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Web-based individual Mindfulness-Based Cognitive Therapy for cancer-related fatigue — A pilot study

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ABSTRACT

Background: Severe fatigue may persist for many years in cancer survivors and has a considerable impact on a patient's life. This condition is called cancer-related fatigue (CRF). Mindfulness-Based Cognitive Therapy has shown to significantly reduce CRF in cancer survivors. Internet-delivered interventions can be valuable for fatigued patients who are not able to travel to a healthcare institute because of the lack of energy and/or physical limitations. Therefore, we have developed a web-based, therapist guided individual 9-week Mindfulness-Based Cognitive Therapy (eMBCT) aimed at diminishing CRF.

Objective: The aim of this study was to evaluate the efficacy of eMBCT in a clinical setting in reducing fatigue severity and distress in cancer survivors.

Methods: This pilot study was based on data from severely fatigued cancer survivors who applied for eMBCT between 2009 and 2013. Our primary outcome measure was the change in self-reported web-assessed fatigue severity, measured with the Fatigue severity subscale of the Checklist Individual Strength before (baseline) and one month after (post-assessment) eMBCT. The secondary outcome was distress (HADS) and the proportion of participants that showed clinically relevant improvement on fatigue severity. Patients' satisfaction with using eMBCT and reasons for non-adherence were studied. Intention-to-treat analyses were performed using multiple imputations to deal with data loss at post-assessment. All patients had to be severely fatigued at baseline ($\geq$35 on the fatigue severity subscale of the Checklist Individual Strength), were >18 years old, had no history of psychosis or current Major Depressive Disorder, finished their last cancer treatment at least six months ago (mixed cancer types), and were not in the terminal phase of illness. Patients were recruited offline as well as online.

Results: Two-hundred fifty-seven patients (age range 22–79 ($M = 50.2$, $SD = 10.7$), 76% women, 44% breast cancer, most had had surgery, chemo- and/or radiotherapy) met our inclusion criteria. Paired samples t-tests showed that fatigue severity was significantly reduced post-assessment ($t(18) = 13.27$, $p < .001$, Cohen's d: 1.45 as well as distress ($t(46) = 7.66$, $p < .001$, Cohen's d: 0.71). Thirty-five percent ($n = 89$) was clinically relevant improved at post-assessment and 62% ($n = 159$) adhered to treatment. This study had a completion rate of 1.5 and a registration rate of 2.3.

Conclusion: These findings suggest that individual eMBCT may be effective in reducing fatigue in cancer survivors. A randomized controlled study with a large sample and longer follow up is needed to demonstrate the effectiveness of eMBCT for CRF.

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1. Introduction

Fatigue is a common side-effect of cancer and its treatment (Servaes et al., 2003; Bower, 2005; Van der Geest et al., 2013). Cancer-related fatigue (CRF) is defined as a distressing persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning (Berger et al., 2014). In about one third of cancer survivors fatigue may persist for months or even years after cancer treatment (Nieboer et al., 2005; Goedendorp et al., 2013; Heutte et al., 2009; Hjermstad et al., 2005; Storey et al., 2012). Fatigue is known as one of the most prevalent and distressing long-term consequences of cancer (Bower, 2008; Díaz et al., 2008; Jansen et al., 2011; Oerlemans et al., 2013). It is associated with high levels of depression and anxiety (Prue et al., 2006; Smets et al., 1993; Goldstein et al., 2006), and has an impact on patient's ability to reintegrate into

Abbreviations: RCT, Randomized Controlled Trial; CRF, Cancer-Related Fatigue; ITT, Intention-To-Treat; MBCT, Mindfulness-Based Cognitive Therapy; CIS, Checklist Individual Strength; HADS, Hospital Anxiety and Depression Scale; CRI, Clinically Relevant Improved; RCI, Reliable Change Index.

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everyday life (Bartsch et al., 2003). It is estimated that in the Netherlands alone, at least 156.000 cancer survivors are suffering from fatigue (Goedendorp et al., 2013; Meulepas et al., 2011a). This number is expected to rise in the next decades, as the number of people surviving cancer is increasing (Meulepas et al., 2011b).

The etiology of CRF is complex and multidimensional (Koornstra et al., 2014), as it most likely involves physiological, biochemical and psychological systems (Ryan et al., 2007). Most commonly identified factors that contribute to CRF include 1) tumor-related factors and complications (e.g. anemia, pain, appetite loss, stress), 2) treatment side effects (e.g. tissue damage due to cytostatica, or radiation, medication side effects), 3) comorbid medical condition (e.g. thyroid dysfunction, diabetes mellitus, chronic obstructive pulmonary disease) 3) exacerbating comorbid symptoms (sleep disturbance, deconditioning, chronic pain) and 4) psychosocial factors (coping with illness, anxiety, depression) (Koornstra et al., 2014; Wagner and Cella, 2004).

In the National Comprehensive Cancer Network (NCCN) guidelines for CRF (Berger et al., 2014) psychosocial interventions are recommended for CRF both during active cancer treatment, as well as after treatment. These interventions are aimed at changing inefficient coping strategies (Berger et al., 2014; Mock, 2003), thus changing the behavioral and cognitive reactions of the patient to cancer-related stressors including fatigue itself (Duijts et al., 2011; Gielissen et al., 2006; Van der Lee and Garssen, 2012). Mindfulness-Based Cognitive Therapy (MBCT) has shown to be effective in reducing severe fatigue in cancer survivors in a randomized controlled trial (Van der Lee and Garssen, 2012). Mindfulness-based interventions have been found to have a positive effect on psychological and physiological symptoms in cancer survivors (Ledesma and Kumano, 2009; Foley et al., 2010; Ott et al., 2006; Hofmann et al., 2010). Baer (2003) proposed that mindfulness skills can lead to symptom reduction and behavior change through exposure, cognitive change, self-management, relaxation and acceptance. In Fig. 1 the proposed mechanisms by Baer are presented, and applied to CRF by the authors.

1.1. Web-based Mindfulness-Based Cognitive Therapy for cancer survivors

Internet-delivered psychosocial interventions can serve as an addition to existing face-to-face interventions (Cuijpers et al., 2008; Andersson et al., 2014; Boettcher et al., 2014). It makes treatment available for patients who are unable to travel to a healthcare institute, because of lack of energy or physical limitations. Also, internet interventions may be suitable for patients who seek treatment that is easy to integrate into daily life activities, as one can follow the program when and wherever preferred. We have developed a web-based individual MBCT aimed at alleviating CRF called eMBCT. The eMBCT is characterized by personal contact with one assigned therapist via e-mail and follows the same protocol as face-to-face MBCT for CRF (see Appendix A) (Van der Lee and Garssen, 2012). MBCT is originally delivered in a group format. Individual MBCT can be beneficial for patients who are reluctant to treatment in a group, for instance because they fear being confronted with stories of fellow patients. Individual MBCT has been shown to be effective in reducing depression in patient with diabetes (Tovote et al., 2014). As far as we know, this pilot study is the first to investigate a web-based individual MBCT for CRF.

1.2. Development of eMBCT

In the development of eMBCT, we originally adopted the 9-week face-to-face MBCT protocol for CRF (Van der Lee and Garssen, 2012), and made the following adaptations: We re-designed the reader with a professional lay-out, and added a written introduction which was originally given in the group face-to-face. The weekly reader was divided in paragraphs, describing each psycho-educational theme separately, and thereby improving readability. We transformed the audio files from the face-to-face MBCT to digital MP3 files. We added written instructions for the exercises 'eating with awareness' and 'walking meditation', as these exercises were originally done in the group in the face-to-face MBCT. We illustrated the yoga exercises in the reader so patients could easily copy the yoga postures.

I. Exposure	The ability to observe fatigue sensations non-judgmentally is believed to reduce distress associated with fatigue through desensitization.
II. Cognitive change	The practice of mindfulness may lead to changes in one's attitude towards one's thoughts. Fatigue-related thoughts like: "I am useless, feeling so fatigued all the time" are 'just thoughts' rather than reflections of truth or reality. Patients are stimulated to cognitively defuse from these thoughts.
III. Self-management	Through the practice of mindfulness a patient can learn to raise awareness to the present experience and becomes aware of potentially maladaptive coping strategies (e.g. irritation in social contact, catastrophizing about fatigue, being overactive, or being too inactive). By raising awareness people are able to choose a more helpful coping strategy.
IV. Relaxation	By raising awareness to bodily sensations such as muscle tension, autonomic arousal, and racing thoughts, mindfulness exercises may lead to relaxation. Relaxation has a beneficial effect on quality of sleep and rest.
V. Acceptance	Mindfulness meditation includes acceptance of fatigue-related thoughts, feelings, urges, or other bodily, cognitive and emotional reaction. In that way the patients can save energy which is otherwise spilled on trying to change, escape, or avoid fatigue.

Fig. 1. How MBCT may help Ott et al., 2006 — applied to cancer-related fatigue by the authors.

We designed a website (www.mindermoebijkanker.nl Helen Dowling Institute, 2009) (SSL encrypted) with the help of an ICT company called Studio2 (Studio2 Communications BV, 2015) (see Appendix D for screenshots). The 9-week protocol, the readers, MP3 files, and log boxes were implemented. On this website, patients as well as therapists could log in on their personal webpage with a username and password. In the log boxes patients could write down their experiences with doing the exercises. An e-mailbox was implemented on the webpage, so patients could securely correspond with their personal therapist, and receive feedback on their log files. An extensive intake procedure containing state and trait questionnaires was designed and put on the webpage. See Section 2.3 for more information about setting and intervention.

Five fatigued cancer patients, who had previously followed face-to-face MBCT for CRF (Van der Lee and Garssen, 2012), volunteered to follow the first version of eMBCT and gave feedback about user friendliness and usability. Following their feedback, we added MP3 files of the same exercises (male voice, female voice, and shorter versions) so patients could choose which exercise they preferred. We added an option to print out the log files and e-mail correspondence with the therapist. We improved navigation on the webpage and enlarged the log boxes. An online forum was suggested to share experiences with mindfulness, and to help continue practicing after the intervention had finished. Though, as the costs of a moderator would not be compensated by the health insurance companies, we instead referred to a website for the patient to find mindfulness meetings nearby.

1.3. Aim of this study

The aim of this study was to evaluate the efficacy of eMBCT in a clinical setting in reducing fatigue severity and distress in cancer survivors.

2. Material and methods

2.1. Patients

Participants in this pilot study had to meet the following inclusion criteria: they (a) were a cancer survivor (all cancer types included), meaning either they had cancer but were not in the terminal phase of illness, or had suffered from cancer in the past (b) had completed their last cancer treatment at least six months before the start of eMBCT (hormonal treatment excluded); (d) were older than 18 years; (e) scored ≥ 35 on the severity of fatigue subscale of the self-report Checklist Individual Strength (CIS) at baseline (Vercoulen et al., 1999); (f) had no history of psychosis or current Major Depressive Disorder. If patients followed any other form of psychological care for fatigue or changed their medication considerably during the eMBCT, this was registered at post-assessment (self-report). Patients who reported they had cancer recurrence or started a cancer treatment during the study were excluded from analysis. Co-morbid somatic diseases that were a possible cause for fatigue were no exclusion criterion, but were registered during the study (self-reported).

