

RCT of an Online MBSR Intervention with Metastatic Breast Cancer Patients

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Abstract

Purpose

The diagnosis and treatment of cancer can result in an array of psychological and physical sequelae for patients. Mindfulness-Based Stress Reduction (MBSR) is a well-validated intervention aimed at reducing emotional distress and improving long-term treatment effects in cancer patients. Further studies employing more powerful control group designs are needed to validate MBSR in patients with advanced disease and in novel clinical settings that facilitate enrollment. Patients diagnosed with metastatic disease are highly impacted by their disease and treatment and are an under-examined high-risk population.

Methods

This study aimed to determine the efficacy of a 6-week modified online MBSR intervention in improving psychological and physical symptoms associated with quality-of-life, as well as biomarkers associated with their disease trajectory, in patients diagnosed with metastatic breast cancer.

Results

The 6-week online intervention was found to significantly improve measures of mindfulness and several psychological/quality of life indices. There were no intervention effects on biomarkers of stress or inflammation, although improved levels of mindfulness due to the intervention were negatively correlated with several pro-inflammatory cytokines, including IL-6, IL-8, and TNF α . Patients indicated high satisfaction with the content and delivery method of the intervention.

Conclusions

Addressing the multidimensional needs of metastatic patients requires service delivery models that integrate powerful interventions into care settings while minimizing participant burden. This study developed a novel online MBSR treatment for distressed metastatic breast cancer patients that was found to be effective in improving mindfulness and several areas pertinent to patient quality of life.

Background

A cancer diagnosis is a life-changing and highly stressful event for most patients, often resulting in marked declines in quality-of-life (QOL) both during and after treatment. Prevalence estimates suggest that up to 35% of cancer patients report symptoms of depression and/or anxiety.¹ Additionally, up to 40% of patients report chronic cancer-related fatigue², 30–50% report chronic sleep impairment, and 33% of patients continue to experience pain.³ These rates are often higher in patients with metastatic illness, with 42% meeting criteria for a psychiatric disorder, at least 50% reporting fatigue, up to 60% reporting sleep impairment⁴, and 64% experiencing pain.^{4,5} There are approximately 3.8 million women living with

a history of invasive breast cancer in the U.S., with over 150,000 living with metastatic disease. The average woman with metastatic breast cancer will live 2–3 years, with 25% living 4+ years.⁵ With ever-increasing advances in targeted therapies, survival with metastatic disease will continue to improve.

In recognition of the need to address these long-lasting symptoms of cancer treatment, the NCCN developed Clinical Practice Guidelines for Survivorship in 2013, most recently updated in 2021. These guidelines focus on several areas that patients often continue to struggle with post-treatment: cardiotoxicity, anxiety, depression, cognitive function, fatigue, pain, sexual function, and sleep disorders.⁶ While the Survivorship Guidelines provide algorithms for the assessment and treatment of each of these areas, efforts to develop validated measures and interventions are ongoing. Patient preferences indicate a high need for non-pharmacologic, complementary and alternative medicine (CAM) interventions to address these chronic symptoms. Unique to the metastatic population is the experience of chronic symptomatology and treatment course – a ‘living with’ rather than ‘living after’ cancer.

Many interventions have been developed aimed at improving these symptoms in cancer patients, with mindfulness-based interventions (MBIs) showing particular promise. Mindfulness-Based Stress Reduction (MBSR) and Mindfulness-Based Cancer Recovery (MBCR) are two well-validated MBI treatments shown to be effective for the improvement of stress, mood, fatigue, and QOL, that can affect several biomarkers related to cancer.^{7–10} MBSR was developed by Kabat-Zinn and focuses on one’s present awareness, with a view toward life circumstances that is open, accepting, and non-judgmental.¹¹ This was later adapted by Carlson and Speca with the creation of MBCR to assist patients undergoing cancer treatment in managing symptom burden.¹² It has been widely supported as a beneficial intervention in improving patient’s experience of pain, anxiety, depression, sleep concerns, fatigue, and health-related QOL^{13–15}, as well as with patients dealing with metastatic breast cancer.^{16,17}

While evaluations of MBIs have been promising, most MBI psychological interventions are almost exclusively delivered face-to-face, often in a group format. As a result, high attrition rates are often reported as patients experiencing ongoing side effects or living a distance from the hospital may find it difficult to adhere to a time-intensive treatment.¹⁷ In addition, MBIs are typically validated on earlier-stage cancer patients, and those that do include patients with metastatic illness often result in very low enrollments and/or high attrition rates. Metastatic patients are highly impacted by chronic symptoms, yet paradoxically, are often the least-studied.

In addition, MBSR may improve physiological outcomes and biomarkers associated with disease outcomes. Breast cancer patients with advanced disease often have high circulating levels of pro-inflammatory cytokines, which are consistently associated with increased levels of stress, pain, depression, and fatigue,^{18,19} that may be associated with breast cancer progression and poorer prognosis in patients with metastatic breast cancer.^{20,21} Reductions in pro-inflammatory cytokine levels or expression, including IL-6 and TNF α have occurred following participation in MBIs that are as short as 6 weeks in length.^{22,23} No studies, however, have broadly examined the potential impact of MBSR training

on pro- and anti-inflammatory cytokines that can affect disease prognosis and none have examined the impact of MBSR on biomarkers associated with regulating stress response that may play a role in modulating inflammation among patients with metastatic disease.²⁴⁻²⁶

