Effects of Internet Training in Mindfulness Meditation on Variables Related to Cancer Recovery

by

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ABSTRACT

Cancer survivors engaged in either six-week Internet-delivered mindfulness training or a usual-care control and were compared on the following outcome battery: The Hospital Anxiety and Depression Scale, the Profile of Mood States, the Pittsburgh Sleep Quality Index, and the Fatigue Symptom Inventory. Assessments were conducted before and after treatment and intervention compliance was monitored. Mindfulness treatments were delivered at a time and on a computer of the participants' choosing. Multivariate analysis indicated that mindfulness training produced significant benefits on all measures ($p <$ .05). Online mindfulness instruction represents a widely-accessible, cost-effective intervention for reducing psychological distress and its behavioral manifestations in cancer survivors, especially those who are unable to participate in in-person training.

To my father and mother, who have shown me how to persevere throughout difficult circumstances, including cancer.

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CHAPTER 1

EFFECTS OF INTERNET TRAINING IN MINDFULNESS MEDITATION ON VARIABLES RELATED TO CANCER RECOVERY

Receiving a diagnosis of cancer is stressful and in some cases can be perceived as life-threatening. As a result, many patients experience depression, anxiety, and fatigue (Cella, Lai, Chang, Peterman, & Slavin, 2002; de Haes & van Knippenberg, 1985; Derogatis et al., 1983). On a psychological level, patients may experience worries about the future, change in social roles, limitations in physical functioning, and fears about managing symptomology (Burg et al., 2015; Christiansen et al., 2009; Honda & Goodwin, 2004). Biologically, prolonged stress and cancer-related treatments can induce dysregulation of the immune and neuroendocrine systems and a constellation of "sickness-related" symptoms including sleep disturbance, fatigue, depression and cognitive impairment (Miller, Ancoli-Israel, Bower, Capuron, & Irwin, 2008; Ryan et al., 2007). For a significant minority of patients, such symptoms persist for years into remission and survivorship (Bower, 2008; Cella, et al., 2002), lowering quality of life and increasing risk of additional medical problems, possibly even recurrence (Kjaer et. al., 2001; Miller et al., 2008). Methods of reversing chronic stress and reestablishing healthy biorhythms are needed. Mindfulness-based treatments—previously found to reduce stress and mitigate negative mental states (Grossman, Neimann, Schmidt, & Walach, 2004)—have been suggested (Pavlov & Tracey, 2005) and seen increasing use.

Stress and Immunity

Stress can be defined as the body's response to an event that changes or threatens to change its homeostasis. Uncomfortable emotions and physical sensations act as motivation to resolve such threats (Levine & Ursin, 1991). When stressed, the body enables survival-related action by releasing hormones, such as Corticotropin releasing hormone (CRH), that activate the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system (SNS. Lopez, Akil, & Watson, 1999). This activation triggers further hormone secretion, including epinephrine and norepinephrine, which increases heart rate, blood pressure and arousal (Raison & Miller, 2001).

In response to acute stress, the immune system is mobilized to fight possible infection (Sapolsky, 2004). While such activation is adaptive in the short term, chronic immune response poses health risks, heightening risk for autoimmune disease development (Davidson & Diamond, 2001; Sapolsky, Romero, & Munck, 2000) and eventually damaging organs and tissues (Mariotti, 2015). To reduce these risks, the body generates immunosuppressive mechanisms alongside activating ones (Raison & Miller, 2001). For instance, while CRH activates cytokine production, stimulating inflammation and blood flow, it also leads to production of glucocorticoids (including cortisol), which act chiefly as immunosuppressants (Coutinho & Chapman, 2011). In the case of short-lived stressors, this suppression simply returns the immune system to its baseline functioning, and even hones its effectiveness by eliminating older and less effective white blood cells (Sapolsky, 2004). However, when stress persists, immune functioning is

suppressed beneath baseline levels, increasing vulnerability to many diseases, including cancer (Dhabhar, 2009).

This feedback loop of arousal and suppression is expressed behaviorally, as well, allowing the organism to either meet, or retreat from, a stressful situation. HPA-axis activation causes anxiety, hyper-vigilance, and sleep disruption, preparing active coping (Vgontzas et al., 2001). However, when the hypothalamus and vagus nerve detect ongoing elevated cytokine levels (indicating continued immune response), they induce depression, fatigue, and cognitive impairment (Breedlove, Watson & Rosenzweig, 2010), prompting reduction in physical activity and an attempt to reestablish baseline neuroendocrine functioning through rest (Hart, 1988).