2.2. Recruitment

We informed medical doctors about the eMBCT via articles in relevant magazines, and informed patients directly by newsletters of patient associations, and via advertisements on relevant websites in the Netherlands (see Appendix B for advertisement).

2.3. Setting and intervention

Patients were referred to the Helen Dowling Institute (a health care institution, specialized in psycho-oncology, then situated in Utrecht, the Netherlands) by medical doctors and all costs were compensated by health insurance. The intervention was given by eleven therapists (see Appendix C for case volume), who had at least two years of experience with face-to-face MBCT for cancer patients. They were trained in giving the nine-week eMBCT protocol (see Appendix A) and attended supervision bimonthly. Patients registered for eMBCT via the website (www.mindermoebijkanker.nl) (Helen Dowling Institute, 2009). They filled in the fatigue severity subscale and were given immediate automated feedback on their fatigue severity. In case their scores indicated severe fatigue, patients could register for eMBCT. After registration, patients were asked to agree on the general usage conditions and fill in the intake questionnaire on their personal webpage. Then, their personal therapist gave feedback on the intake and judged whether eMBCT would be suitable for them. If the therapist had doubts about whether eMBCT was adequate care for the patient, the therapist contacted patients via telephone for inquiry. To start the intervention, patients could log on to their personal webpage where they could download MP3 files with exercises, read written information about a specific mindfulness theme each week in the weekly reader, and to correspond with their personal therapist via e-mail (see Appendix D for screenshots). Patients were asked to practice the mindfulness exercises six days a week for half an hour, and to document their experiences in their personal log on their webpage. On an agreed day of the week, the therapists replied to this weekly log, thereby guiding the patients through the nine-week program. The therapist encouraged the patient to try out the new mindfulness exercises and also do some of the exercises of the weeks before (see Appendix A). From week 7 on participants could choose which exercises they preferred, and in week 9 they created their own program. The therapist provided the patient with personal support in doing the exercises, and creating a mild and open awareness for thoughts, feelings and behaviors. Patients could continue with the next week's session after they had registered their experiences with each exercise in their log of the previous week. Patients were stimulated to follow the nine-week intervention within the nine weeks period. In case of holidays or illness they could pause for a week or more in consultation with their therapist. At the end of each week patients answered eight questions about their wellbeing using the six items of the outcome rating scale (Miller et al., 2003) and two self-created questionnaires about fatigue and illness, so the therapists could monitor their patients closely. In case a patient reported a drop in wellbeing, the therapist contacted the patient for inquiry, to investigate if (additional) help was needed from their general practitioner or other health professionals nearby. An evaluation questionnaire was sent by e-mail four weeks after the intervention (see 2.4 *Data collection*). The therapist replied to this evaluation questionnaire for one last time, and encouraged the patient to continue practicing after the intervention had finished.

2.4. Data collection

On their personal webpage, patients filled in questionnaires concerning fatigue severity and distress before (baseline intake) the nine-week intervention. One month after the intervention (post-assessment), patients were sent an invitation via e-mail to fill in the post-assessment questionnaire via a password secured online questionnaire. IP addresses were used to distinguish post-assessment questionnaires between patients. Patients were able to review and modify their answers through a 'back' button. All items of the fatigue severity and distress questionnaires were mandatory. Regarding satisfaction with eMBCT, all patients were sent an evaluation questionnaire post-assessment. The data were collected in a clinical setting, and was approved by the ethical board of the Helen Dowling Institute. In the general usage conditions, patients agreed on their answers to the questionnaires being used for research purposes.

2.5. Measures

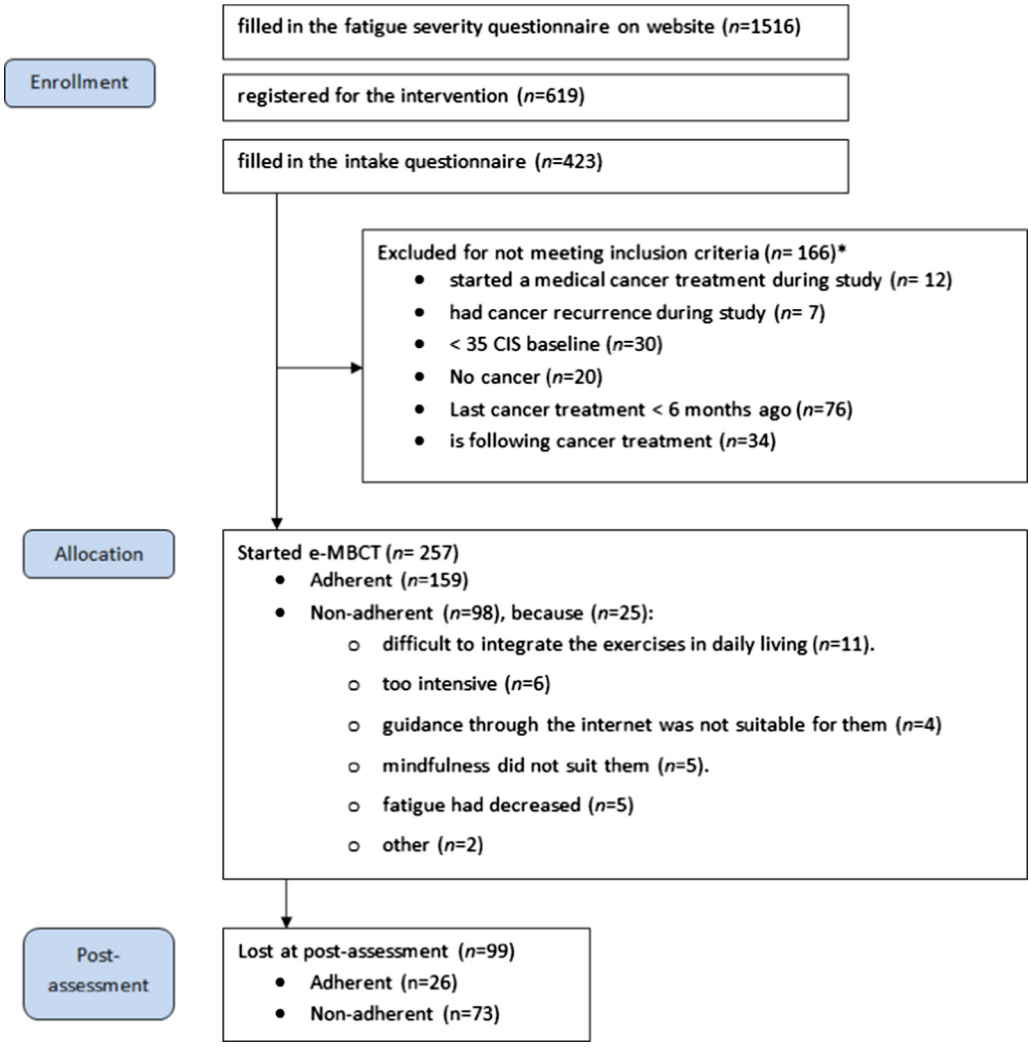
2.5.1. Primary outcome variable: fatigue severity

Fatigue severity was assessed with the fatigue severity subscale of the Checklist Individual Strength (CIS) (Vercoulen et al., 1999). The

subscale fatigue severity consists of eight items, each scored on a 7-point Likert scale and demonstrated acceptable to excellent reliability (Vercoulen et al., 1994) and internal consistency (Stulemeijer et al., 2005). In this study, Guttman's λ_2 (Guttman, 1945; Sijtsma and Emons, 2011) for the CIS subscale fatigue severity was .75 at baseline and .93 at post-assessment. Patients with a score of >35 on this subscale are considered to suffer from severe fatigue (Gielissen et al., 2006; Vercoulen et al., 1994). The CIS has been used to assess fatigue in cancer survivors (Gielissen et al., 2006; Servaes et al., 2002a, 2002b). It closely resembles the Multidimensional Fatigue Inventory (Smets et al., 1996; Smets et al., 1995), which is often used internationally for measuring CRF. We chose the CIS, because a clinical cut off point for severe fatigue is available for Dutch cancer survivors (Gielissen et al., 2006).

2.5.2. Secondary outcome variables: distress, clinically relevant improvement, satisfaction

Distress is a common symptom in cancer patients, and is often associated with fatigue severity (Nieboer et al., 2005; Brown et al., 2013; Brown and Kroenke, 2009). Therefore distress was used as our secondary outcome measure and was assessed with the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983). The HADS is a self-report questionnaire that comprises 14 items measuring feelings of generalized fear and depressive symptoms. The HADS is considered a reliable and valid instrument in medical patients and is sensitive to change (Herrmann, 1997; Bjelland et al., 2002). A Dutch validation study showed good reliability (Spinhoven et al., 1997). Le Fevre et al. (1999) showed that >20 on the total scale is a good cut off point to screen for depression in cancer patients. In this study, Guttman's λ_2 (Guttman, 1945; Sijtsma and Emons, 2011) for the HADS was .85 at baseline and .85 at post-assessment. We calculated the percentage of clinically relevant improved patients at post-assessment on fatigue severity. Also, we calculated how many patients were less fatigued, how many patients did not respond to treatment, and how many patients reported more fatigue after treatment (Rozental et al., 2014). Concerning patients' satisfaction with eMBCT, we asked adherent patients about their opinion on the duration of, the amount of homework, and what grade they would give their therapist on a scale from 1 to 10. Adherent patients were asked about what they thought had helped them most and what they would like to see improved about eMBCT. Non-adherent patients were also asked what they would like to see improved about eMBCT, and were asked for their reason to stop using the intervention. The post-assessment questionnaire for non-adherent



** Numbers do not add up as multiple exclusion criteria are possible*

Fig. 2. Flowchart.

patients was shorter than adherent patients, as we expected that a long evaluation questionnaire would not be filled in by non-adherers, leading to loss at post-assessment. A patient was considered adherent if he or she had followed at least 70% of the intervention. We chose 70%, as we expect that by week 6 patients have experienced enough content of the intervention to could benefit from it (Christensen et al., 2009).

2.5.3. Patient characteristics

Demographic and medical information (marital status, age, gender, work status, education, cancer type, medicine use, treatment, time since treatment) was collected at baseline via self-report.

2.5.4. Control variables

At post-assessment patients registered important changes that could have influenced their fatigue over the last four months, such as changes in medication, following another treatment for fatigue, divorce, starting a new medical treatment, or cancer recurrence.