The area of telemedicine has grown vastly in the past several years and is allowing patients to gain access to clinical trials, psychological treatment, and ongoing medical care that was previously very difficult to engage in, particularly for late-stage patients. Online interventions are becoming increasingly common and show positive effects on emotional health and coping with the effects of cancer treatment.^{14,27}

The objectives of the study were: 1) to test a novel online MBSR treatment for distressed metastatic breast cancer patients who may otherwise be unable to participate in a traditional in-person intervention due to high symptom burden. It was hypothesized that the online format would be accessible to a majority of patients, easily adopted, and would result in high completion rates; and 2) to determine the impact of the intervention on patient self-reported outcomes and on biomarkers of inflammation and sympathetic activation as markers of the stress response. It was hypothesized that patients assigned to the intervention, compared to wait-listed controls, would show improvements in psychological and physical symptoms associated with QOL, including depression, anxiety, fatigue, sleep impairment, and pain; increases in indices of mindfulness; and improvements in blood pressure measurements and immune biomarkers associated with better QOL, reduced levels of stress, and/or better disease prognosis.

Methods

This study was approved by our Center's Institutional Review Board, study #I50317. All patients completed an IRB-approved consent form and were provided a signed copy and were assured that participation or withdrawal from the study would not affect their medical care.

Sample

The study sample consisted of patients diagnosed with metastatic breast cancer within the previous 5 years, either after a diagnosis of localized disease or as an initial diagnosis of metastatic disease and were currently being treated at our center.

Eligibility criteria included an ability to read and understand English to be able to complete study measures and read intervention materials, an ability to access an internet connection with their own device (computer, tablet, smartphone, etc.), not currently involved in an ongoing psychological intervention, and reporting a current distress score of 4+ on the NCCN Distress Thermometer.²⁸

Procedure

The online MBSR intervention was modeled on the work of Carlson and Speca's 8-week MBSR intervention.²⁹ The burden of time and effort involved in prior studies using MBSR or MBSR is a likely

barrier with metastatic patients, necessitating the adaptation of the gold standard with this population. The intervention consisted of 6 weekly, 60-minute sessions (as opposed to a traditional 8 weeks of 90-120-minute sessions). Additionally, the traditional 6 or 7-hour day of mindfulness or mindfulness retreat during week 6 was reduced to a 3-hour period of mindfulness meditation.

All online sessions were accessed using WebEx³⁰, allowing participants to engage in a group-like atmosphere online. Participants randomized to the wait-list control condition were enrolled in the online intervention after the initial 6-week period ended. Groups consisted of up to 10 participants, with 8 groups held throughout the study duration.

A participant study manual and session-by-session facilitator manual were developed by the study Principal Investigator (JH) and research assistant (CE) based on the work of Carlson and Speca to provide written guidance for weekly groups and to ensure standardization of the intervention across sessions. All participants received a study manual along with Carlson and Speca's MBCR book as a companion guide.²⁹ The study PI and research assistant facilitated all online sessions. Fidelity to the study manual was evaluated by a doctoral-level Psychology intern not involved with the study, with core topic areas of each weekly session covered 96% of the time, and within the timeframe goal of each session 73% of the time.

Weekly intervention sessions consisted of approximately 45 minutes of didactic instruction on a topic - including the practice of body scan, sitting and lying meditation, gentle yoga, mindful walking, and acceptance meditation. Each session ended with approximately 15 minutes of practice of that session's topic. During in-person study visits, all participants completed surveys, had their blood pressure measurements taken, and provided blood samples.

Outcome Measures and Covariates

Changes in facets of mindfulness due to the intervention was assessed using the Five Facet Mindfulness Questionnaire³¹ (FFMQ), a 39-item measure assessing five domains of mindfulness and self-awareness, i.e. Observing, Describing, Acting with Awareness, Non-judging, and Non-reacting, that is related to decreases in clinical symptoms of depression, anxiety, and stress.

The primary outcomes of anxiety, depression, and somatic symptoms and severity of symptoms were assessed by the Brief Symptom Inventory³², a 53-item measure covering 9 symptom dimensions and 3 global indices of distress.

Secondary outcomes included overall quality-of-life as measured by the Functional Assessment of Cancer Therapy-Breast³³ (FACT-B), fatigue as measured by the Functional Assessment of Chronic Illness Therapy-Fatigue³⁴ (FACIT-Fatigue), sleep impairment as measured by the General Sleep Disturbance Scale³⁵ (GSDS), and dimensions of pain as measured by visual analog scales per NCCN Guidelines for Adult Cancer Pain.³⁶ Systolic and diastolic blood pressure measurements were completed by a clinic nurse. Two measurements were taken at each study visit to ensure an accurate reading.

Plasma biomarkers of inflammation and stress were also assessed as secondary outcomes to assess the impact of MBSR treatment on physiologic pathways that may play a role in breast cancer outcomes. These included C-reactive protein (CRP, Milliplex HCVD3MAG), as a marker of systemic inflammation, a panel of pro- (TNF α , IL-1 β , IL-6, IL-8, IL-21) and anti-inflammatory (IL-10) cytokines (HSTCMAG-6k: Milliplex MAP Human High Sensitivity T-cell Panel), as well as several pituitary hormones and neurotrophic factors related to stress-induced sympathetic activation, i.e. agouti-related peptide (AgRP)²⁴, ciliary neurotrophic factor (CNTF)^{25,26}, and thyroid stimulating hormone (TSH)^{25,26} (HPTP1MAG: MILLIPLEX MAP Human Pituitary Magnetic Bead Panel).

