Article Type: Review Article

Mindfulness-based stress reduction for menopausal symptoms after risk-reducing salpingo-oophorectomy (PURSUE study): a randomized controlled trial

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Running title: MBSR for menopausal symptoms

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/1471-0528.15471

Abstract

Objective: To assess the short- and long-term effects of mindfulness-based stress reduction (MBSR) on the resulting quality of life, sexual functioning, and sexual distress after risk-reducing salpingo-oophorectomy (RRSO).

Design: Randomized controlled trial.

Setting: A specialized family cancer clinic of the university medical center Groningen.

Population: 66 women carriers of the *BRCA1/2* mutation who developed at least two moderate-to-severe menopausal symptoms after RRSO.

Methods: Women were randomized to an 8 week MBSR training or care as usual (CAU).

Main outcome measures: Change in the Menopause-Specific Quality of Life Questionnaire (MENQOL), the Female Sexual Function Index, and the Female Sexual Distress Scale administered from baseline at 3, 6, and 12 months. Linear mixed modeling was applied to compare the effect of MBSR with CAU over time.

Results: At 3 and 12 months there were statistically significant improvements in the MENQOL for the MBSR group compared with the CAU group (both $p = 0.04$). At 3 months, the mean MENQOL scores were 3.5 (95% confidence interval [95%CI], 3.0–3.9) and 3.8 (95%CI, 3.3–4.2) for the MBSR and CAU groups, respectively; at 12 months, the corresponding values were 3.6 (95%CI, 3.1–4.0) and 3.9 (95%CI, 3.5–4.4). No significant differences were found between the MBSR and CAU groups in the other scores.

Conclusions: MBSR was effective at improving quality of life in the short- and long-term for patients with menopausal symptoms after RRSO. However, it was not associated with improvement in sexual functioning or distress.

Funding: C&W de Boer Foundation

Keywords: Mindfulness, *BRCA1/2*, salpingo-oophorectomy, surgical menopause, menopausal symptoms, sexual functioning.

Trial registration: ClinicalTrials.gov (https://clinicaltrials.gov/ct2/show/NCT02372864)

Tweetable abstract (110 characters max):

Mindfulness improves menopause related quality of life in women after risk-reducing salpingo-oophorectomy

Introduction

Women carrying a *BRCA1* or *BRCA2* mutation have an increased lifetime risk of developing breast and ovarian cancer compared with the general population.[1–4] At present, because ovarian cancer screening is ineffective for early detection, offering risk-reducing salpingo-oophorectomy (RRSO) is standard practice to reduce the incidence of ovarian cancer in these women.[5–8] RRSO is recommended at the ages of 35 to 40 years for *BRCA1* mutation carriers and at 40 to 45 years for *BRCA2* mutation carriers, provided there is no desire to have more children.[9–13] There is good evidence that the procedure reduces the risk of ovarian cancer by up to 96% when performed within these age ranges.[14–17]

The acute surgical menopause induced by RRSO is associated with sequelae, of which hot flashes, (night) sweats, vaginal dryness, loss of sexual desire, and pain during intercourse are the most frequent.[18–27] Moreover, it is reported that menopausal symptoms are more severe after acute surgical menopause than after natural menopause.[28] Although hormone replacement therapy (HRT) can alleviate the symptoms, they only do so partially, and symptom levels remain above those of premenopausal women.[22] Confounding this issue is the fact that one-third of *BRCA1/2* mutation carriers who undergo RRSO have had breast cancer, contraindicating HRT use.[29,30] Therefore, non-hormonal methods are needed to alleviate menopausal symptoms induced by RRSO in breast cancer survivors.

A possible non-hormonal alternative could be a psychological intervention that targets perception and acceptance, such as mindfulness-based training. The goal of such training is to help the patient pay full attention to the present moment in a non-judgmental, accepting way.[31] Specifically, the mindfulness-based stress reduction (MBSR) method achieve this through a well-described, protocol-based training program over an eight-week period. The program consists of meditation, gentle yoga poses, and body awareness exercises. In studies carried out in women experiencing menopausal symptoms after breast cancer treatment or natural menopause, MBSR has shown promise for both reducing difficulty with hot flushes and improving menopause-specific quality of life.[32–35] However, these studies were not carried out in women with RRSO-induced menopause, and they were either uncontrolled or had short follow-up periods.