2.6. Statistical analysis

A paired samples *t*-test was used to investigate changes on the primary outcome CIS fatigue severity subscale, and secondary outcome HADS, both between baseline and post treatment. We used multiple imputation algorithms (Predictive Mean Matching) to deal with missing values at post-assessment (Schenker and Taylor, 1996; Heitjan and Little, 1991). Firstly, we performed an intention-to-treat (ITT) analysis including both adherent and non-adherent patients. Secondly, we analyzed change scores for only adherent patients. To measure the effect size for the dependent samples *t*-test analyses, Cohen's *d* was calculated as followed: Cohen's d = mean difference/standard deviation of the difference (Borenstein et al., 2009). Significance level was set at $p \leq .05$. To assess clinical relevance in fatigue severity change, a patient was considered clinically improved if the following two conditions were met: 1) the reliable change index (RCI) should be more than 1.96 (Jacobson and Truax, 1991), and 2) the post score should be within the normal range, that is a score < 1 standard deviation above the mean of a normative group (Servaes et al., 2002c), i.e. a score < 30.4 on CIS fatigue severity subscale. Moreover, we used the RCI to calculate the number of patients who were less fatigued (RCI > 1.96), did not respond to treatment (RCI between 1.96 and −1.96), and who were more fatigued after treatment (RCI < −1.96). The demographic, medical history and outcome variables were described using frequency and descriptive statistics. To see if there were differences at baseline between non-adherent and adherent patients, we checked the following characteristics using *t*-tests and χ^2-tests: depression (HADS ≥ 20), fatigue severity at baseline, prognosis, marital status, age, gender, employment, education, cancer type, medicine use, treatment type, previous experience with meditation, and time since cancer treatment. Analyses were performed using SPSS Version 19 for Windows package (SPSS Inc, Chicago, IL).

3. Results

Between October 2009 and February 2013 1516 people filled in the fatigue severity subscale on the website (www.mindermoebijkanker.nl), of which 98% ($n = 1485$) scored > 35 and thus were given the automated feedback that they could apply for eMBCT. Eventually, 619 patients registered for the intervention, out of which 423 filled in the intake questionnaire (see Fig. 2 for flowchart). This gives a registration rate of 2.3 (ratio unique visits to website/registered) and a completion rate of 1.5 (ratio agreed to participate/finished survey). For this study, we had to exclude 169 patients, leaving 257 patients that were eligible and started the intervention. Of these, 38.1% ($n = 98$) were not adherent as they stopped using the intervention before completing 70%, including 15.6% ($n = 40$) that did not start the intervention after they

Table 1
Baseline characteristics of study participants (n = 257).

	Mean (SD)/%
Age (years)	50.2 (10.7)
Women	76.3
Dutch nationality	97.7
Living with partner and/or children	69.6
Education	
Low	5.8
Middle	37.7
High	50.6
Employment[a]	
Paid job	54.5
Disability insurance act	29.2
Absenteeism from work	36.2
Cancer type[a]	
Breast	44.0
Blood bone marrow, Hodgkin	12.1
Digestive system	6.6
Reproductive organs	7.0
Head and neck	4.7
Other	8.1
More than one cancer type	11.3
Cancer recurrence	6.6
Heredity form of cancer	3.5
Lymph nodes affected	42.0
Metastases	16.0
Type of cancer treatment[a]	
Surgery	67.7
Chemotherapy	60.3
Radiotherapy	55.3
Hormonal therapy	28.4
Immunotherapy	7.8
Stem cell transplantation	2.7
No treatment: wait and see	0.8
Other	5.4
Suffer from co morbidity	27.2
Of these, percentage that suffers from two or more co morbidities	18.6
Co morbidity[b]	
Infection	20.7
Spine	13.4
Blood	9.8
Thyroid	8.5
Lung	8.5
Diabetes	7.3
Chronic fatigue syndrome, myalgic encephalomyelitis	6.1
Pain, fibromyalgia	6.1
Fear or mood disorder	2.4
Psoriasis, eczema	2.4
Migraine	2.4
Other	12.4
Medicine use[a]	
Pain	24.1
Tension	7.0
Sleep	13.2
Antidepressants	10.1
For cancer	23.7
Time since last cancer treatment (years)	2.93(3.29) (range 0.5–22)
Time since diagnosis (years)	3.44 (2.42) (range 0.08–22.75)
HADS ≥20 at baseline	26.46
Duration of fatigue	4.11 (1.29)
1 = 0–5 months	9.0
2 = 6 months–1 year	22.6
3 = 1–2 years	24.9
4 = 2–5 years	26.8
5 = more than 5 years	14.8
Patient's own estimated prognosis	
Positive	56.8
Unclear, uncertain	17.1
Negative	2.3
I don't know	8.9
No experience with attention-focused exercises, such as meditation or yoga	31.1
Duration completing 70% of intervention (weeks)	15.53 (10.12), ranging from 7 to 64

Table 1 (*continued*)

	Mean (SD)/%
Non-adherent	38.1
Followed any other form of psychological care for fatigue at baseline	15.5
Changed medication considerably during the eMBCT	8.9

eMBCT = web-based Mindfulness Based Cognitive Therapy; M = mean; SD = standard deviation; HADS = Hospital Anxiety Depression Scale.

[a] Percentages do not add up to 100% because multiple options are possible.

[b] Infection including Sarcoidosis, Bechterew's disease, Crohn's disease, Graves' disease, rheumatoid arthritis. Spine injury including whiplash and hernia. Blood including heart problems, high blood pressure, polycytemia vera. Lung diseases including fibrosis, asthma, bronchitis, emphysema.

had filled in the intake. On average, patients completed 70% of the intervention within 16 weeks. Demographic characteristics at baseline are presented in Table 1.

3.1. Multiple imputation of missing data using predictive mean matching and predictors of dropout

To select auxiliary variables for multiple imputation, we investigated differences between *dropouts* (patients who did not fill in the post-assessment questionnaire, Christensen et al., 2009) and non-dropouts, using independent samples *t*-tests and χ^2-tests. This showed that dropouts had been suffering from fatigue shorter ($\chi^2(6) = 14.96$, $p = .021$), had relatively lower education ($\chi^2(2) = 15.71$, $p < .001$), were more often men ($\chi^2(1) = 3.846$, $p < .05$), had less often breast cancer ($\chi^2(1) = 5.00$, $p = .025$), had 'other' cancer type more often ($\chi^2(1) = 6.99$, $p = .008$), had a less good prognosis ($\chi^2(4) = 11.13$, $p = .025$), suffered from comorbidity more often ($\chi^2(1) = 5.52$, $p = .019$), were less often occupied with household activities ($\chi^2(1) = 4.96$, $p = .026$), and reported a poorer quality of life at baseline (measured with one 10-point scale question: *How would you rate your quality of life?*) ($t(164) = -2.64$, $p = .009$). These variables were used as auxiliary variables for imputation fatigue and distress scores at post-assessment. The pooled mean of the imputed dataset consisting of 5 iterations, was used for the analyses.

3.2. The efficacy of eMBCT on fatigue severity and distress

Paired samples *t*-test in the ITT analysis indicated that patients experienced less fatigue severity after the intervention than before the intervention, with a large effect size (see Table 2a). Analysis of adherent patients gave comparable results (see Table 2b). The proportion of clinically relevant improved patients in the ITT analysis was 34.9% ($n = 89$) and for the adherent patients 36.8% ($n = 59$).

Concerning our secondary outcome distress, paired samples *t*-test in the ITT analysis indicated that on average, patients experienced less distress after the intervention than before the intervention with a moderate effect size (see Table 2a). The number of patients who were less fatigued after treatment was 82.5% ($n = 212$). We found that 6.5% ($n = 17$) did not respond to treatment, and 11.0% ($n = 28$) was more fatigued after treatment.

3.3. Satisfaction with eMBCT

Adherent patients who filled in the post-assessment questionnaire ($n = 133$) rated the guidance by the therapist with an average grade of 8.0 ($SD = 1.2$) on a scale from 1 to 10. Most of these patients found the duration of eMBCT (78.9%; $n = 105$), and the amount of homework adequate (66.9%; $n = 89$). Patients reported that doing the exercises (especially breathing, yoga, body scan and meditation), writing down their experiences (reflect on their thoughts, feelings and behaviors), and receiving feedback from their therapist (feeling supported, receiving mild, understanding feedback) were factors that were most helpful in eMBCT. Patients wrote that eMBCT had helped them by learning to accept their fatigue, recognizing which factors (situations, thoughts, feelings, behaviors) are energy giving or energy taking, letting go of energy consuming thoughts, recognizing their boundaries and pitfalls, managing communicating their boundaries with others, and accepting not being the same person as before the cancer and treatments. We asked both adherent as well as non-adherent patients to give their feedback on what they would improve about e-MBCT. This question was answered by 158 patients (25 non-adherent and 133 adherent). The majority (55.1%; $n = 87$) said the intervention did not need improvement. The following issues were suggested for improvement: a) *Usability of webpage*: Patients said it was difficult to navigate on the webpage, and the box for the log file was too small to write down long texts ($n = 27$); b) *Intensity*: Patients reported that they needed more time to do the 9-weekly intervention program, as the program was too intensive, both emotional, as well as due the many assignments they had to do ($n = 21$); c) *Guidance through the internet*: Patients said they had difficulty in explaining themselves in written words, and would prefer face-to-face contact with their therapist or contact by telephone ($n = 8$).

We asked non-adherent patients ($n = 25$) for their reason to stop using the intervention before completing 70%. Most patients stopped because they found it difficult to integrate the exercises in daily life ($n = 11$). The second most frequent reason was that the intervention was too intensive ($n = 6$). Other reasons were that fatigue had decreased or that a co-morbid illness had gotten worse, mindfulness or online help did not suit them, or that the intervention was not what they had expected.

3.4. Differences in demographics and baseline characteristics of adherent and non-adherent patients

In Tables 3a and 3b the results of the *t*-tests and χ^2 -tests are presented, with ϕ as a measure of strength of the correlation between adherence and variables that have two categories, and Cramer's *V* for variables which have more than two categories. Significant differences between adherent and non-adherent patients were found on several demographic characteristics. The group of non-adherent patients were more often depressed at baseline ($\chi^2(1) = 23.44$, $p < .001$, $V = .30$, were often more men ($\chi^2(1) = 14.79$, $p < .001$, $V = -.24$), and had lower education ($\chi^2(2) = 7.97$, $p = .019$, $V = -.18$). They had a paid job less often ($\chi^2(1) = 4.46$, $p = .035$, $V = -.13$), used sleeping medication less often ($\chi^2(1) = 3.91$, $p = .048$, $V = -.14$), and had no previous experience with mindfulness ($\chi^2(2) = 11.30$, $p = .004$,

Table 2a
Intention-to-treat analysis. Paired samples *t*-test results of baseline and post assessment fatigue severity (CIS fatigue severity subscale) and distress (HADS) of the imputed dataset.

	n	Baseline	Post assessment	*t*-test	*p*	Cohen's *d*
		M (SD)	M (SD)			
CIS–fatigue severity	257	46.53 (5.70)	33.89 (10.67)	$t(18) = 13.27$	<.001	1.45
HADS	257	15.48 (6.76)	10.90 (6.10)	$t(46) = 7.66$	<.001	0.71

CIS–fatigue severity = Checklist Individual Strength–Fatigue severity subscale; HADS = Hospital Anxiety and Depression Scale; *M* = mean (standard deviation).

Table 2b
Adherent patients. Paired samples *t*-test results of baseline and post assessment fatigue severity (CIS fatigue severity subscale) and distress (HADS) of the imputed dataset.

	n	Baseline	Post assessment	*t*-test	*p*	Cohen's *d*
		M (SD)	M (SD)			
CIS–fatigue severity	159	46.12 (5.52)	34.02 (10.70)	$t(160) = 13.37$	< .001	1.37
HADS	159	15.63 (6.66)	11.14 (5.75)	$t(561) = 7.46$	< .001	0.72

CIS–fatigue severity = Checklist Individual Strength–Fatigue severity subscale; HADS = Hospital Anxiety and Depression Scale; *M* = mean (standard deviation).

