., Schroevers, M.J., 2015. The therapeutic alliance predicts outcomes of cognitive behavior therapy but not of mindfulness-based cognitive therapy for depressive symptoms. *Psychother. Psychosom.* 84, 314–315.
- Spielberger, D., Gorsuch, R.L., Lushene, P.R., Vagg, P.R., Jacobs, G.A., 1983. *State-Trait Anxiety Inventory for Adults*. 76.
- Stanton, A.L., 2006. Psychosocial concerns and interventions for cancer survivors. *J. Clin. Oncol.* 24, 5132–5137.
- Steketee, G., Chambless, D., 1992. Methodological issues in prediction of treatment outcome. *Clin. Psychol. Rev.* 12, 387–400.
- Sucala, M., Schnur, J.B., Constantino, M.J., Miller, S.J., Brackman, E.H., Montgomery, G. H., 2012. The therapeutic relationship in e-therapy for mental health: a systematic review. *J. Med. Internet Res.* 14, 175–187.
- Thewes, B., Rietjens, J.A.C., van den Berg, S.W., Compen, F.R., Abrahams, H., Poort, H., van de Wal, M., Schellekens, M.P.J., Peters, M.E.W.J., Speckens, A.E.M., Knoop, H., Prins, J.B., 2018. One way or another: the opportunities and pitfalls of self-referral and consecutive sampling as recruitment strategies for psycho-oncology intervention trials. *Psychooncology*. 27, 2056–2059.
- Titov, N., Dear, B., Nielssen, O., Staples, L., Hadjistavropoulos, H., Nugent, M., Adlam, K., Nordgreen, T., Bruvik, K.H., Hovland, A., Repål, A., Mathiasen, K., Kraepelien, M., Blom, K., Svanborg, C., Lindefors, N., Kaldo, V., 2018. ICBT in routine care: a descriptive analysis of successful clinics in five countries. *Internet Interv.* 13, 108–115.

- Verbeke, G., Molenberghs, G., 2000. *Linear Mixed Models for Longitudinal Data*. Springer, New York.
- Zernicke, K.A., Campbell, T.S., Speca, M., McCabe-Ruff, K., Flowers, S., Carlson, L.E., 2014. A randomized wait-list controlled trial of feasibility and efficacy of an online mindfulness-based cancer recovery program: the eTherapy for cancer applying mindfulness trial. *Psychosom. Med.* 76, 257–267.
- Zernicke, K. A., T. S. Campbell, M. Speca, K. M. Ruff, S. Flowers, R. Tamagawa, and L. E. Carlson. 2016. The eCALM Trial: eTherapy for cancer applying mindfulness. Exploratory analyses of the associations between online mindfulness-based cancer recovery participation and changes in mood, stress symptoms, mindfulness, posttraumatic growth, and spiritual. *Mindfulness* (N. Y). 7: 1071–1081.