While each of the aforementioned behavioral symptoms harms quality of life, disrupted sleep-wake rhythm is a key risk factor in cancer progression (Sephton & Spiegel, 2003). The hormone melatonin, created only during night-time sleep, counteracts incipient tumor creation, and its absence impairs T-cells and reduces anti-cancer cytokine levels (Blask, 2009). Unsurprisingly, shift-workers are at increased risk for a variety of cancers, including breast, colon, prostate and endometrial (Schernhammer et al., 2003; Kubo, Ozasa, Mikami, Wakai & Fujino, 2006 Schernhammer, Kroenke, Laden & Hankinson, 2006; Viswanathan, Hankinson, Schernhammer, 2007). Other individuals with disrupted cortisol and sleep-wake patterns evidence similar cancer risks (Sephton, Sapolsky, Kraemer & Spiegel, 2000; Sephton et al., 2013)

In summary, chronic stress is detrimental and the body employs biological, and resulting behavioral, mechanisms to relieve it. For cancer survivors, however, stress is

often not caused by an external (objective) stressor that can be surmounted or avoided, but by the ongoing, subjective, fear of recurrence (Allen, Savadatti, & Levy, 2009; Koolhaas et al., 2015). Effective coping, therefore, must therefore include adaptation not only to external events, but to the internal experience of anxiety. Mindfulness-based treatments, designed to help individuals cope with distressing thoughts and feelings, are uniquely suited to this need. Before discussing these treatments, let us examine more fully the sources of stress that cancer survivors experience.

Cancer Survivorship

Cancer patients experience heightened stress for a number of reasons. First, biologically, the presence of the disease impels an immune response to find and destroy tumors (Breedlove, Watson & Rosenzweig). In addition, treatments such as chemotherapy, radiation and surgery have variable effects, at times suppressing and at others inciting immune response, but throughout, taxing the body's resources (Abbas & Lichtman, 2010; Scholl, Bekker & Babu, 2012, Miller et al., 2008). Finally, conditions comorbid with cancer and its treatment, such as anemia, further contribute to physiological stress (Bower, 2008; Stein, Syrjala, & Andrykowski, 2008).

Psychological stressors can be prominent and persistent throughout the course of the disease as well. Fear of death, change in social roles, and limitations in physical functioning all cause worry and may be sufficient to produce a persistent SNS and immune response (Bower, 2007; Ganz, 2009).

Even when cancer no longer poses a threat to life, the transition from cancer patient to survivor can be challenging. Survivors may feel they have lost their "action

plan" for combating the disease (Allen, Savadatti, & Levy) and the support of fellow patients with whom they are now in less frequent contact (Arnold, 1999). In addition, many survivors report feeling pressured to resume work and "life as usual" before they have integrated the psychological impact of their experience (Tesauro, Rowland, & Lustig, 2002). Further, reduced medical visits leave survivors with increased responsibility for monitoring their physical condition and heightened vigilance about symptoms and the possibility of recurrence (Cordova et al., 1995).

Fear of recurrence is almost universal and can be triggered by symptoms that are unexplained or similar to the previous cancer experience (Allen, Savadatti, & Levy). Unfortunately, this fear can activate the SNS, leading to the release of stress hormones and further inducing the feared physical symptoms (Rabin, 1999). Interrupting the cycle of worry and symptomology is imperative for helping survivors achieve a life free from both cancer and its specter. Mindfulness based treatments (MBTs) offer hope for breaking this cycle.

Before discussing treatments, it is important to note that research linking stress, immune activation and medical outcomes has focused predominantly on patients with breast cancer, due to the prevalence of the condition (see Bower, 2007 for a review). Researchers must be wary of generalizing treatments for one type of cancer to others, since the biology of diverse cancers (and to some extent, even cancers in the same site) can vary considerably (Weinberg, 2013). Despite these biological differences, considerable evidence suggests that the stress response is similar across diverse cancer survivors, as are the reasons for this stress (Crist & Grunfeld, 2013). The current study

focuses on the stress of the cancer and survivorship experience and its reduction, and therefore includes survivors of diverse cancer type.