$V = -.18$). Depression at baseline has a moderate correlation, meaning there is a moderate association between depression at baseline and non-adherence. All other correlations were small.

4. Discussion

4.1. Principal results

In this study, the efficacy of an individual internet-delivered Mindfulness-Based Cognitive Therapy for the treatment of cancer-related fatigue, called eMBCT, was investigated in a clinical setting ($n = 257$). As far as we know, this is the first study to evaluate an internet-delivered individual MBCT for CRF. Fatigue severity and distress significantly decreased from baseline to post-assessment, with a high effect size of 1.45 (Cohen's *d*). Intention-to-treat analysis showed that in 34.9% of the patients, fatigue severity was clinically relevant decreased, meaning they no longer reported fatigue complaints. In 82.5% of the patients fatigue decreased post-assessment, 6.5% did not respond to treatment, and 11.0% was more fatigued after treatment.

Adherent patients (61.9%) reported that eMBCT had helped learning 1) to accept their fatigue or being the same person as before the cancer and treatments (acceptance, see Fig. 1), 2) recognizing and managing their boundaries and pitfalls (self-management), and 3) letting go of energy consuming thoughts (relaxation). Most patients were satisfied with eMBCT, though some made suggestions for improving the usability of the webpage, lowering the intensity of the intervention, and providing additional face-to-face contact or contact by telephone. Non-adherent patients said they stopped using the intervention because they found it difficult to integrate the intervention in daily life activities, and/or found the intervention too intensive. We found a moderate correlation between depression at baseline and non-adherence, therefore these patients may need to be cautiously monitored by the therapist during the intervention.

4.2. Strengths and limitations

As this study was based on data assessed in a clinical setting, our research design has several limitations. First of all, we used a design without a control group and therefore cannot control for other factors that could explain change in fatigue and distress other than the intervention. Second, a follow-up measurement is lacking. As fatigue is variable in time, a follow-up is essential for evaluating the long term effects of eMBCT. Third, the questionnaires were assessed by the same institute that provided the intervention, therefore social desirability may have influenced the results. The influence of social desirability may be less if another party would assess the pre- and post-data. Unfortunately 38.5% patients did not fill in the evaluation questionnaire, thus we could not find out their satisfaction with eMBCT. Monitoring adherent and non-adherent patients is essential to get a clear view on the overall patient's satisfaction with the intervention.

4.3. Comparison with prior work of others

As this is the first study to investigate online individual web-based MBCT for CRF, we will compare our results to other (online) mindfulness-based interventions, or other online interventions.

Our findings concerning the proportion of clinically relevant improved patients (Jacobson and Truax, 1991) is slightly greater than in group face-to-face MBCT for CRF (30%) (Van der Lee and Garssen, 2012), and individual face-to-face MBCT for depression in diabetes patients (26%) (Tovote et al., 2014). It is slightly lower than the 40% that Boettcher et al. (2014) found in their online mindfulness-based intervention for lowering severity of somatic and cognitive anxiety symptoms in patients suffering from an anxiety disorder. Yun et al. (2012) found that 56% of moderate to severely fatigued cancer survivors were clinically meaningfully improved after a web-based tailored education program. Though, they used a different fatigue severity inventory and used a different statistical method for clinically relevant improvement: they did not use the criterion that the post-assessment fatigue severity score was within the normal range. Thus their definition of clinically relevant improvement was less stringent than used in the current study and others (Van der Lee and Garssen, 2012; Tovote et al., 2014).

Our non-adherence rate of 38.1% is within the found range of a meta-analysis of face-to-face mindfulness-based interventions for several disorders (anxiety depression, chronic pain, psoriasis) (3–40%, $M = 25\%$ (8.91) (Baer, 2003). Though, our non-adherence rate is slightly higher than the results of a meta-analysis of nine web-based cognitive behavior therapies for depression and anxiety (3–34%, $M = 18\%$) (Spek et al., 2007). Also, compared to studies investigating face-to-face mindfulness-based interventions (Van der Lee and Garssen, 2012;

Table 3a
Cross tabulation of adherence and demographics.

Demographics	Adherence		χ^2	*Cramer's V*
	Adherent	Non-adherent		
Depressed (HADS ≥ 20)	40 (−2.4)	54 (3.0)	23.44*	.30
Male gender	25 (−2.1)	36 (2.6)	14.79*	.24
Living with partner	110 (−.1)	69 (.1)	0.04	.01
No paid job	61 (−.9)	46 (1.3)	4.46*	.13
High education	92 (1.1)	38 (−1.5)	7.97*	.18
Type of cancer treatment	113 (.6)	61 (−.7)	2.78	−.11
Surgery	100 (−.6)	55 (−.6)	1.48	.08
Chemotherapy	91 (.4)	51 (−.5)	0.86	.06
Radiotherapy	48 (.4)	25 (−.6)	0.75	.06
Hormonal therapy	14 (.5)	6 (−.6)	0.65	.05
Immunotherapy	10 (.5)	4 (−.6)	0.60	.05
Other				
Cancer type				
Breast	86 (.7)	43 (−.9)	2.92	.11
Blood bone marrow, Hodgkin	22 (.4)	11 (−.5)	0.41	.04
Digestive system	13 (−.2)	9 (.2)	0.07	.01
Reproductive organs	12 (−.9)	13 (1.1)	2.19	.10
Head and neck	9 (−.8)	10 (1.0)	1.77	.09
Good prognosis	99 (.6)	47 (−.8)	3.23	.12
Medicine use	42 (−.3)	10 (.5)	0.52	.05
Pain	13 (.1)	5 (−.1)	0.01	.01
Tension	29 (1.0)	5 (−1.5)	3.91*	.14
Sleep	19 (.1)	7 (−.2)	0.05	.02
Antidepressants	44 (.1)	17 (−.1)	0.03	.01
For cancer				
No previous experience with meditation	40 (−1.5)	40 (1.9)	11.30*	.24

Note. Adjusted standardized residuals appear in parentheses next to group frequencies.
* $p < .05$.

Table 3b
Demographic means for adherence.

	Adherence		*t*	*df*
Demographics	Adherent	Non-adherent		
Fatigue at baseline	46.12 (5.52)	47.19 (5.95)	−1.47	255
Age	49.29 (9.89)	51.63 (11.81)	−1.71	255
Time since cancer treatment	35.13 (41.56)	35.18 (35.58)	−.01	150

Note. * = p < .05. Standard deviations appear in parentheses next to means. *df* = degrees of freedom.

Johns et al., 2014) more patients were non-adherent in our study. It should be noted that the ease to access online interventions (such as the one evaluated in this study) may invite patients to apply, who would never usually consider accessing a psychological face-to-face intervention. Therefore online interventions may show higher non-adherence rates (Christensen et al., 2009).

We need to learn from the feedback patients gave us on the use of eMBCT. We have created a new version of eMBCT in a new ICT environment, as quite a large sample suggested improving the usability of the webpage. We launched this new version in April 2013 and expect it to be more user friendly. Regarding the intensity of the intervention, we agree that eMBCT is an intensive course. The therapists encouraged the patients to practice at least half an hour a day for six days a week, try out the new mindfulness exercises and also do some of the exercises of the weeks before, but in the same time respect their own boundaries. Better informing the patients beforehand about the intensity of the program may help decreasing disappointment, stress and non-adherence rate. As the average duration of the intervention was 16 weeks, we consider spreading the protocol over a longer time period.

5. Conclusion

These findings indicate promising possibilities for eMBCT in treatment of CRF. This pilot study involved a large sample size, the found significant decrease in fatigue severity had a high effect size, and a substantial proportion was clinically relevant improved. The results of this study are therefore informative, and suggest that individual eMBCT may be effective in reducing fatigue in cancer survivors. A randomized controlled study with a longer follow up is needed to demonstrate the effectiveness of eMBCT. Moreover, it would be valuable to investigate for which CRF patient eMBCT may be helpful in decreasing fatigue severity, and how the decrease in fatigue severity is established. Investigating the written correspondence between the therapist and the patient, would be of great value in understanding the role of the therapist and a possible variation in outcome between therapists. Currently, we are investigating the newly designed eMBCT in a three-armed randomized controlled trial funded by Alpe d'HuZes/KWF fund (Wolvers et al., in press). This trial is registered in the Dutch Trial Registry, trial number 3483: www.trialregister.nl, and results are expected in 2016.

Conflicts of interest

None of the authors are owners or employees of Internet companies that market the services described in the manuscript. Eltica de Jager Meezenbroek, Anette Pet, and Marije van der Lee have developed eMBCT. Fieke Bruggeman-Everts has outlined this manuscript, and performed the analysis. Marije van der Lee and Eltica de Jager Meezenbroek gave critical revision on this manuscript.

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Appendix A. EMBCT protocol

Overview of the e-MBCT protocol with the specific mindfulness themes of each week Van der Lee and Garssen, 2012.

Week 1: Theme: the automatic pilot, do not strive.

Information about the stress-coping model and the 'automatic pilot mode'. Introduction to 'eating with awareness' and 'body scan'. Homework: 'eating with awareness' and 'body scan'. Addition: psychoeducation about coping with stress and fatigue and cancer-related fatigue.

MP3 files: Body scan (32 min, woman)

Week 2: Theme: the body and the breath, do not judge.

Information about how to cope with pain and fatigue during the body-scan exercise and how to handle thoughts during the 'awareness of breathing' exercise. Homework: 'breathing exercise' and the 'body scan' and noticing thoughts and feelings at nice or happy moments. Addition: tips for a better sleep quality.

MP3 files: Body scan with muscle tension, Jacoben (22 min. – man), Attention to your breathing (14 min.- woman)

Week 3: Theme: accepting boundaries, acceptance.

Recognizing unpleasant experiences. Becoming aware of how one deals with physical and emotional boundaries and cultivating acceptance. Three minute exercise focusing on breathing. Homework: 'yoga exercise', 'body scan', 'breathing exercises'. Addition: psychoeducation about how to build up energy and condition after cancer.

MP3 files: Yoga (32 min. – woman), Three minute breathing exercise (4 min. – woman)

Week 4: Theme: patience, attention.

Recognizing automatic negative cognitions, recognizing daily stress inducing experiences and their emotional impact, promoting free choice how to handle daily stress. Homework: 'sitting with awareness',' walking with awareness', alternated with previous learned exercises.

MP3 files: Sitting meditation (47 min. – man), Sitting meditation (30 min. – woman)

Week 5: Theme: letting go, accept things as they are.

Learning how to cope with negative emotions through acceptation. Keeping a diary of negative emotions. Homework: 'accepting what is in the present', alternated with previous learned exercises.

MP3 files: Accepting what is in the present (23 min. – woman)

Week 6: Theme: dealing with thoughts and fear, trust.

Explanation how thoughts, behavior and emotions interact and how one can choose to stop automatic reactions. Physiology of fear. Fear of cancer recurrence. Dealing with loss. Homework: 'walking with awareness' and 'sitting with awareness', alternated with previous learned exercises.