Data Analysis

Data were analyzed for patients completing 4/6 of the online interventions only. Patient demographic and clinical characteristics were summarized using mean and standard deviations for continuous variables and frequencies for categorical variables. Comparisons were made using the Mann-Whitney U or Fisher's exact tests, as appropriate.

The global and sub-scale scores for survey data and biomarker levels (log-transformed) were summarized by intervention arm and time-point using the mean and standard error. Survey scores and biomarker levels were modeled as a function of intervention arm, time-point, their two-way interaction, and a random subject effect using linear mixed models. Multivariate models involving biomarker data were adjusted for age and BMI. Additionally, associations between pre-post changes in psychological/QoL measures and post-intervention biomarker levels (log-transformed) were evaluated using Spearman correlation, with adjustments for biomarker values at baseline, age, and BMI. Individual survey responses were summarized by intervention arm and time-point using the mean, median, and standard deviation or frequencies and relative frequencies, as appropriate.

All analyses were conducted in SAS v9.4 (Cary, NC) at a significance level of 0.05 (SAS Institute, 2013).³⁷

Results

Patient characteristics and satisfaction with intervention

A total of 146 patients were approached at a visit to the Breast Center to assess their interest in the study, with 28 patients completing the intervention (see Fig. 1 for study flow). Study participants were primarily White, approximately 55 years of age, and showed no statistical differences in ECOG performance status, blood pressure, or mean BMI levels by intervention arm. No significant baseline differences were observed between patients randomized to the MBSR intervention or the wait-list control groups on all psychological/QoL measures (Table 1). Overall, participants rated the practical and content aspects of the online study intervention very highly (see Table 2).

Psychological/QoL outcomes

Several significant findings were found for psychological and quality of life indices (see Table 3). Patients enrolled in the waitlist condition showed no significant effects on any study measure while enrolled in the control portion of their study arm.

Post-intervention scores on 5 of 6 of the FFMQ mindfulness subscales were higher among the MBSR group compared to the wait-listed group, including Observing (+ 24%, $p < 0.001$), Acting with Awareness (+ 8.7%, $p = 0.032$), Nonjudging (+ 12.5%, $p = 0.014$), Nonreactivity to Inner Experience (+ 17.1%, $p = 0.001$), and Total Score (+ 13%, $p < .001$). There was borderline significant improvement for the mindfulness subscale Describing (+ 6.1%, $p = .051$). All subscales of the Brief Symptom Inventory were significantly lower among the intervention group compared to the wait-listed group, including a lower score for Depression (-51%, $p < .001$), Anxiety (-37%, $p = .019$), Somatization (-34%, $p < 0.001$), and for the Global Severity Index (-41%, $p < 0.001$). Overall QoL as measured by the FACT-B Total Score was higher among the MBSR group post-intervention compared to those randomized to the wait-listed intervention (+ 12.9%, $p < 0.001$). Higher scores were observed for 4 of the 5 FACT-B subscales, including Physical Well-Being (+ 19.7%, $p < .0001$), Emotional Well-Being (+ 21.1%, $p < 0.001$), Functional Well-Being (+ 21.1%, $p < .001$), as well as the Breast Cancer Subscale (+ 8.7%, $p = 0.008$). The MBSR intervention was also associated with significantly better FACIT-Fatigue QoL scores (+ 33.6%, $p < .001$) as well as lower overall levels of sleep disturbance as measured by the GSDS (-46.8%, $p < 0.001$) compared to the waitlisted group. All indices of reported pain, including worst pain over the past 24 hours and 1 week period, were significantly lower or showed a trend towards lower levels in the MBSR group ($p = 0.071$) compared to the wait-listed group except for levels of Least Pain over the past 24 hours ($p = 0.414$).

Physiologic outcomes

Effects of the MBSR intervention on blood pressure levels and circulating plasma biomarkers of inflammation and stress are presented in Table 4. All analyses of post-intervention values were adjusted for age, body mass index, and baseline biomarker levels (which differed significantly at baseline for IL-1 β and IL-8). No significant differences were observed between the MBSR and Waitlisted groups for levels of CRP, as a biomarker of systemic inflammation, or for any of the pro- (TNF α , IL-1 β , IL-6, IL-8, IL-21) or anti-inflammatory (IL-10) cytokines assayed. AgRP levels, which are downregulated by acute stress³⁸, was higher among the MBSR group ($P = 0.03$), but no other differences were noted for other biomarkers of stress assayed. Blood pressure measurement also did not differ by intervention group.

Associations between pre- and post-interventional changes in psychological/QoL measures and post-intervention biomarker levels of inflammation and stress

Associations between changes in psychological/QoL measures and biomarker levels after receiving the MBSR intervention were assessed by Spearman correlation, with adjustments for baseline biomarker levels, age, and body mass index as shown in Fig. 2. Increases in the FFMQ mindfulness factors Observing ($r = -0.47$, $p = 0.023$) and Describing ($r = -0.52$, $p = 0.011$) were negatively correlated with circulating IL-6 levels, a proinflammatory cytokine, and total FFMQ scores were negatively correlated with both the proinflammatory cytokine IL-8 ($r = -0.50$, $p = 0.02$) and TNF α ($r = -0.41$, $p = 0.05$). Higher levels of

CRP were associated with increases in Depression ($r = 0.37$, $p = 0.08$), BSI Somatization ($r = 0.41$, $P = 0.055$), and BSI Global Severity ($r = 0.40$, $p = 0.06$), although none reached statistical significance at $P = 0.05$. Positive correlations were also suggested between increased IL-6 levels and Somatization ($r = 0.39$, $p = 0.07$) and global BSI score ($r = 0.38$, $p = 0.07$). Improved Emotional Well-Being was associated with higher levels of both CNTF ($r = 0.48$, $P = 0.02$) and TSH ($r = 0.57$, $P = 0.004$), and increased sleep disturbance was positively associated with increased levels of CRP ($r = 0.43$, $P = 0.042$). Increases in several pain indices were positively correlated with pro-inflammatory cytokines, including IL-1 β , IL-21, IL-6, and TNF- α . Levels of IL-1 β were correlated with increases in worst pain over the past 24 hours ($r = 0.64$, $P = 0.001$), increased pain with movement ($r = 0.42$, $P = 0.048$), and increased levels of average pain over the past 24 hours ($r = 0.48$, $P = 0.025$).