In the present study, we aimed to investigate the short- and long-term effects of MBSR compared to care as usual (CAU) in *BRCA1/2* mutation carriers after RRSO. Specifically, we were interested in the effects on menopause-specific quality of life (primary outcome) and on sexual functioning and sexual distress (secondary outcomes).

Patients and Methods

Study Design

The randomized controlled trial, "Psychosexual conseqUences of Risk-reducing Salpingo-oophorectomy in *BRCA1/2* mUtation carriErs" (PURSUE) study is an open label trial and was approved by the Medical Ethical Committee of the University Medical Center Groningen on November 14, 2014 (registration number NL46796.042.14). It was conducted in accordance with the principles of the Declaration of Helsinki (as amended in 2013) and the relevant Dutch legislation (the Medical Research Involving Human Subjects Act). The ClinicalTrials.gov Identifier for the trial is NCT02372864. Women were recruited for participation from January 2015 to October 2015, and were followed for one year after randomization. Patients were not involved in the development of the study.

Participants

The clinical data for women referred to the Family Cancer Clinic of the University Medical Center Groningen at increased risk of developing breast or ovarian cancer, including *BRCA1/2* mutation carriers, have been prospectively recorded in a database since 1994.[36] We contacted *BRCA1/2* mutation carriers who underwent RRSO at an age younger than 52 years by letter detailing the possibility of receiving MBSR training aimed at alleviating menopausal symptoms after RRSO. The letter included a purpose-designed questionnaire (see Appendix S1) about the presence and severity of menopausal symptoms. Cancer history and current psychiatric and cancer treatment were recorded on the questionnaire. Women were eligible for participation if they had undergone RRSO before the age of 52 years and reported at least two moderate-to-severe menopausal symptoms in the two preceding weeks. We excluded the following groups: those who were undergoing cancer treatment at the time of inclusion, apart from those receiving adjuvant hormonal or immune therapy; those who were receiving

psychiatric care; and those who had insufficient understanding of the Dutch language to complete questionnaires. We did not exclude women using HRT, non-hormonal medications (e.g. clonidine), or dietary or herbal remedies (e.g. soy, black cohosh), or those with a history of breast cancer. All eligible women were invited for an intake visit, and after giving written informed consent, were randomized to an intervention or a control group. The intervention group received an eight-week MBSR training course, plus CAU, whereas the control group received only CAU.

Interventions

Participants in the MBSR group received an eight-week MBSR training course (Appendix S2). This comprised weekly sessions lasting two and half hours each, a silent retreat evening lasting four hours, and a commitment to performing mindfulness exercises at home for 30–45 minutes on six days of the week using instructions on a provided MP3 player.[31] The MBSR training was a standard training program and not specifically adapted to focus on menopausal symptoms. In total, six MBSR training classes were organized, each with four to seven study participants only. Training classes took place at three locations in the north of the Netherlands to reduce travel time for participants, and all were led by one of three certified and experienced MBSR trainers.

Care as Usual

CAU consisted of information provided by a specialist nurse during the intake visit. This covered lifestyle advice for hot flashes, night sweats, vaginal dryness, sexual functioning, cardiovascular health, and bone health. An information booklet summarizing this information was provided to participants in both groups. Approximately 12 weeks after randomization, all participants were offered a repeat appointment with the nurse to address any remaining issues.

Randomization

We used block randomization stratified by HRT use. Randomization was done by the independent trial coordination center of the University Medical Center Groningen via a web-application, using a computerized random number generator. After randomization, an e-mail was automatically sent to the research nurse and researchers detailing the group allocation of that particular study participant. The participants were informed about their allocation group by the research nurse.

Assessments

Questionnaires were sent by mail at randomization (T0, baseline), and at three (T1), six (T2) and twelve (T3) months thereafter. If participants did not respond, a second request was sent after four weeks and a third request after eight weeks. If no response was received after twelve weeks, or the data was unclear, the participant was contacted by e-mail and/or phone by a researcher.

Baseline Descriptive Measures

The following baseline characteristics were collected: age, weight, height, marital or cohabitating status, parity, number of children living at home, highest completed education, employment, smoking history, alcohol consumption, exercise behavior, breast cancer history, mastectomy history, and HRT use. In addition, anxiety and depression were screened for using the Generalized Anxiety Disorder 7 (GAD-7) questionnaire[37] and the Patient Health Questionnaire-2 (PHQ-2),[38] respectively.