MP3 files: Silence (20 min)

Week 7: Theme: silence and compassion, loving kindness towards oneself.

Patients plan half a day with several awareness and compassion exercises at home in silence.

MP3 files: Mountain (16 min. — woman), Lake (20 min. — woman), Lake (21 min. — man), Flower (15 min. — woman), Metta-meditation (36 min. — woman)

Week 8: Theme: seeing from a new perspective: taking good care of myself.

Participants make their own program of exercises and plan how they will continue the exercises without therapist feedback. Making a list of the top ten of helpful cognitions. Accepting stress as a part of life. Homework: practice your own program of exercises.

Week 9: Theme: from stress to inner strength.

Repetition of previous themes. Recommended literature.

Appendix B. Advertisement (in Dutch)

We informed medical doctors about the eMBCT via articles in relevant magazines, and informed patients directly by newsletters of patient associations, and via advertisements on relevant websites in the Netherlands.

Minder Moe bij Kanker

behandeling via internet bij het Helen Dowling Instituut (HDI)

Vermoeidheid is één van de meest voorkomende klachten bij kanker.
Heeft u ernstige vermoeidheidsklachten? U kunt wat doen!
Volg negen weken de training en ervaar het verschil.

Hoe werkt het?

Extreem moe zijn, kan alles overheersen. Veel energie gaat ongemerkt verloren aan niet helpende emoties, gedachten en gedragspatronen. Wat is uw energielek? Tijdens de aandachtgericht Cognitieve Therapie (aCT) leert u zich bewust te worden van automatische reacties die uw vermoeidheid versterken. Onder behandeling van uw eigen therapeut gaat u aan de slag met een vrij intensieve therapie; hou rekening met een tijdsinvestering van driekwartier per dag. Door opdrachten, oefeningen en informatie leert u in negen weken effectiever om te gaan met uw energie.

Wie behandelen u?

Het valt niet mee om automatische patronen te wijzigen. Maar u doet het niet alleen. De aCT wordt begeleid door BIG geregistreerde therapeuten, die ruime ervaring hebben in het behandelen van kankerpatiënten en het geven van aandachtgerichte Cognitieve Therapie. En het werkt. Acht op de tien deelnemers is minder moe na afloop. Bij maar liefst de helft van de deelnemers van de internettherapie is na afloop van de therapie de vermoeidheid verdwenen. Zie ook het persbericht: > Internettherapie zeer succesvol

Wanneer kunt u starten?

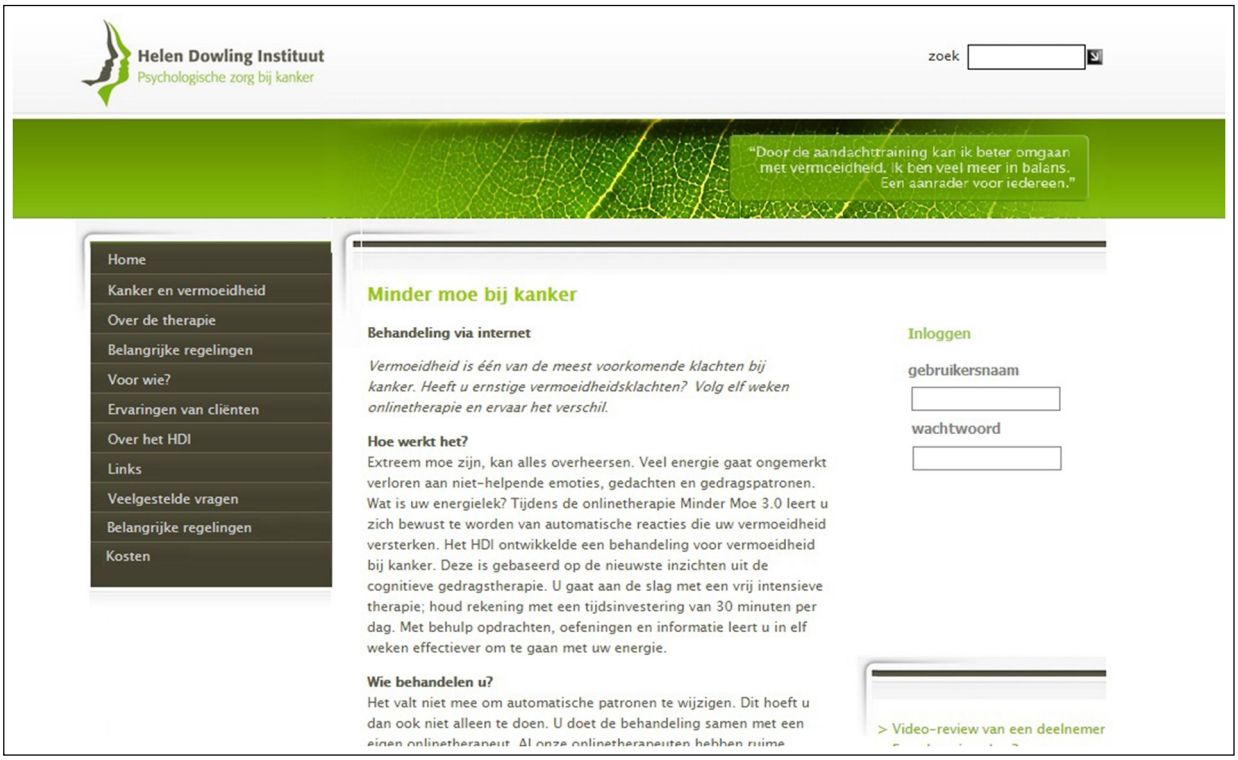
Na de aanmelding volgt nog een online intake. Als uw therapeut de behandeling voor u geschikt vindt, kunt u direct starten en werken aan uw oefeningen wanneer het u uitkomt.

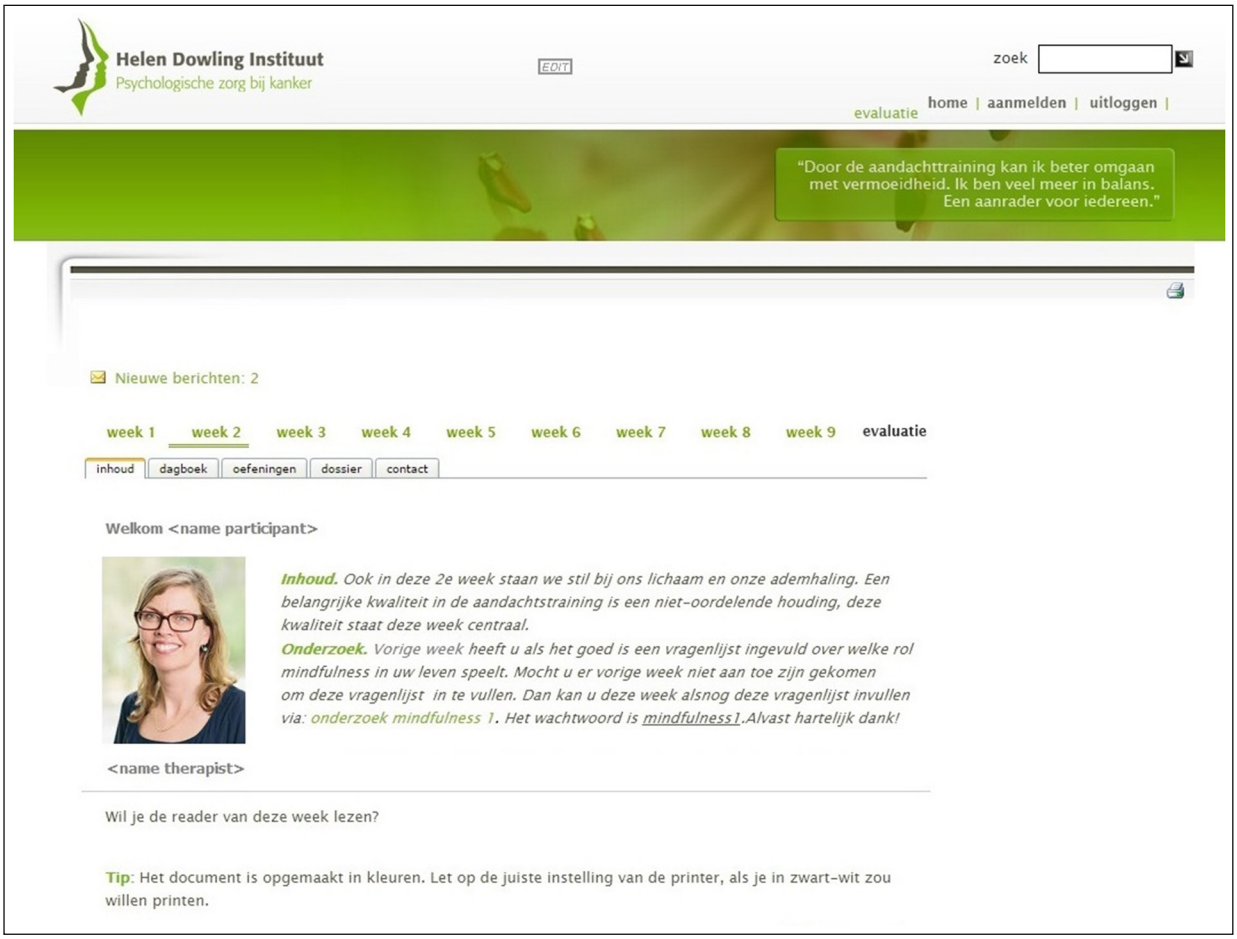
Appendix C. Case volume

In this table the number of patients treated by each therapist is shown.