Discussion

Our modified MBSR intervention was found to be highly effective in improving measures of mindfulness and several indices of emotional health and quality of life, including physical, emotional, and functional well-being, anxiety, depression, sleep, experience of pain and fatigue among metastatic breast cancer patients. MBIs continue to show promising effects on several QOL indices for oncology patients³⁹, and are becoming more easily integrated into healthcare delivery systems.⁴⁰ Patients indicated that the practice of non-judgment was found to be particularly transformative, with several women describing a newfound ability to make room for feelings previously experienced as unwanted and uncomfortable. The positive findings related to psychosocial measures and quality of life highlight the significance and benefit, in terms of real-life outcomes, of continuing to develop pragmatic interventions that improve coping and ameliorate the high symptom burden experienced by patients diagnosed with metastatic illness.

Despite several promising effects of the intervention on emotional and physical health measures, we did not find intervention effects for inflammatory cytokine measures or blood pressure, although against expectation, AgRP concentrations, which are reduced in preclinical models of chronic unpredictable stress, was higher among the MBSR group.⁴¹ The general lack of association with biomarkers of stress and inflammation may be due to the short 6-week follow-up period and the limited sample size. When changes in mindfulness and QoL measures due to the MBSR intervention were correlated with changes in biomarker levels, we found that increased measures of overall mindfulness as well as specific mindfulness factors were negatively correlated with several pro-inflammatory cytokines, including IL-6, IL-8, and TNF α . This is the first study to show that measures of mindfulness are negatively correlated with inflammatory markers, which is consistent with findings from a recent meta-analysis of mindfulness-based randomized controlled trials that found reductions in IL-6 and CRP.⁴² This may be clinically significant given that reduced inflammation among metastatic breast cancer patients may translate into better disease prognosis given associations between inflammation and reduced breast cancer survival.⁴³ The MBSR intervention was found to be associated with improved emotional well-being and higher levels of TSH and CNTF, which was somewhat unexpected given that both TSH and CNTF have been

associated with higher levels of stress.⁴⁴ Only a small number of studies have investigated the relationship between mindfulness interventions and biomarkers, however, with most focused on inflammatory cytokines and CRP. Larger studies examining the impact of MBSR on biological biomarkers of stress are still needed.⁴⁵

Our study aimed in part to validate a modified version of Carlson and Speca's MBSR intervention with patients diagnosed with metastatic breast cancer using an online format. Primary outcomes of feasibility and patient satisfaction came with mixed results. While many patients that were approached for the study were initially interested, a number did not meet eligibility criteria due to feeling too unwell to participate, not having a device or internet access, or already participating in a mindfulness practice. For a number of patients, the technology requirements felt too difficult to engage with and/or they did not wish to have additional bloodwork or questionnaires to complete. Of those that were interested and eligible, however, 100% chose to enroll and a majority completed the intervention. For many of our patients, increasing symptom burden, hospitalization, or death were reasons for study dropout, pointing to the precarious nature of these patients' health and life circumstances.

In addition, we received very positive feedback regarding the practical and content aspects of the intervention. Patients felt that it was convenient for them to participate at home, they appreciated the online group format in which they could interact with other patients, and found the content to be very helpful in learning about mindfulness and in starting a consistent mindfulness practice. Anecdotal evidence from these patients indicated that they found it to be especially helpful in remaining in the present when struggling with upcoming scans or worry about their future. From these feasibility and satisfaction data, it appears that patients experiencing high symptom burden greatly appreciate the option of an online platform to participate in a group mindfulness practice. It is likely that without the bloodwork component of this study, additional patients may have participated as well.

Study limitations

A major limitation of the present study is in the small sample size, most likely due to patients' reluctance to complete additional bloodwork or become involved in an additional study. Many of our patients with metastatic illness are enrolled in clinical trials and attend a myriad of medical appointments regularly. It is likely that more patients would enroll in this type of intervention without this study aspect.

In addition, many patients were not interested in engaging in an online intervention, or did not have access to the technology or consistent Internet to complete the intervention. This may likely be due to the older age of this client population that may not be as comfortable with interacting with online content. This study was conducted before the Covid pandemic and it may be reasonable to think that patients have gained more comfort in online interactions since this time. Further research will need to consider ways in which we may help older patients to gain confidence in interacting with technology, or consider in-person groups for those more comfortable with this format.

Clinical implications

This study provides strong evidence for the benefit of an online MBSR intervention for patients coping with metastatic breast cancer. Patients were highly satisfied with the content and delivery format, scores on mindfulness and several psychological and quality of life measures were improved, and we showed for the first time that improved measures of mindfulness are associated with reduced systemic inflammation, which may impact breast cancer outcomes. This type of intervention could be easily implemented in clinics treating breast cancer patients with facilitation by a staff mental health provider or nurse trained in MBSR.