Primary Outcome Measure

The primary outcome of interest was menopause-specific quality of life, as measured by the Menopause-specific Quality of Life questionnaire (MENQOL). The MENQOL is a self-administered 29-item questionnaire that assesses quality of life in menopausal women over the preceding four weeks.[39] It records the presence and the severity of menopausal symptoms as the degree of perceived burden (or bother) women experience from menopausal symptoms, using seven-point scales per item. It consists of four domains: vasomotor (three items), psychosocial (seven items), physical (16 items), and sexual (three items). The domain scores range from one to eight, with one reflecting an absence of symptoms and eight reflecting extremely bothersome symptoms. A cut-off score is not available.

Secondary Outcome Measures

The Female Sexual Function Index questionnaire (FSFI) consists of 19 items on six sub-domains: desire, arousal, lubrication, orgasm, satisfaction, and pain.[40] Each domain is scored on a Likert-type scale from zero to five. Higher scores indicate better sexual functioning in the prior four weeks, and a score <26.55 indicates sexual dysfunction.[41]

Sexual distress was determined using the Female Sexual Distress Scale questionnaire (FSDS) for the preceding four weeks. The FSDS consists of 12 items scored on a five-point Likert scale from zero (no distress) to four (always experiencing distress).[42] A score of 11 or higher indicates sexual distress.[43]

Sample Size Calculation

The minimum sample size was calculated as 64 with and 60 without correcting for 10% attrition based on a minimal clinically relevant difference of 1.0 on the MENQOL, a standard deviation of 1.36 based on a previous RCT that compared the change in MENQOL score between a MBSR intervention group and a waiting list control group at 20 weeks in naturally post and perimenopausal women[33], a statistical power of 80% and an α of 0.05.[33]

Quality Control

To improve consistency and uniformity of the MBSR training sessions, three meetings were organized with the trainers under the supervision of an experienced MBSR trainer (MS), and adherence to the protocol was assessed by audio recordings of 6/48 (12.5%) of all training sessions. Protocol adherence was defined as the weighted average of agreement between the specified and actual exercise duration. Participant attendance was recorded by trainers at start of each session, and participants were asked to report the frequency and duration of daily home exercises on weekly evaluation forms during the intervention period.

Statistical Analysis

In case of missing items in the questionnaires, scores were calculated using mean imputation if at least 80% of the answers had been given. Baseline characteristics were described for each treatment arm using means and standard deviations for continuous variables and using frequencies for categorical variables. The primary and secondary outcomes were analyzed by linear mixed modeling to allow for the inclusion of women with missing time points for longitudinal data. The scores on the MENQOL, FSDS, FSFI, and their sub-domains at T0, T1, T2, and T3 were modeled as a function of the treatment arm,

the time moment, and the interaction between the treatment arm and the time moment. An unstructured data matrix was assumed because the data did not indicate another correlation structure. All analyses were performed on an intention-to-treat basis. The normality of the outcome measures will be determined by visual inspection of a Q-Q plot. We used IBM SPSS version 23 (IBM Corp., Armonk, NY, USA) for all analyses. All p-values were two-tailed and considered significant if $p < 0.05$.

Funding

The C&W de Boer Foundation provided funding for the research. The funding source had no role in the study design, collection, analysis, or interpretation of data, or in the writing of the manuscript or in the decision to submit it for publication. The corresponding author had full access to all study data and has final responsibility for the decision to submit for publication.

Results

Recruitment and Attrition

Of the 365 women informed about the study, 218 women completed and returned the questionnaires on the presence and severity of menopausal symptoms (Figure 1); of these, 197 met the inclusion criteria and 66 agreed to participate and be randomized to the MBSR (n = 34) and CAU (n = 32) groups. One participant in the CAU group did not return the questionnaire at T0 or at subsequent time points for unknown reasons, so baseline data were available for 65 participants (34 MBSR, 31 CAU). At inclusion, the average age of the participants was 47.7 ± 5.2 years, and 19 out of 65 (29%) women used HRT (Table 1). Furthermore, 17 out of 65 women (26%) had a history of breast cancer.