Mindfulness Based Treatments

Derived from Buddhist meditation practices, Mindfulness-based treatments (MBTs) teach individuals to tolerate psychological distress, reduce rumination and calm anxiety. Meditators are instructed to accept their thoughts, feelings and sensations and abstain from attempting to change, judge or mentally elaborate on their internal experience. Further, they are asked to maintain a sense of curiosity and sensitivity to the uniqueness of the particular moment, and to refocus on the current moment if their attention wanders (Bishop et al., 2004; Linehan, 1993). MBTs can include additional mental training, as in the case of Mindfulness Based Cognitive Therapy (MBCT, Segal, Williams & Teasdale, 2002) or gentle physical exercise, as in Mindfulness Based Stress Reduction (MBSR, Kabat-Zinn, 1982) to help patients regulate emotions and release physical tension. MBTs do not require acceptance of a particular religious worldview, but rather act as a skill set that can be used to cope with daily stressors throughout the course of a chronic disease.

Such skills may benefit cancer survivors, for a number of reasons. First, personality research has demonstrated a small but consistent link between repressive/avoidant coping style and increased glucocorticoid levels and speed of mortality, once diagnosed with cancer (Baltrusch, Stangel, & Titze, 1991). Hence, mindfulness, which teaches individuals to accept and observe distress rather than avoid it, may be of benefit. Second, viewing one's physical symptoms without reactivity or

judgment may inhibit otherwise frequent worries about recurrence. Third, mindfulness practice offers a method of improving health once conventional treatments have ceased, which may confer a sense of perceived control over one's recovery (Andreu et al., 2012; Marshall, 2012). Fourth, on a physiological level, the autogenic training inherent in the practice, involving synchronization of breath, touch, and attention (Schultz & Luthe, 1959), has been found to calm hyper-arousal and hypertension (Astin, Shapiro, Eisenberg, & Forys, 2003; Linden & Chambers, 1994), reduce stress hormones (Gaab et al., 2003; Kamei et al., 2000), improve phagocytic efficacy (Peavey, Lawlis, & Goven, 1985) and facilitate processing of stressful life events (van der Kolk, 2000. For a full review of the effects of mind-body therapies on cancer and immunity, see Larkey, Greenlee, & Mehl-Madrona, 2005). Finally, increases in attention, intelligence and cognition associated with mindfulness practice (Sedlmeier, 2012) may counteract cognitive impairment and improve one's ability to manage his or her recovery.

Mindfulness-Based Stress Reduction is the most thoroughly researched cancer care MBT. In randomized controlled trials, patients with diverse cancer types have shown improved emotion regulation and stress management capability (Labelle, Campbell, Faris & Carlson, 2015; Rush & Sharma, 2017) reductions in anxiety and depression (Piet, Wurtzen, & Zachariae, 2012), sleep disturbance (Lengacher et al., 2015; Shapiro, Bootzin, Fiueredo, Lopez, & Schwartz, 2003), fatigue (Johns et al., 2015; Speca, Carlson, Goodey & Angen, 2000), and physical complaints (Monti et al., 2006), and enhanced quality of life (Musial, Bussing, Huesser, Choi & Ostermann, 2011), cognition (Johns et al., 2016), self-kindness (Boyle et al., 2017), and post-traumatic growth (Shiyko,

Hallinan, & Naito, 2017), with some evidence that improvements may persist over time (Carlson et al, 2016). Improvements in immune response and disease markers are beginning to be found (Bower et al. 2015; Carlson et al, 2015) though the majority of studies have not found such changes (Ledesma & Kumano, 2009; Matchim, Armer, & Stewart, 2011). Continued investigation in this area is warranted.

MBSR consists of eight weekly group meetings and a day-long retreat, totaling 26 hours of in-person instruction (Carmody & Baer, 2009). While beneficial, this treatment's time requirements may be too extensive for patients managing complex treatment protocols or survivors reclaiming the responsibilities of daily life. A more convenient delivery mode may increase use and thereby improve outcomes. Self-guided mindfulness training, presented over the internet, is one such possibility.

Only two studies have examined the feasibility of online mindfulness training for cancer patients. Participants in Altschuler, Rosenbaum, Gordon, Canales, & Avins (2011) listened daily to 20-minute guided meditations over three months and showed improvements in anxiety, depression and quality of life. This initial, exploratory study lacked a comparison group and had limited compliance from self-selected patients. Still, positive participant feedback and the potential to scale the asynchronous (non-live) intervention's effects warrants further investigation.