Declarations

Conflict of interest statement

All study authors have no conflicts of interest to disclose. The primary author is in possession of all study data, which is available upon request.

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Availability of Data and Material

All data and material are accessible through the principle author upon request.

Code Availability

Not applicable

Author Contributions

All authors contributed to the study conception and design. Material preparation and data collection were performed by Jennifer Hydeman and Carrie Ernhout. Data analysis was performed by Kristopher Attwood and Chi-Chen Hong. The first draft of the manuscript was written by Jennifer Hydeman, Kristopher Attwood, and Chi-Chen Hong and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Roswell Park Comprehensive Cancer Center (7/2017; #I50317).

Consent to Participate

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

Consent to Publish

The authors affirm that human research participants provided informed consent for publication of any study data.

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Tables

Table 1. *Patient characteristics at randomization*

	Wait-list Control (N=22)	MBSR Intervention (N=22)	P- value ¹
	N (%)	N (%)	
Race			
White	20 (90.9%)	19 (86.4%)	1.00
Non-white	2 (9.1%)	3 (13.6%)	
ECOG Performance Status			
0	0 (0%)	1 (4.8%)	0.17
1	11 (57.9%)	16 (76.2%)	
2	8 (42.1%)	4 (19.0%)	
	Mean (SD)	Mean (SD)	
Age, Years	57.3 (11.4)	54.7 (11.5)	0.40
Blood Pressure, Mm Hg			
Systolic	123.1 (3.9)	124.1 (3.7)	0.96
Diastolic	78.1 (2.1)	78.4 (2.0)	0.86
BMI, Kg/m ²	28.8 (7.3)	31.4 (7.6)	0.34
FACT-B Total	96.9 (21.1)	91.2 (18.7)	0.34
Physical Well-Being	19.2 (5.0)	16.7 (6.3)	0.31
Social/Family Well-Being	20.8 (6.2)	21.1 (3.8)	0.42
Emotional Well-Being	15.4 (4.1)	13.3 (5.7)	0.33
Functional Well-Being	16.5 (6.2)	16.6 (4.7)	0.88
Breast Cancer	25.0 (6.7)	23.5 (6.0)	0.44
GSDS Total Score	31.9 (19.6)	33.5 (19.4)	0.77
FFMQ			
Observing	23.2 (6.3)	24.0 (4.9)	0.82
Describing	24.6 (7.1)	28.0 (5.3)	0.06
Acting with awareness	26.3 (7.7)	26.8 (4.9)	0.72
Nonjudging of inner experience	30.3 (8.1)	27.5 (6.5)	0.21
Nonreactivity to inner experience	18.2 (4.1)	20.4 (5.3)	0.08

Total FFMQ	122.5 (20.0)	126.6 (17.7)	0.30
Brief Symptom Questionnaire			
Somatization	4.5 (3.4)	6.3 (4.1)	0.17
Depression	3.5 (3.5)	5.7 (3.7)	0.03
Anxiety	4.3 (4.3)	6.0 (4.6)	0.2
Global Severity Index	12.3 (9.3)	18.0 (10.2)	0.07
Pain			
Pain at Rest	2.8 (2.3)	1.6 (1.8)	0.09
Pain with Movement	4.1 (2.9)	3.1 (2.2)	0.3
Current Pain	2.6 (2.8)	2.5 (2.0)	0.66
Worst Pain (1 week)	5.8 (2.9)	5.0 (2.8)	0.35
FACIT-Fatigue	29.9 (9.4)	25.7 (9.6)	0.22
¹ Comparisons between the wait-list control and MBSR intervention group were made using the Mann-Whitney U test for continuous variables and Fisher's Exact test for categorical variables.			

Table 2. *Participant satisfaction with online MBSR program*

		All Women (N=26)	Initially Randomized to Wait-list arm (N=11)	Initially Randomized to MBSR arm (N=15)	P- value ¹
How satisfied were you with:					
the ease of setting up the webcam?	Mean (SD)	8.0 (2.6)	6.7 (3.3)	8.8 (1.7)	0.09
	Median (Min, Max)	9.5 (1.0, 10.0)	7.0 (1.0, 10.0)	10.0 (5.0, 10.0)	
the ease of accessing the online program?	Mean (SD)	8.0 (2.6)	7.4 (3.1)	8.5 (2.1)	0.27
	Median (Min, Max)	9.5 (1.0, 10.0)	8.0 (1.0, 10.0)	10.0 (4.0, 10.0)	
your ability to interact with others using the online format?	Mean (SD)	8.6 (2.2)	7.7 (2.8)	9.3 (1.3)	0.16
	Median (Min, Max)	10.0 (3.0, 10.0)	9.0 (3.0, 10.0)	10.0 (6.0, 10.0)	
the convenience of the program?	Mean (SD)	9.1 (1.9)	8.8 (2.1)	9.3 (1.8)	0.58
	Median (Min, Max)	10.0 (3.0, 10.0)	10.0 (3.0, 10.0)	10.0 (3.0, 10.0)	
the content of the program?	Mean (SD)	9.3 (1.3)	9.1 (1.3)	9.5 (1.3)	0.17
	Median (Min, Max)	10.0 (5.0, 10.0)	10.0 (6.0, 10.0)	10.0 (5.0, 10.0)	
How helpful was the program:					
in learning about mindfulness?	Mean (SD)	9.0 (1.4)	9.1 (1.3)	8.9 (1.5)	0.82
	Median (Min, Max)	9.5 (5.0, 10.0)	10.0 (6.0, 10.0)	9.0 (5.0, 10.0)	
in establishing a personal mindfulness practice?	Mean (SD)	8.5 (2.0)	8.2 (2.1)	8.7 (1.9)	0.62
	Median	9.0/3.0/10.0	8.0/4.0/10.0	9.0/3.0/10.0	