Six participants did not complete the intervention, with two citing scheduling conflicts, two citing that it was too time consuming, and two citing that they were not expecting a benefit. At each time point, at least 70% of participants returned their questionnaires, and the reasons for non-response are shown in Figure 1. In total, 53 women completed the MENQOL questionnaire at T1 resulting in a statistical power of 76%.

Quality Control

Adherence by the trainers to the MBSR protocol, based on the audio recordings of several training sessions, was 80%. Participants receiving MBSR attended 79% of the MBSR sessions. The patient-reported adherence to daily homework was 75% during the intervention period, with participants reporting practicing for 33 minutes on average per day.

Primary and Secondary Outcomes

Table 2 summarizes the results of linear mixed modeling of the primary and secondary outcomes as a function of time, treatment, and interaction between time and treatment. Figure 2 visualizes the primary outcome estimates per time point and arm.

At randomization (T0), 63% (41/65) of participants reported five or more complaints with a bother score of six or higher (scale one to eight, data not shown). Statistically significant differences in improvements were found for the MENQOL total score (T1: 0.56, $p = 0.04$, T3: 0.56, $p = 0.04$) and the vasomotor (T1: 0.93, $p = 0.04$, T3: 0.98, $p = 0.02$) and physical (T1: 0.65, $p = 0.01$, T3: 0.69, $p = 0.03$) subscales in the MBSR group compared with the CAU group at three and 12 months after the start of the intervention (Table 2). At six months, there was a non-significant trend for improvement in the MBSR group compared with the CAU group ($p = 0.31$), but there were no statistically significant differences in the psychosocial and sexual subscales of the MENQOL between the MBSR and CAU groups at

any assessment point. A statistically non-significant but clinically relevant improvement (≥1 improvement in MENQOL total score) was also seen in 28.6% of the MBSR group compared with 16.7% of the CAU group at T1.

Regarding the secondary outcomes, 94% (61/65) of participants reported clinically relevant sexual dysfunction and 65% (42/65) reported clinically relevant sexual distress at randomization (T0; data not shown). However, no statistically significant differences were observed between the MBSR and CAU groups for the FSDS and FSFI total scores or subscales at any assessment point (Table 2).

After visual inspection of their respective Q-Q plots, the MENOL and FSDS could be considered to be normally distributed, but some non-normality could be observed in the distribution of FSFI scores at baseline (Figure S1).

Discussion

Main Findings

In this randomized study, we showed that MBSR improved menopause-specific quality of life over both the short- and long-term in women with at least two moderate-to-severe menopausal symptoms after RRSO. However, MBSR did not improve sexual functioning or sexual distress.

Strengths and Limitations

The main strengths of this study are its randomized controlled design, the long-term follow-up over 12 months and that MBSR was conducted by certified trainers with high protocol adherence. Furthermore, this study is the first RCT to test a psychological

intervention for alleviating menopausal complaints after RRSO, and is among the first to test the effect of that intervention on sexual symptoms associated with menopause.

The CAU group did not receive a blinded placebo intervention because it was impossible to blind participants to treatment allocation, which could induce a placebo effect. The use of a non-active control group receiving CAU and no other attention during the intervention period means that there was no control for the non-specific effects of MBSR (e.g., repeated contact with MBSR trainers and other group participants). Although no adverse effects were reported during the intervention, this was not routinely monitored or recorded, so cannot be excluded as a possibility. The FSFI questionnaire was observed to have some non-normality which could have resulted in an optimistic p-value estimation. Since the FSFI was not found to be statistically significantly improved more in the MBSR arm compared to the CAU arm this would not impact the conclusions of the study. Finally, only one third of the eligible women chose to participate in this study, therefore a self-selection bias is plausible which could have caused an overestimation of the intervention effect.

Interpretation

This is the first study reporting the long-term effects of MBSR in women with menopausal symptoms after RRSO. Consistent with previous studies, we showed short-term improvement at three months (T1).[32,33] However, our study is the first to report a persisting effect after one year, with improvement in menopause-specific quality of life at 12 months (T3) in the MBSR group compared with the CAU group. Although there was improvement from baseline in the MBSR group compared with the CAU group at the intermediate period of six months (T2), this was not statistically significant. Given that the change in effect at six months (T2) is small but in the same direction as the short- and long-term significant effect, it

is likely that this is merely due to a statistical issue that could be solved with a larger sample size.