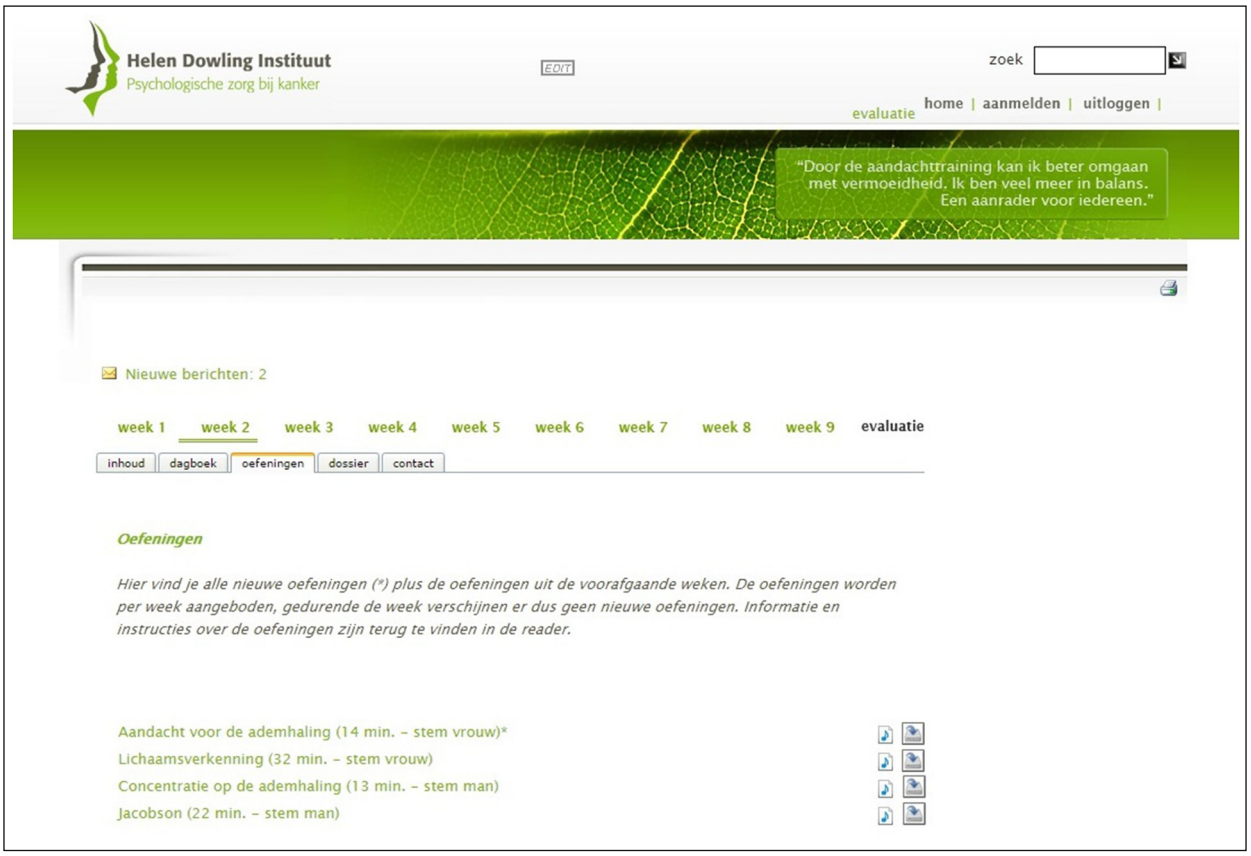
Therapist	Male/Female	*n*
Therapist 1	F	3
Therapist 2	F	6
Therapist 3	F	20
Therapist 4	F	16
Therapist 5	F	6
Therapist 6	F	47
Therapist 7	F	61
Therapist 8	M	46
Therapist 9	F	35
Therapist 10	F	14
Therapist 11	M	2