Zernicke et al. (2014), meanwhile, provided a synchronous (real-time), practitioner-led MBSR program consisting of eight two-hour trainings and a six-hour online retreat. Compared with treatment-as-usual, the training improved mood, stress, and spirituality, and subsequent analysis revealed benefits for some subgroups of participants

(Zernicke, Campbell, Speca, Ruff, & Flowers, 2016). Moreover, attrition—a common issue in online interventions—was low. However, mindfulness itself was inconsistently affected by the intervention, drawing into question the theoretical basis for improvements on the primary outcome variables. Research to rule out nonspecific group effects appears warranted. In addition, few if any studies have investigated behavioral or physiological outcomes resulting from online cancer-care MBTs.

Self-guided and Internet-delivered mindfulness training, while new to cancer treatment, has a small but growing literature base with healthy adults and those suffering other ailments, and its effects rival in-person training. In Wolever et al. (2012), adults dealing with workplace stress received 12 weeks of either traditional group or internet-based mindfulness training. The two conditions showed similar improvements on perceived stress, mindfulness, and sleep quality when compared to wait-list controls and the internet condition showed lower attrition and improvement in heart rate variability. Online mindfulness training, combined with other elements, has led to symptom improvement in heart disease (Younge et al., 2015), irritable bowel syndrome (Ljottson et. al., 2010, 2011), epilepsy (Thompson et al., 2010), depression (Meyer et al., 2009) and chronic pain (Dowd et al., 2015). Training though media such as books, CDs and automated phone calls, has led to improvements in emotional and physical health of the elderly (Zatura et al., 2012), clinically anxious outpatients (Herzberg et al., 2012), and those treated for psoriasis (Kabat-Zinn et al., 1998).

Online mindfulness training may be a convenient and cost-effective method of reducing stress for cancer survivors experiencing depression, anxiety, sleep disturbance,

and fatigue. The current study is a randomized controlled trial assessing psychological and behavioral outcomes in this population.

Method

Participants

Eleven participants were recruited through researcher announcements at major cancer hospitals, including Cancer Treatment Centers of America and Banner Health in central Arizona and southern Wisconsin. Ten additional participants were recruited via the survey firm, Qualtrics. Seventy-six percent identified as female, and 80% as white, with a mean age of 51.0 years. No incentive was offered for study completion. Rather, participation, and mindfulness meditation more broadly, were presented as a method of coping with daily stressors and reentry into post-treatment life. Eligibility criteria are listed in Appendix A.

Procedure

Interested participants were directed to visit the study website from a personal computer. Upon arrival at the website, participants created an identification/login code, provided informed consent and were screened for eligibility—including age, disease and treatment history, and computer literacy—all online. Eligible participants were randomly assigned to treatment or care-as-usual condition, provided directions for study completion, and prompted to take pre-intervention assessments. Ineligible participants were thanked and provided access to the mindfulness intervention and additional mindfulness-related web resources.

Participants in the treatment condition were asked to engage in daily guided mindfulness exercises, available on the website, at a time and place of their choosing. Treatment compliance was tracked by users clicking on a link after listening to each exercise. This link appeared only after an exercise finished playing and, if not clicked within ten minutes, disappeared. Participants in the usual care condition were not asked to complete any exercises.

Participants received one "welcome" email after registering for the study and one "thank you" email six weeks later, prompting them to complete their post-assessments. Following study completion, all participants were provided access to the mindfulness intervention.

Mindfulness training included six guided meditation audio clips and brief textual lessons, based on Kabat-Zinn's (1982) Mindfulness-Based Stress Reduction curriculum. Each week, a new exercise and lesson were presented. Participants were asked to read the lesson and listen, daily, to the exercise. The first exercise guided participants in noticing their surroundings through sight, hearing, and touch. In week two, participants performed the body scan, focusing on and relaxing areas of the body. In week three, participants were led to observe their thoughts, emotions and impulses with acceptance. Week four provided instruction in breath awareness, week five in loving-kindness meditation, and week six in integrating mindfulness practice into daily life. Exercises range from 8 to 17 minutes in length, with an average duration of 12 minutes.