	(Min, Max)				
instructor?	Mean (SD)	9.7/0.8/26	9.5/1.2/11	9.9/0.4/15	0.34
	Median (Min, Max)	10.0/6.0/10.0	10.0/6.0/10.0	10.0/9.0/10.0	
How likely would you be to recommend this treatment to others?	Mean (SD)	9.3/1.8/26	8.8/2.6/11	9.6/0.7/15	0.82
	Median (Min, Max)	10.0/2.0/10.0	10.0/2.0/10.0	10.0/8.0/10.0	
¹ Comparisons between those initially randomized to the wait-list control vs the MBSR intervention group were made using the Mann-Whitney U test for continuous variables. Higher values indicate increased satisfaction.					

Table 3. *Psychological and QOL measures at baseline and post-intervention*

Outcome Measures	Randomization Arm	Time-point ^a			Post-Intervention Least Squares Mean (SE) ^c		
		Mean (SE)			Wait-Listed Control	MBSR	P-value
		T1	T2	T3			
FFMQ							
Observing	Wait-list (C → I)	23.2 (1.3)	22.6 (1.4)	29.5 (1.5)	23.4 (0.8)	29.2 (1.0)	<.001
	MBSR (C → I)	24.0 (1.2)	29.0 (1.4)				
Describing	Wait-list (C → I)	24.6 (1.5)	24.2 (1.6)	25.9 (1.7)	26.2 (1.0)	27.8 (1.1)	0.051
	MBSR (C → I)	28.0 (1.4)	29.5 (1.5)				
Acting with Awareness	Wait-list (C → I)	26.3 (1.5)	25.8 (1.6)	30.2 (1.7)	26.4 (1.0)	28.7 (1.1)	0.032
	MBSR (C → I)	26.8 (1.4)	27.5 (1.6)				
Nonjudging of inner experience	Wait-list (C → I)	30.3 (1.7)	29.3 (1.8)	34.2 (2.0)	28.7 (1.0)	32.3 (1.3)	0.014
	MBSR (C → I)	27.5 (1.5)	30.6 (1.8)				
Nonreactivity to inner experience	Wait-list (C → I)	18.2 (1.2)	18.7 (1.3)	23.4 (1.4)	19.3 (0.8)	22.6 (0.9)	0.001
	MBSR (C → I)	20.4 (1.1)	22.3 (1.3)				
Total FFMQ	Wait-list (C → I)	122.5 (4.6)	120.7 (5.1)	143.0 (5.6)	124.1 (3.0)	140.2 (3.7)	<.001
	MBSR (C → I)	126.6 (4.3)	138.3 (5.1)				
BSI							
Depression	Wait-list (C → I)	3.5 (0.8)	3.3 (0.8)	2.1 (0.9)	4.5 (0.5)	2.2 (0.6)	<.001
	MBSR (C → I)	5.7 (0.7)	2.5 (0.8)				
Anxiety	Wait-list (C → I)	4.3 (1.0)	3.7 (1.0)	3.6 (1.1)	4.9 (0.6)	3.1 (0.8)	0.019
	MBSR (C → I)	6.0	2.7				

		(0.9)	(1.0)				
Somatization	Wait-list (C → C → I)	4.5 (0.8)	4.4 (0.9)	2.8 (0.9)	5.3 (0.5)	3.5 (0.6)	<.001
	MBSR (C → I)	6.3 (0.7)	4.2 (0.8)				
BSI Global Severity Index	Wait-list (C → C → I)	12.3 (2.0)	11.3 (2.2)	8.4 (2.4)	14.7 (1.3)	8.7 (1.6)	<.001
	MBSR (C → I)	18.0 (1.9)	9.3 (2.2)				
FACT-B							
Physical Well-Being	Wait-list (C → C → I)	19.2 (1.2)	18.3 (1.4)	21.6 (1.5)	17.8 (0.8)	21.3 (1.0)	<.001
	MBSR (C → I)	16.7 (1.2)	20.8 (1.3)				
Social/Family Well-Being	Wait-list (C → C → I)	20.8 (1.3)	20.0 (1.4)	21.1 (1.5)	20.8 (0.9)	21.5 (1.0)	0.342
	MBSR (C → I)	21.1 (1.2)	21.6 (1.4)				
Emotional Well-Being	Wait-list (C → C → I)	15.4 (1.1)	14.9 (1.2)	17.0 (1.3)	14.2 (0.7)	17.2 (0.9)	<.001
	MBSR (C → I)	13.3 (1.0)	17.1 (1.2)				
Functional Well-Being	Wait-list (C → C → I)	16.5 (1.2)	16.8 (1.3)	20.6 (1.4)	16.6 (0.8)	20.1 (0.9)	<.001
	MBSR (C → I)	16.6 (1.1)	19.8 (1.3)				
Breast Cancer	Wait-list (C → C → I)	25.0 (1.4)	24.4 (1.5)	27.3 (1.6)	24.1 (0.9)	26.2 (1.1)	0.008
	MBSR (C → I)	23.5 (1.3)	25.3 (1.5)				
FACT-B Total Score	Wait-list (C → C → I)	96.9 (4.8)	94.4 (5.0)	107.3 (5.3)	93.5 (3.1)	105.6 (3.5)	<.001
	MBSR (C → I)	91.2 (4.4)	103.8 (4.8)				
FACIT-Fatigue Score	Wait-list (C → C → I)	29.9 (2.2)	33.4 (2.4)	40.5 (2.6)	28.6 (1.4)	38.2 (1.7)	<.001
	MBSR (C → I)	25.7 (2.0)	36.2 (2.3)				
GSDS Total Score	Wait-list (C →	31.9	24.4	12.4	31.2 (3.2)	16.6	<.001