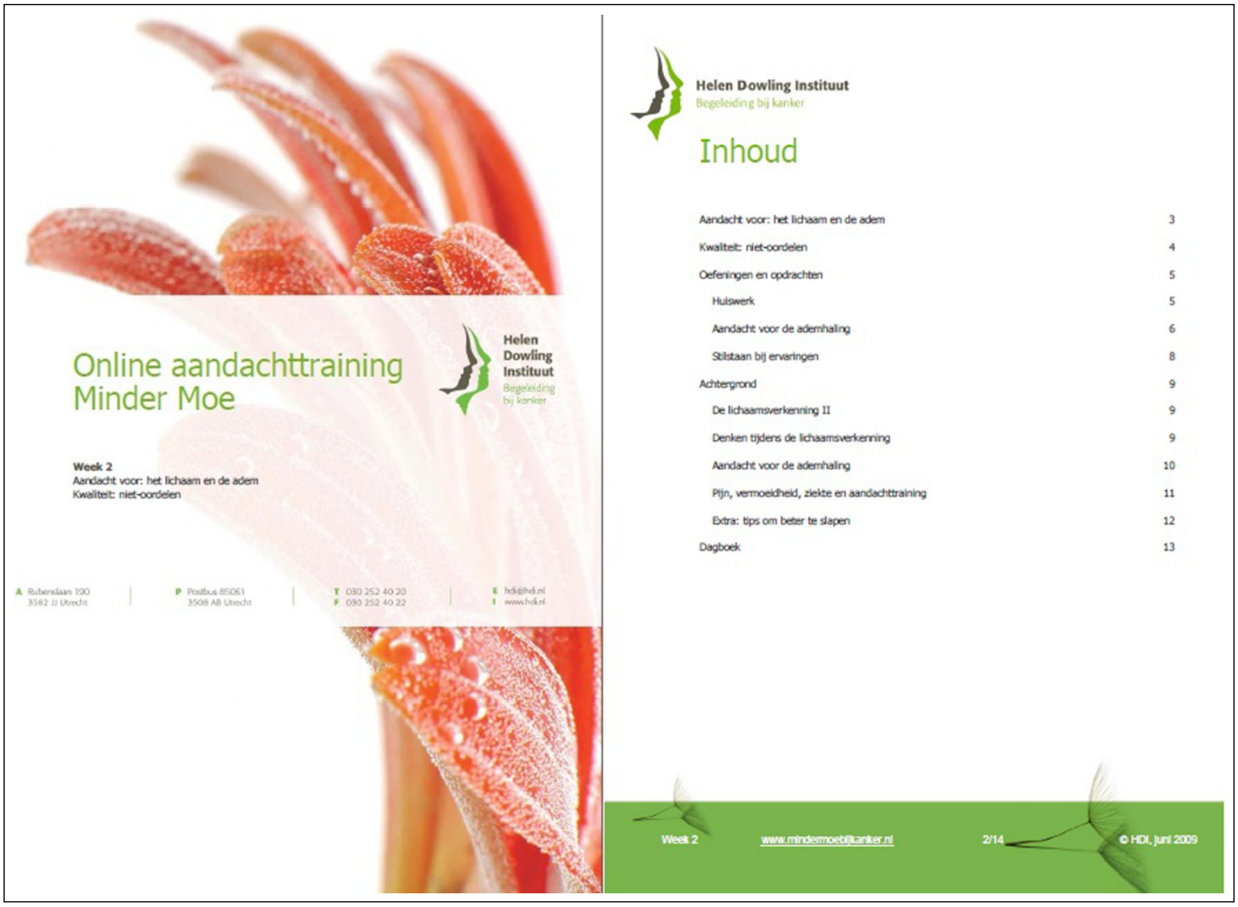
Appendix D. Screenshots of eMBCT



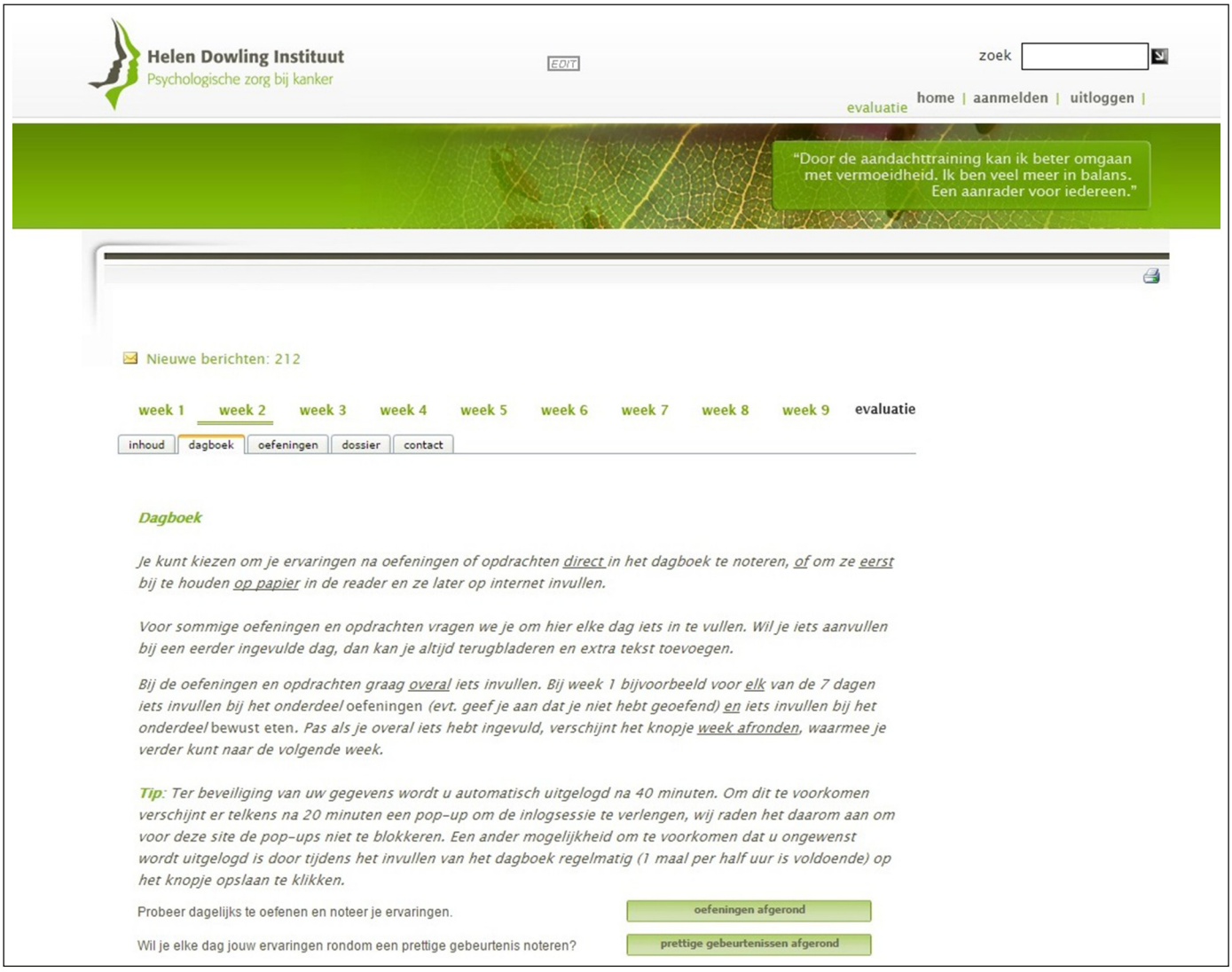


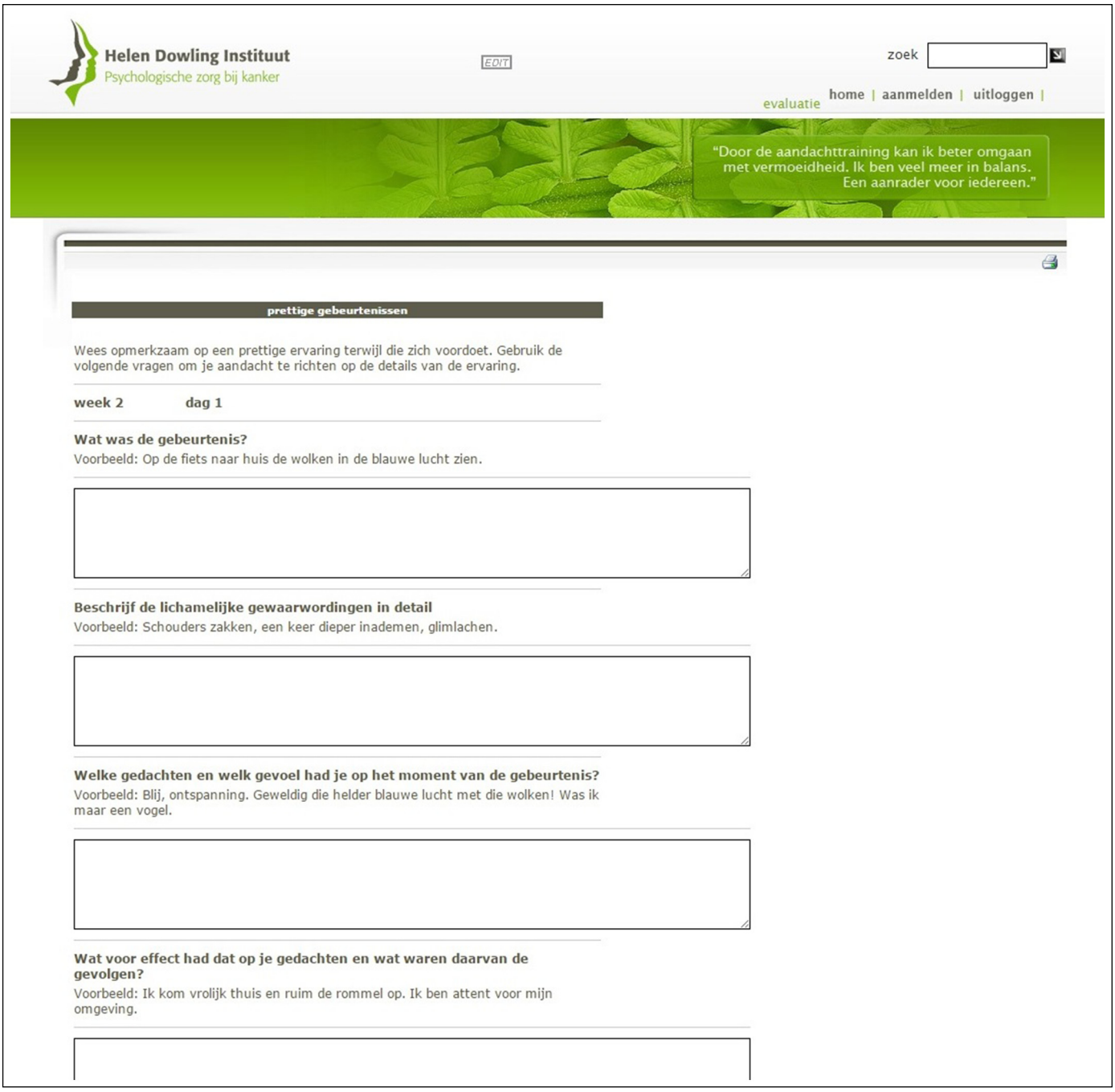
Figs. D.1 and D.2: Patients could log in on their personal password-protected webpage (D.1). where patients were introduced to the new mindfulness theme by their therapist (D.2).





Figs. D.3 and D.4: Patients downloaded mindfulness audio files (D.3), and downloaded written information following the specific mindfulness theme of the week (D.4).


Helen Dowling Instituut
Psychologische zorg bij kanker
EDIT
zoek
evaluatie
home | aanmelden | uitloggen |
"Door de aandachttraining kan ik beter omgaan met vermoeidheid. Ik ben veel meer in balans. Een aanrader voor iedereen."
Nieuwe berichten: 212
week 1 week 2 week 3 week 4 week 5 week 6 week 7 week 8 week 9 evaluatie
inhoud dagboek oefeningen dossier contact
Dagboek
Je kunt kiezen om je ervaringen na oefeningen of opdrachten direct in het dagboek te noteren, of om ze eerst bij te houden op papier in de reader en ze later op internet invullen.
Voor sommige oefeningen en opdrachten vragen we je om hier elke dag iets in te vullen. Wil je iets aanvullen bij een eerder ingevulde dag, dan kan je altijd terugbladeren en extra tekst toevoegen.
Bij de oefeningen en opdrachten graag overal iets invullen. Bij week 1 bijvoorbeeld voor elk van de 7 dagen iets invullen bij het onderdeel oefeningen (evt. geef je aan dat je niet hebt geoefend) en iets invullen bij het onderdeel bewust eten. Pas als je overal iets hebt ingevuld, verschijnt het knopje week afronden, waarmee je verder kunt naar de volgende week.
Tip: Ter beveiliging van uw gegevens wordt u automatisch uitgelogd na 40 minuten. Om dit te voorkomen verschijnt er telkens na 20 minuten een pop-up om de inlogsessie te verlengen, wij raden het daarom aan om voor deze site de pop-ups niet te blokkeren. Een ander mogelijkheid om te voorkomen dat u ongewenst wordt uitgelogd is door tijdens het invullen van het dagboek regelmatig (1 maal per half uur is voldoende) op het knopje opslaan te klikken.
Probeer dagelijks te oefenen en noteer je ervaringen.
oefeningen afgerond
Wil je elke dag jouw ervaringen rondom een prettige gebeurtenis noteren?
prettige gebeurtenissen afgerond



Figs. D.5 and D.6: On their personal log on their webpage, patients wrote down their experiences after doing the mindfulness exercises and reading the weekly information. On an agreed day of the week, the therapists replied to this log, thereby guiding the patients through the nine-week program.

References

Andersson, G., Cuijpers, P., Carlbring, P., Riper, H., Hedman, E., 2014. Internet-based vs. face-to-face cognitive behaviour therapy for psychiatric and somatic disorders: a systematic review and meta-analysis. World Psychiatry 13 (3), 288–295. http://dx.doi.org/10.1002/wps.20151.

Baer, R.A., 2003. Mindfulness training as a clinical intervention: a conceptual and empirical review. Clin. Psychol. Sci. Pract. 10 (2), 125–143. http://dx.doi.org/10.1093/clipsy.bpg015.

Bartsch, H.H., Weis, J., Moser, M.T., 2003. Cancer-related fatigue in patients attending oncological rehabilitation programs: prevalence, patterns and predictors. Onkologie 26 (1), 51–57. http://dx.doi.org/10.1159/000069864.

Berger, A., Mooney, K., Alvarez-Perez, P., et al., 2014. NCCN Clinical Practice Guidelines In Oncology: Cancer- Related Fatigue. http://dx.doi.org/10.1002/cncr.27475.

Bjelland, I., Dahl, A.A., Haug, T.T., Neckelmann, D., 2002. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J. Psychosom. Res. 52 (2), 69–77. http://dx.doi.org/10.1016/S0022-3999(01)00296-3.

Boettcher, J., Aström, V., Påhlsson, D., Schenström, O., Andersson, G., Carlbring, P., 2014. Internet-based mindfulness treatment for anxiety disorders: a randomized controlled trial. Behav. Ther. 45 (2), 241–253. http://dx.doi.org/10.1016/j.beth.2013.11.003.

Borenstein, M., Hedges, L.V., Higgins, J.P.T., Rothstein, H.R., 2009. Effect sizes based on correlations. Introduction To Meta-Analysis, pp. 21–32 http://dx.doi.org/10.1002/9780470743386 (ch6).

Bower, J.E., 2005. Prevalence and causes of fatigue after cancer treatment: the next generation of research. J. Clin. Oncol. 23 (33), 8280–8282. http://dx.doi.org/10.1200/JCO.2005.08.008.

Bower, J.E., 2008. Behavioral symptoms in patients with breast cancer and survivors. J. Clin. Oncol. 26 (5), 768–777. http://dx.doi.org/10.1200/JCO.2007.14.3248.