Unlike standard MBSR, our mindfulness treatment involved no meditative movement. Including such movement in a mindfulness curriculum, while likely

therapeutic (Carmody & Baer, 2008; Smith & Pukall, 2009), risks confounding the benefit of exercise with that of mindfulness. Similarly, our treatment provided no training in assertiveness and conflict resolution, as MBSR does. Such training, though potentially useful for cancer survivors (Hinnen, Hagedoorn, Ranchor, & Sanderman, 2008), seemed outside the scope of a basic mindfulness curriculum. The current study aimed to examine the effect of mindfulness practice independent from additional fortifying elements.

Usual care control condition participants were asked to complete all pre and post-assessments but were not asked to complete any exercises.

Measures

The Hospital Anxiety and Depression Scale (HADS, Zigmond & Snaith; 1983) is a 14-item Likert measure frequently used to assess psychological distress in individuals with cancer. Patients endorse statements regarding their past week, such as "I feel tense or wound up," on a 4-point scale ranging from 0 (*Not at all*) to 3 (*Most of the time*). Anxiety and depression subscales each yield scores from 0-21, with higher scores indicating greater strain. Scores from 0-7 are considered "normal," 8-11 "mild," 11-14 "moderate," and 15-21 "severe." These subscales are then summed to provide a full-scale score of overall distress.

Depression and anxiety are important indicators of well-being for cancer survivors, and amenable to change via mindfulness practice (Piet, Wurtzen, & Zachariae, 2012). As such, the HADS was the primary instrument used to screen patients for study inclusion. In analysis of past studies, the optimal point for discerning clinical disorder was found to be a score of 8 on both the anxiety and depression subscales. To avoid

possible floor effects and measure this intervention's effects on those in need of treatment, the inclusion criterion were set at this score. This device has shown strong concurrent validity and internal consistency and a stable factor structure across ages and genders (Bjelland, Dahl, Haug, & Neckelmann, 2002).

The Profile of Mood States-Short Form (POMS-SF, Shacham, 1983) is a shortened version of the original, 65-item instrument (McNair, Lorr & Droppelman, 1971) used to assess quality of life and mood variation in cancer patients. In this 37-item instrument, patients rate the presence of current feelings (e.g. "Lively," "Listless" etc.) on a 5-point scale anchored by 1 (*Not at all)* and 5 (*Extremely)*. Six subscales measuring Tension-Anxiety, Depression-Dejection, Anger-Hostility, Fatigue-Inertia, Vigor-Activity, and Confusion-Bewilderment sum to yield a Total Mood Disturbance score. In clinical populations studied, correlations between POMS short and long form scales exceeded .95, with subscale internal consistencies ranging from Cronbach's alpha .78-91 (Baker, Denniston, Zabora, Polland & Dudley, 2002) and concurrent and discriminant validity demonstrated for both physical and mental symptoms (Curran, Andrykowsky, & Studts, 1995).

The Pittsburgh Sleep Quality Index (PSQI, Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) is a 19-item self-report instrument measuring seven components of sleep: subjective quality, latency, duration, efficiency, disturbance, use of medication, and daytime dysfunction. Component scales sum to yield a total sleep quality score, ranging from 0-21 with higher scores indicating poorer sleep quality. The PSQI has been

found to accurately differentiate between people with and without clinical sleep disorders and shows acceptable reliability and validity in clinical populations (Buysse et al., 1989).

The Fatigue Symptom Inventory (FSI, Hann et al., 1998) was developed for use with cancer patients and measures fatigue duration (two items) severity (four items) and interference with quality of life (seven items). Participants are asked to respond to questions such as "Rate how much, in the past week, fatigue interfered with your mood," on 11-point scales ranging from 0 (*not at all fatigued/no interference*) to 10 (*as fatigued as I could be/extreme interference*). Items are summed to yield total subscale scores. In addition, we calculated an overall fatigue score by computing the average on each subscale and summing these scores. The FSI has been validated on patients with diverse cancer diagnoses, stages of treatment, ages and genders. It has demonstrated convergent validity with previously established fatigue measures and acceptable test-retest reliability (Hann, Denniston, & Baker, 2000).

Research Questions and Hypotheses

This study examines the question: Can internet-delivered mindfulness training reduce stress in cancer survivors? If so, this reduction should be discernable through improvements in symptoms that result from such stress, including depression/anxiety, mood disturbance, sleep disturbance, and fatigue. Therefore, we hypothesize that treatment condition participants, when compared pre to post with usual care participants, will evidence: 1) Reduced anxiety and depression, as measured by the HADS (Zigmond & Snaith), 2) Reduced total mood disturbance as measured by the POMS-SF (Shacham),

3) Reduced sleep disturbance, as measured by the PSQI (Buysse et al.), and (4) Reduced fatigue, as measured by the FSI (Hann et al.).