	C → I)	(4.9)	(5.3)	(5.6)		(3.8)	
	MBSR (C → I)	33.5 (4.7)	19.3 (5.2)				
Pain							
Pain at Rest	Wait-list (C → C → I)	2.8 (0.4)	2.4 (0.5)	1.7 (0.5)	2.1 (0.3)	1.7 (0.3)	0.048
	MBSR (C → I)	1.6 (0.4)	1.4 (0.4)				
Pain with movement	Wait-list (C → C → I)	4.1 (0.6)	4.6 (0.7)	2.8 (0.7)	3.8 (0.4)	2.9 (0.5)	0.071
	MBSR (C → I)	3.1 (0.6)	3.0 (0.7)				
Current Pain	Wait-list (C → C → I)	2.6 (0.5)	3.4 (0.6)	1.6 (0.6)	2.8 (0.3)	1.9 (0.4)	0.022
	MBSR (C → I)	2.5 (0.5)	2.1 (0.6)				
Worst Pain (24 hours)	Wait-list (C → C → I)	4.5 (0.7)	4.9 (0.7)	3.4 (0.8)	4.7 (0.4)	3.2 (0.5)	0.002
	MBSR (C → I)	4.7 (0.6)	3.0 (0.7)				
Average Pain (24 hours)	Wait-list (C → C → I)	3.4 (0.6)	3.5 (0.6)	2.6 (0.7)	3.4 (0.4)	2.7 (0.4)	0.055
	MBSR (C → I)	3.4 (0.5)	2.6 (0.6)				
Least Pain (24 hours)	Wait-list (C → C → I)	1.9 (0.4)	2.0 (0.5)	1.5 (0.5)	1.7 (0.3)	1.5 (0.3)	0.414
	MBSR (C → I)	1.4 (0.4)	1.4 (0.4)				
Worst Pain (1 week)	Wait-list (C → C → I)	5.8 (0.7)	5.7 (0.7)	4.4 (0.8)	5.4 (0.4)	4.4 (0.5)	0.013
	MBSR (C → I)	5.0 (0.6)	4.3 (0.7)				

^aSurvey outcomes are summarized by study arm (waitlisted controls vs MBSR) and time-point (T1, T2, T3) using means and standard errors. T1 = baseline; T2 = week 6; T3 = week 12. Participants randomized to the MBSR group provided control (C) data at baseline and post-intervention (I) data at week 6. Those randomized into the waitlist group provided control (C) data at baseline and week 6 (averaged), and postintervention (I) data at week 12.

^bPost-intervention least square mean estimates were obtained using linear mixed models and compared between the control and MBSR intervention conditions.

Table 4. *Physiologic outcomes at baseline and post-intervention*

Measure	Randomization Arm	Time-point ^a Mean (SE)			Post-Intervention Least Squares Mean (SE) ^c		
		T1	T2	T3	Wait-Listed Control	MBSR	P-value
Plasma Biomarkers of Inflammation							
CRP	Wait-list (C → C → I)	9.21 (0.41)	8.90 (0.41)	8.95 (0.43)	9.30 (0.27)	9.16 (0.28)	0.357
	MBSR (C → I)	9.55 (0.39)	9.29 (0.39)				
TNF α	Wait-list (C → C → I)	2.15 (0.08)	2.05 (0.08)	2.07 (0.09)	2.09 (0.05)	2.10 (0.06)	0.773
	MBSR (C → I)	2.04 (0.08)	2.15 (0.08)				
IL-1 β	Wait-list (C → C → I)	0.22 (0.16)	0.31 (0.16)	0.34 (0.17)	0.10 (0.10)	0.07 (0.11)	0.691
	MBSR (C → I)	-0.00 (0.15)	-0.21 (0.15)				
IL-6	Wait-list (C → C → I)	1.02 (0.33)	0.98 (0.33)	0.84 (0.34)	0.69 (0.23)	0.80 (0.23)	0.357
	MBSR (C → I)	0.37 (0.31)	0.68 (0.31)				
IL-8	Wait-list (C → C → I)	2.19 (0.23)	2.11 (0.23)	2.14 (0.23)	1.71 (0.16)	1.73 (0.16)	0.675
	MBSR (C → I)	1.27 (0.21)	1.32 (0.22)				
IL-10	Wait-list (C → C → I)	2.56 (0.19)	2.67 (0.19)	2.70 (0.20)	2.40 (0.13)	2.40 (0.14)	0.974
	MBSR (C → I)	2.21 (0.18)	2.10 (0.18)				
IL-21	Wait-list (C → C → I)	2.14 (0.15)	2.29 (0.15)	2.28 (0.15)	2.11 (0.10)	2.08 (0.10)	0.692
	MBSR (C → I)	2.03 (0.14)	1.90 (0.14)				
Plasma Biomarkers of Stress							
AgRP	Wait-list (C → C → I)	4.24 (0.24)	4.20 (0.24)	4.40 (0.25)	4.07 (0.16)	4.24 (0.17)	0.03
	MBSR (C → I)	3.91 (0.22)	4.08 (0.23)				