Brown, L.F., Kroenke, K., 2009. Cancer-related fatigue and its associations with depression and anxiety: a systematic review. Psychosomatics 50 (5), 440–447. http://dx.doi.org/10.1176/appi.psy.50.5.440.
Brown, L.F., Rand, K.L., Bigatti, S.M., et al., 2013. Longitudinal relationships between fatigue and depression in cancer patients with depression and/or pain. Health Psychol. 32 (12), 1199–1208. http://dx.doi.org/10.1037/a0029773.
Christensen, H., Griffiths, K.M., Farrer, L., 2009. Adherence in internet interventions for anxiety and depression: systematic review. J. Med. Internet Res. 11 (2), e13. http://dx.doi.org/10.2196/jmir.1194.
Cuijpers, P., van Straten, A., Andersson, G., 2008. Internet-administered cognitive behavior therapy for health problems: a systematic review. J. Behav. Med. 31 (2), 169–177. http://dx.doi.org/10.1007/s10865-007-9144-1.
Díaz, N., Menjón, S., Rolfo, C., et al., 2008. Patients' perception of cancer-related fatigue: results of a survey to assess the impact on their everyday life. Clin. Transl. Oncol. 10 (11), 753–757. http://dx.doi.org/10.1007/s12094-008-0282-x.
Duijts, S.F., Faber, M.M., Oldenburg, H.S., Van, B.M., Aaronson, N.K., 2011. Effectiveness of behavioral techniques and physical exercise on psychosocial functioning and health-related quality of life in breast cancer patients and survivors — a meta-analysis. Psychooncology 20 (2), 115–126. http://dx.doi.org/10.1002/pon.1728.
Foley, E., Baillie, A., Huxter, M., Price, M., Sinclair, E., 2010. Mindfulness-based cognitive therapy for individuals whose lives have been affected by cancer: a randomized controlled trial. J. Consult. Clin. Psychol. 78 (1), 72–79. http://dx.doi.org/10.1037/a0017566.
Gielissen, M.F.M., Verhagen, S., Witjes, F., Bleijenberg, G., 2006. Effects of cognitive behavior therapy in severely fatigued disease-free cancer patients compared with patients waiting for cognitive behavior therapy: a randomized controlled trial. J. Clin. Oncol. 24 (30), 4882–4887. http://dx.doi.org/10.1200/JCO.2006.06.8270.
Goedendorp, M.M., Gielissen, M.F.M., Verhagen, C.A., Bleijenberg, G., 2013. Development of fatigue in cancer survivors: a prospective follow-up study from diagnosis into the year after treatment. J. Pain Symptom Manag. 45 (2), 213–222. http://dx.doi.org/10.1016/j.jpainsymman.2012.02.009.
Goldstein, D., Bennett, B., Friedlander, M., Davenport, T., Hickie, I., Lloyd, A., 2006. Fatigue states after cancer treatment occur both in association with, and independent of, mood disorder: a longitudinal study. BMC Cancer 6. http://dx.doi.org/10.1186/1471-2407-6-240 (article 240).
Guttman, L., 1945. A basis for analyzing test-retest reliability. Psychometrika 10, 255–282.
Heitjan, D., Little, R., 1991. Multiple imputation for the fatal accident reporting system. J. Stat. Soc. 40 (1), 13–29. http://dx.doi.org/10.2307/2347902.
Helen Dowling Institute, 2009. www.mindermoebijkanker.nl (http://www.webcitation.org/6UN6KukON. Accessed November 26, 2014).
Herrmann, C., 1997. International experiences with the Hospital Anxiety and Depression Scale — a review of validation data and clinical results. J. Psychosom. Res. 42 (1), 17–41. http://dx.doi.org/10.1016/S0022-3999(96)00216-4.
Heutte, N., Flechtner, H.H., Mounier, N., et al., 2009. Quality of life after successful treatment of early-stage Hodgkin's lymphoma: 10-year follow-up of the EORTC-GELA H8 randomised controlled trial. Lancet Oncol. 10 (12), 1160–1170. http://dx.doi.org/10.1016/S1470-2045(09)70258-X.
Hjermstad, M.J., Fosså, S.D., Oldervoll, L., Holte, H., Jacobsen, A.B., Loge, J.H., 2005. Fatigue in long-term Hodgkin's disease survivors: a follow-up study. J. Clin. Oncol. 23 (27), 6587–6595. http://dx.doi.org/10.1200/JCO.2005.09.936.
Hofmann, S.G., Sawyer, A.T., Witt, A.A., Oh, D., 2010. The effect of mindfulness-based therapy on anxiety and depression: a meta-analytic review. J. Consult. Clin. Psychol. 78 (2), 169–183. http://dx.doi.org/10.1037/a0018555.
Jacobson, N.S., Truax, P., 1991. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J. Consult. Clin. Psychol. 59 (1), 12–19.
Jansen, L., Herrmann, A., Stegmaier, C., Singer, S., Brenner, H., Arndt, V., 2011. Health-related quality of life during the 10 years after diagnosis of colorectal cancer: a population-based study. J. Clin. Oncol. 29 (24), 3263–3269. http://dx.doi.org/10.1200/JCO.2010.31.4013.
Johns, S.A., Brown, L.F., Beck-Coon, K., Monahan, P.O., Tong, Y., Kroenke, K., 2014. Randomized controlled pilot study of mindfulness-based stress reduction for persistently fatigued cancer survivors. Psychooncology http://dx.doi.org/10.1002/pon.3648.
Koornstra, R.H.T., Peters, M., Donofrio, S., Van Den Borne, B., De Jong, F.A., 2014. Management of fatigue in patients with cancer — a practical overview. Cancer Treat. Rev. 40 (6), 791–799. http://dx.doi.org/10.1016/j.ctrv.2014.01.004.
Le Fevre, P., Devereux, J., Smith, S., Lawrie, S.M., Cornbleet, M., 1999. Screening for psychiatric illness in the palliative care inpatient setting: a comparison between the Hospital Anxiety and Depression Scale and the General Health Questionnaire-12. Palliat. Med. 13 (5), 399–407.
Ledesma, D., Kumano, H., 2009. Mindfulness-based stress reduction and cancer: a meta-analysis. Psychooncology 18 (6), 571–579. http://dx.doi.org/10.1002/pon.1400.
Meulepas, J.M., Kiemeney, L.A.L.M., Benraadt, J., 2011a. Cancer in the Netherlands until 2020. Trends and Prognoses (Kanker in Nederland Tot 2020: Trends En Prognoses). In: Van Driel, F., Knoop, L. (Eds.), Signaleringscommissie Kanker van KWF Kankerbestrijding, Vereniging van Integrale Kankercentra, Amsterdam, the Netherlands., p. 37.
Meulepas, J.M., Kiemeney, L.A.L.M., Benraadt, J., 2011b. Cancer In The Netherlands Until 2020. Trends And Prognoses (Kanker in Nederland Tot 2020: Trends En Prognoses). Signaleringscommissie Kanker van KWF Kankerbestrijding, Vereniging van Integrale Kankercentra, Amsterdam, the Netherlands, p. 39.
Miller, S.D., Duncan, B.L., Brown, J., Sparks, J.A., Claud, D.A., 2003. The Outcome Rating Scale: a preliminary study of the reliability, validity, and feasibility of a brief visual analog measure. J. Brief Ther. 2 (2), 91–100.
Mock, V., 2003. Cancer-related fatigue. In: Given, C.W., Given, B., Champion, V.L., S K, DN D (Eds.), Evidence-Based Cancer Care And Prevention: Behavioral Interventions. Springer Publishing, New York, pp. 242–273.
Nieboer, P., Buijs, C., Rodenhuis, S., et al., 2005. Fatigue and relating factors in high-risk breast cancer patients treated with adjuvant standard or high-dose chemotherapy: a longitudinal study. J. Clin. Oncol. 23 (33), 8296–8304. http://dx.doi.org/10.1200/JCO.2005.10.167.
Oerlemans, S., Mols, F., Issa, D.E., et al., 2013. A high level of fatigue among long-term survivors of non-Hodgkin's lymphoma: results from the longitudinal population-based PROFILES registry in the south of the Netherlands. Haematologica 98 (3), 479–486. http://dx.doi.org/10.3324/haematol.2012.064907.
Ott, M.J., Norris, R.L., Bauer-Wu, S.M., 2006. Mindfulness meditation for oncology patients: a discussion and critical review. Integr. Cancer Ther. 5 (2), 98–108. http://dx.doi.org/10.1177/1534735406288083.
Prue, G., Rankin, J., Allen, J., Gracey, J., Cramp, F., 2006. Cancer-related fatigue: a critical appraisal. Eur. J. Cancer 42 (7), 846–863. http://dx.doi.org/10.1016/j.ejca.2005.11.026.
Rozental, A., Andersson, G., Boettcher, J., et al., 2014. Consensus statement on defining and measuring negative effects of Internet interventions. Internet Interv. 1 (1), 12–19. http://dx.doi.org/10.1016/j.invent.2014.02.001.
Ryan, J.L., Carroll, J.K., Ryan, E.P., Mustian, K.M., Fiscella, K., Morrow, G.R., 2007. Mechanisms of cancer-related fatigue. Oncologist 12 (Suppl. 1), 22–34. http://dx.doi.org/10.1634/theoncologist.12-S1-22.
Schenker, N., Taylor, J., 1996. Partially parametric techniques for multiple imputation. Comput. Stat. Data Anal. 22 (4), 425–446. http://dx.doi.org/10.1016/0167-9473(95)00057-7.
Servaes, P., Prins, J., Verhagen, S., Bleijenberg, G., 2002a. Fatigue after breast cancer and in chronic fatigue syndrome: similarities and differences. J. Psychosom. Res. 52 (6), 453–459.
Servaes, P., Verhagen, C., Bleijenberg, G., 2002b. Fatigue in cancer patients during and after treatment: prevalence, correlates and interventions. Eur. J. Cancer 38, 27–43.
Servaes, P., Verhagen, S., Bleijenberg, G., 2002c. Determinants of chronic fatigue in disease-free breast cancer patients: a cross-sectional study. Ann. Oncol. 13 (4), 589–598. http://dx.doi.org/10.1093/annonc/mdf082.
Servaes, P., Verhagen, S., Schreuder, B., Veth, R.P.H., Bleijenberg, G., 2003. Fatigue after treatment for malignant and benign bone and soft tissue tumors. J. Pain Symptom Manag. 26, 1113–1122. http://dx.doi.org/10.1016/j.jpainsymman.2003.03.001.
Sijtsma, K., Emons, W.H.M., 2011. Advice on total-score reliability issues in psychosomatic measurement. J. Psychosom. Res. 70 (6), 565–572. http://dx.doi.org/10.1016/j.jpsychores.2010.11.002.
Smets, E.M., Garssen, B., Schuster-Uitterhoeve, A.L., de Haes, J.C., 1993. Fatigue in cancer patients. Br. J. Cancer 68 (2), 220–224. http://dx.doi.org/10.1038/bjc.1993.319.
Smets, E.M., Garssen, B., Bonke, B., De Haes, J.C., 1995. The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. J. Psychosom. Res. 39 (3), 315–325. http://dx.doi.org/10.1016/0022-3999(94)00125-O.
Smets, E.M., Garssen, B., Cull, A., De Haes, J.C., 1996. Application of the Multidimensional Fatigue Inventory (MFI-20) in cancer patients receiving radiotherapy. Br. J. Cancer 73 (2), 241–245. http://dx.doi.org/10.1038/bjc.1996.42.
Spek, V., Cuijpers, P., Nyklíček, I., Riper, H., Keyzer, J., Pop, V., 2007. Internet based cognitive behaviour therapy for symptoms of depression and anxiety: a meta analysis. Psychol. Med. 37 (3), 319–328. http://dx.doi.org/10.1017/S0033291706008944.
Spinhoven, P., Ormel, J., Sloekers, P.P., Kempen, G.I., Speckens, A.E., Van Hemert, A.M., 1997. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. Psychol. Med. 27 (2), 363–370.
Storey, D.J., McLaren, D.B., Atkinson, M.A., et al., 2012. Clinically relevant fatigue in recurrence-free prostate cancer survivors. Ann. Oncol. 23 (1), 65–72. http://dx.doi.org/10.1093/annonc/mdr034.
Studio2 Communications BV, 2015. www.studio2.nl (http://www.webcitation.org/6WdGMH05g. Accessed February 26, 2015).
Stulemeijer, M., de Jong, L.W., Fiselier, T.J., Hoogveld, S.W., Bleijenberg, G., 2005. Cognitive behaviour therapy for adolescents with chronic fatigue syndrome: randomised controlled trial. BMJ 330, 14 (1468-5833 (Electronic)).
Tovote, A.K., Fleer, J., Snippe, E., et al., 2014. Individual mindfulness-based cognitive therapy and cognitive behavior therapy for treating depressive symptoms in patients with diabetes: results of a randomized controlled trial. Diabetes Care 37 (9), 2427–2434. http://dx.doi.org/10.2337/dc13-2918.
Van der Geest, I.C.M., Knoop, H., Veth, R.P.H., Schreuder, H.W.B., Bleijenberg, G., 2013. High fatigue scores before and after surgical treatment of bone and soft tissue tumors. Exp. Ther. Med. 5 (1), 205–208. http://dx.doi.org/10.3892/etm.2012.786.
Van der Lee, M.L., Garssen, B., 2012. Mindfulness-based cognitive therapy reduces chronic cancer-related fatigue: a treatment study. Psychooncology 21 (3), 264–272. http://dx.doi.org/10.1002/pon.1890.
Vercoulen, J.H.M.M., Swanink, C.M.A., Fennis, J.F.M., Galama, J.M.D., van der Meer, J.W.M., Bleijenberg, G., 1994. Dimensional assessment of chronic fatigue syndrome. J. Psychosom. Res. 38, 383–392.
Vercoulen, J.H.M.M., Alberts, M., Bleijenberg, G., 1999. De Checklist Individual Strength (CIS). Gedragstherapie 32, 131–136.
Wagner, L.I., Cella, D., 2004. Fatigue and cancer: causes, prevalence and treatment approaches. Br. J. Cancer 91 (5), 822–828. http://dx.doi.org/10.1038/sj.bjc.6602012.
Wolvers, M.D.J., Bruggeman-Everts, F.Z., Lee, M.L. van der, Vollenbroek-Hutten, M.M.R., et al., 2015. Effectiveness, mediators, and effect predictors of internet interventions for chronic cancer-related fatigue: the design and an analysis plan of a three-armed randomized controlled trial. J Med Internet Res — Res Protoc. http://dx.doi.org/10.2196/resprot.4363 (in press).
Yun, Y.H., Lee, K.S., Kim, Y.-W., et al., 2012. Web-based tailored education program for disease-free cancer survivors with cancer-related fatigue: a randomized controlled trial. J. Clin. Oncol. 30 (12), 1296–1303. http://dx.doi.org/10.1200/JCO.2011.37.2979.
Zigmond, A.S., Snaith, R.P., 1983. The Hospital Anxiety and Depression Scale. Acta Psychiatr. Scand. 67 (6), 361–370.