Results

Preliminary Analyses

Pretreatment equivalence. Analyses of variance (ANOVAs) conducted on pretest scores of all participants who provided posttest data found no differences on any measure. Participants, thus, appeared equivalent at the start of the study.

Attrition. Of 56 pretested participants, 21 (38%) completed treatment and posttesting. Dropout from the two conditions was essentially equivalent (37% for the treatment, 39% for care-as-usual).

Reliabity. Pretest internal consistencies on the HADS, POMS FSI, PSQI were .82, .93, .90, .77, and respectively.

Statistical power. Meta-analyses suggest that mindfulness training with cancer patients confers an effect of about Hedge's g = .4 for anxiety, depression, and mood. Analysis conducted using G*Power 3.1 (Faul, Erdfelder, Lang & Buchner, 2007) suggests that 42 participants were needed to yield sufficient power (i.e., > .8) to detect effects at an alpha level of .05.

Recruitment of participants was gradual, permitting ongoing analysis of potential outcome effects. At midpoint in the recruiting process, it became apparent that the treatment was highly successful. We thus cancelled study recruitment and assigned all further interested participants to the active treatment.

Treatment Effects

Appendix B presents the means and standard deviations of each condition at pre and posttest.

Repeated measures multivariate analysis of variance (RM MANOVA) was performed on pre and posttreatment outcome measures of the HADS, POMS, FSI, and PSQI. Assumptions of normality and sphericity were checked and met. A treatment condition by time interaction was found, indicative of differential improvement, over time, attributable to condition membership, $F(4, 16) = 4.98$, $p < .01$. Subsequent univariate RM ANOVAS found that, for each variable studied, mindfulness training conferred more benefit than care-as-usual. Effect sizes appropriate for correlated samples designs are notated below by g_{av} (Lankin, 2013).

Consistent with this study's hypothesis, mindfulness training appeared to reduce anxiety and depression, as measured by the full-scale HADS $F(1, 19) = 7.33$, $p < .05$, $g_{av} = .64$ and total mood disturbance, as measured by the POMS $F(1, 19) = 4.67$, $p < .05$ $g_{av} = .67$. In addition, mindfulness-training participants reported large improvements on sleep, as measured by the PSQI $F(1, 19) = 12.44$, $p < .01$, $g_{av} = 1.14$ and fatigue, as measured by the FSI $F(1, 19) = 5.96$, $p < .05$, $g_{av} = 1.03$.

Treatment Adherence

Mindfulness-training participants completed an average of 13.0 exercises over the course of the study, or approximately two per week. Two-thirds of participants engaged with the treatment on a weekly basis or more frequently. Pearson product-moment correlations indicated that for all variables, greater exercise completion was related to

improved outcomes, either significantly or marginally (HADS, $p < .05$, $r = -.45$; POMS, $p < .01$, $r = -.56$; PSQI, $p < .05$, $r = -.39$; FSI, $p < .07$, $r = -.34$).

Exploratory Subscale Analyses

Our hypotheses specifically and exclusively concerned outcome effects on the total scores of all measures. Such effects occurred and reflect strong promise for Internet delivered mindfulness training in cancer recovery.

Each of the four measures used in this study are composed of subscales that vary in psychometric strength, within themselves and among the battery of devices. Exploratory univariate analyses were conducted on the subscales of each measure to examine the possibility that noteworthy patterns might emerge, of relevance to future research.

The HADS consists of two subscales, measuring anxiety and depression. Exploratory analysis indicated that mindfulness-training had a stronger impact on symptoms of anxiety $F(1, 19) = 7.91$, $p = .01$, $g_{av} = .59$, than those of depression $F(1, 19) = 3.48$, $p < .08$.

All six of the POMS's subscales showed shifts in the expected direction, with three reaching significance at the .05 level: fatigue $F(1, 19) = 7.40$, $p = .01$ $g_{av} = .82$, confusion $F(1, 19) = 5.96$, $p < .01$ $g_{av} = .83$, and vigor $F(1, 19) = 4.31$, $p = .05$ $g_{av} = .64$.