CNTF	Wait-list (C → C → I)	3.73 (0.36)	3.24 (0.36)	3.30 (0.39)	3.06 (0.23)	3.23 (0.26)	0.462
	MBSR (C → I)	2.62 (0.34)	3.01 (0.34)				
TSH	Wait-list (C → C → I)	1.59 (0.14)	1.54 (0.14)	1.40 (0.15)	1.42 (0.09)	1.41 (0.10)	0.947
	MBSR (C → I)	1.28 (0.13)	1.36 (0.13)				
Blood Pressure							
SBP	Wait-list (C → C → I)	123.1 (3.9)	126.9 (4.2)	120.3 (4.5)	124.7 (2.5)	121.5 (2.9)	0.215
	MBSR (C → I)	124.1 (3.7)	123.2 (4.1)				
DBP	Wait-list (C → C → I)	78.1 (2.1)	78.0 (2.3)	74.5 (2.4)	78.5 (1.4)	76.7 (1.6)	0.197
	MBSR (C → I)	78.4 (2.0)	79.2 (2.2)				
<p><i>Note.</i> The cytokines are summarized by study arm and time-point using means and standard errors. Using linear mixed models, least square mean estimates of the cytokines are obtained and compared for the control and intervention conditions.</p>							

Figures

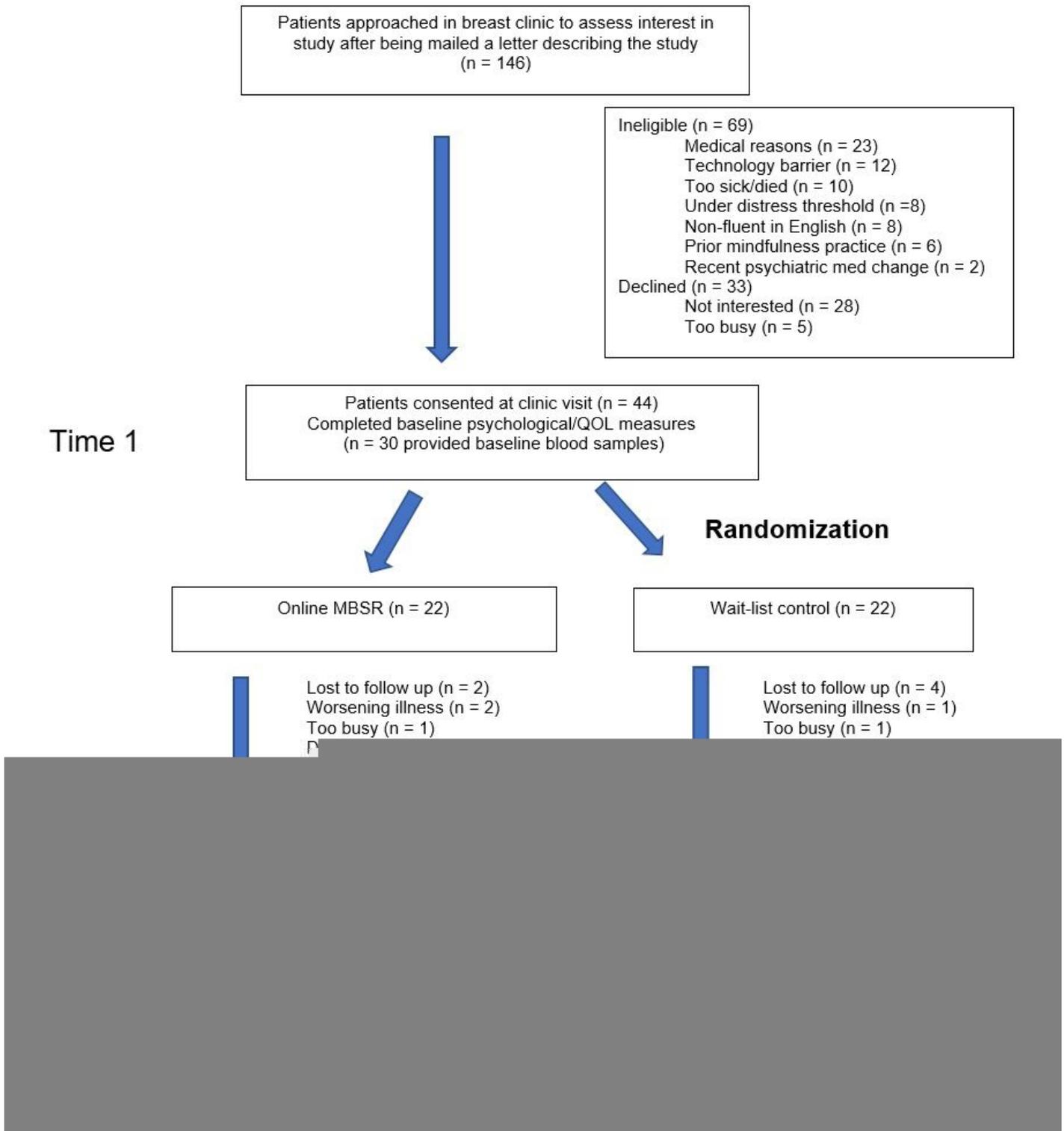


Figure 1

CONSORT diagram

Figure 2

Heat map indicating correlations between changes in psychological/QOL measures and changes in biomarker levels and blood pressure

Presented as partial correlations, adjusting for age and BMI.

* indicates $p < 0.05$; ** indicates $p < 0.005$.