Similarly, all seven component scales of the PSQI showed movement in the expected direction, with three reaching significance. These were overall sleep quality $F(1, 19) = 9.20$, $p < .01$ $g_{av} = 1.04$, sleep latency $F(1, 19) = 8.57$, $p < .01$ $g_{av} = -1.52$, and use of sleeping medication $F(1, 19) = 6.47$, $p < .05$ $g_{av} = -.95$.

The FSI contains three component scales, measuring fatigue duration, severity, and interference with quality of life. Analysis revealed significant or marginal improvements on the first two subscales (duration, $F(1, 19) = 7.60$, $p < .05$ $g_{av} = .95$, and severity, $F(1, 19) = 3.39$, $p = .08$) but no effect on the third.

In summary, despite these subtests' attenuated reliabilities, their outcome patterns were consistent with the total score analyses. Beneficial shifts emerged on all subscales for every measure, with many reaching significance (n = 8) or marginal (n = 4) levels. These findings essentially echoed those of the full score analyses, not altering the scope or focus of intended follow up research.

Discussion

For a significant subset of cancer survivors, depression, anxiety, sleep disturbance, and fatigue persist for years after treatment, compromising quality of life and triggering further health problems. The goal of this study was to determine whether online mindfulness training could reduce psychological distress and its behavioral manifestations in these patients.

Summary of Findings

Our data indicate that online mindfulness training benefits cancer survivors' anxiety and depression, mood, sleep, and fatigue. Clear and consistent positive results across all variables led us to cancel study recruitment early and offer all subsequent interested participants the active treatment.

Anxiety and depression (measured by the HADS) was our primary outcome variable, given its frequency and salience in the lives of cancer survivors. Mindfulness

training participants reported significant reductions on this measure, relative to controls. The magnitude of this reduction (g_{av} = .64) falls in the medium range and is similar to what has been reported in previous in-person (Ledesma & Kumano, 2009; Musial et al., 2011) and synchronous online (Zernicke et al., 2014) trainings. Such change is notable given that the current intervention is asynchronous and therefore both cost-effective and easily scalable.

Our second outcome variable, the POMS, measured mood broadly, assessing additional facets of mental state (e.g. vigor, confusion, etc.) relevant to the experience of cancer survivors. Mindfulness training, when compared to care as usual, led to moderate improvements on the POMS as well (g_{av} = .67), suggesting that the training benefits overall mental health beyond its effects on anxiety and depression.

Mindfulness training participants evidenced large improvements in sleep on the PSQI relative to controls (g_{av} = 1.14) as well. The magnitude of this change (3.16 points) translates to a shift of nearly half of the difference separating the normed scores of disordered sleepers (10.38) and healthy ones (2.67; Buysse et al., 1989). As noted previously, sleep disturbance leads to fatigue and somatic complains and has been associated with increased cancer risk (Sapolsky, 2004). Improvements in sleep are, therefore, important not only for quality of life, but for ongoing health.

Aligned with our findings on sleep, participants in the active treatment condition reported reductions in fatigue, as measured by the FSI, relative to controls. Fatigue is a key factor impacting cancer patients' quality of life, independence, and ability to pursue

life goals (Hann, Denniston, & Baker, 2000). As in the case of sleep, the large magnitude of this effect (g_{av} = 1.03) has both clinical significance and real life import.

Finally, as an independent variable manipulation check, we tracked treatment compliance. Most participants engaged with the treatment weekly or more frequently. While excluding participants who chose to engage less frequently did not change the overall pattern of results, greater meditation practice was associated with improved outcomes on each variable.

Advantages, Limitations, and Avenues for Further Research

This study differed in certain respects from others in the cancer care MBT literature, conferring both advantages and limitations.

First, our intervention did not include meditative movement or communication skills training, common to most MBSR-derived trainings. This exclusion allowed us to measure the benefit of mindfulness, separate from additional fortifying elements. Future studies may wish to reintroduce meditative movement or communication training to evaluate supplementary gains, particularly in populations experiencing chronic physical complaints or those experiencing relationship distress.

Second, this intervention was shorter than most MBTs, for example, MBSR. While longer treatments are the norm, brief treatments have shown efficacy (Carmody & Baer, 2009; Shao, Gao, & Cao, 2016; Vettese, Toneatto, Stea, Nguyen, and Wang; 2009) and deserve continued investigation, since they may encourage participation and limit cost.

Third, our study delivered an asynchronous treatment in randomized-controlled fashion—the first such trial in the MBT cancer-care literature, to our knowledge—allowing us to rectify methodological issues frequent to in-person mindfulness training: We delivered treatments individually, avoiding use of a small number of multi-person groups, whose resultant sample size may quickly violate ANOVA's independence-of-observation assumption, and provided double-blind treatment to rule out the effects of non-specific group factors. Asynchronous treatments have been found to provide other benefits, as well, including individualized pacing, greater time for reflection, and the chance to focus soley on one's own development (Simonson, Smaldino, Albright, & Zvacek, 2012), but also drawbacks, such as reduced social encouragement to engage and persist with training (Er, Ozden, & Arifoglu, 2009; Harris, Mishra, & Koehler, 2009). Developers of online medical interventions should consider not only what content they wish to include, but also what delivery format will best engender use, persistence and long-term skill acquisition for learners. While little has been written about the relative merits of synchronous vs. asynchronous online learning for cancer care, researchers might look to the field of education, where online learning has been explored in greater depth. Blended e-learning, which combines aspects of both synchronous and asynchronous environments and adaptive e-learning, in which interventions respond uniquely to learner needs, are ideas worthy of study (Er, Ozden, & Arifoglu, 2009; O'Donnell, Lawless, Sharp, & Wade, 2015).

Finally, there are two additional, important, avenues for MBT cancer-care research. First, we recommend that researchers investigate how patients' stress

symptoms and responses to treatment vary based on individual characteristics, such as cancer type, stage of progression, major treatment procedures undergone, and even non-medical life events experienced during the course of cancer (e.g. changes in one's work or relationships). Second, we believe that evaluation of MBTs should include not only psychological outcomes, as has been the norm, but behavioral and physiological ones as well. Such multiple-method assessment would help clarify the biological processes through which mindfulness training reduces chronic stress and the medical conditions for which this training is most useful. The current study's investigation of sleep, though self-reported, is a step in this direction.

Implications

Mindfulness training—with emerging evidence of health benefits and a focus on helping patients manage anxiety and depression—has seen increasing use in cancer care, answering the call for greater attention to patients' psychosocial needs. As explicated in the recent Institute of Medicine Report of the National Academies (Adler & Paige, 2008), psychologically healthy patients can more easily seek medical care, comply with treatments, manage their recovery and enjoy life. To achieve these goals, cancer centers have been asked to assess and refer individuals for psychosocial support. Online mindfulness training represents a widely-accessible, cost-effective intervention for survivors who cannot, or prefer not to, participate in in-person MBTs, such as MBSR. Whether offered in stand-alone fashion or incorporated into existing hospital-based care, online mindfulness training represents an important emerging resource for doctors and their patients.

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APPENDIX A

ELIGIBILITY CRITERIA

Inclusion Criteria

1. Aged 35 or older
2. Previous cancer diagnosis, stage I-III with major treatment complete and entering remission in the previous three years
3. HADS score above 7 for depression, anxiety, or both
4. English Literacy
5. Ownership of a computer and confidential, individual, email address
6. Computer proficiency defined as the ability to operate a web-browser

Exclusion Criteria

1. Impaired hearing
2. Current daily mindfulness practice
3. Current autoimmune disorder
4. Non-melanoma skin cancer patients

APPENDIX B

MEAN SCORES AND STANDARD DEVIATIONS ON ANXIETY/DEPRESSION, MOOD, SLEEP, AND FATIGUE SCALES

Variable	Mean Score ± (SD)			
	Mindfulness		Care as Usual	
	Pretest	Posttest	Pretest	Posttest
HADS[a]	16.87 (3.72)	10.00 (2.49)	18.50 (6.36)	17.80 (10.52)
POMS[b]	58.07 (15.63)	37.47 (12.20)	71.42 (28.01)	63.50 (36.90)
PSQI[c]	10.57 (3.45)	8.50 (3.14)	12.67 (3.07)	12.75 (3.02)
FSI[d]	20.78 (4.33)	11.58 (4.98)	19.39 (4.59)	16.25 (7.92)

[a] Higher scores reflect greater anxiety/depression. [b] Higher scores reflect greater mood disturbance. [c] Higher scores reflect higher sleep disturbance. [d] Higher scores reflect greater fatigue