On the interpretation of the MENQOL score, no specific studies have been published. However, the authors of the MENQOL questionnaire have suggested that a relevant clinical difference in MENQOL score could be 0.5 point change[39]. This suggestion was based on previous publications that compared patient-rated relevant change in symptoms with the corresponding change on a 7-point scale in other disease-specific QOL questionnaires (similar to the MENQOL questionnaire)[44,45]. A change of 0.5 or of 1.0 was equivalent to patients reporting their symptoms to be 'A little better' and 'Moderately better', respectively[44,45].

In the current study the improvement in the total MENQOL score was mainly due to the improvement in the subscales of vasomotor symptoms (i.e. burden caused by hot flushes, night sweats and sweating in general) and physical symptoms (e.g. burden caused by stamina reduction, aches, urination frequency). The average difference on a 7-point scale in the vasomotor subscale and the physical subscale was 0.93 and 0.65 points, respectively. Therefore clinicians and patients could expect a modest to moderate reduction of perceived burden (i.e. bother) by vasomotor and physical symptoms of approximately 13% and 9% respectively.

Clinicians and patients might want to be able to interpret the clinical impact of MBSR in terms of symptom frequency reduction. The MENQOL questionnaire only measures bother by menopausal symptoms, not frequency of menopausal symptoms. However some direction on the relationship between bother by and frequency of menopausal symptoms can be given. In an earlier RCT that recorded both the change in hot flush frequency and change in MENQOL score, an improvement of approximately one point in the MENQOL score was

found together with a 45% reduction of the hot flush frequency (an estimated reduction of approximately four hot flushes per day). However, the conclusion that one point change in MENQOL score represents the aforementioned reduction in hot flushes is too simplified. Changes in the other symptom domains or other (unknown) factors influence the total MENQOL score as well and therefore the relation between MENQOL score and hot flush frequency could be different in other circumstances.

The baseline level of sexual dysfunction was very high in this study, comparable to that reported after RRSO in other research, but much higher than that reported in the general population.[27,46] Unfortunately, our MBSR intervention did not improve this sexual dysfunction or distress. In contrast to this, previous controlled studies of mindfulness-based therapy for low sexual desire and arousal have found significant improvements in sexual functioning after the intervention.[47,48] Differences in study populations could explain the results, because the sexual problems in previous studies were of a psychological nature (e.g., lack of desire or low arousability), whereas the problems in the current population may have been of a mixed psychological and physiological nature (e.g., vaginal discomfort and loss of desire due to estrogen deprivation).[47,48] However, consistent with our study, the earlier research also failed to show any improvement in sexual distress.[47,48] In a single-armed pilot study, mindfulness-based therapy did improve sexual functioning after RRSO, but that study used an intervention specifically targeting sexual difficulties, rather than a general MBSR protocol as we used in this study.[49]

It has been proposed that mindfulness facilitates a more accepting, even-tempered state of being that helps decrease reactivity to stimuli.[50] Therefore, MBSR could work by reducing the degree to which vasomotor and physical symptoms are experienced as problematic or bothersome; in other words, by dampening the perceived severity of symptoms.[51] Indeed, it might be that MBSR also primarily affects the psychological aspects

of sexual problems by improving cognitive appraisal rather than the by altering the actual physiological symptoms. This would explain why a previous study on the effect of MBSR on physiological arousal, as measured by vaginal photoplethysmography, did not find an improvement[47]. However, another hypothesis is that by decreasing stress, MBSR could diminish the frequency of hot flushes at a physiological level, because stress is thought to lower the threshold for heat dissipation responses.[51,52] Moreover, the effect of MBSR on the physiological stress response has been suggested by preliminary research indicating that it produces statistically significant reductions in cortisol levels and non-significant improvements in dehydroepiandrosterone-sulfate levels.[53,54]

Conclusion

This study indicates that MBSR improves short- and long-term menopause-specific quality of life in women with menopausal complaints after surgical menopause induced by RRSO. We recommend that healthcare providers advocate MBSR in conjunction with HRT. However, MBSR may be especially relevant for breast cancer survivors or in other settings when HRT is contraindicated.

Acknowledgments

We thank Dr Robert Sykes (www.doctored.org.uk) for providing editorial services.

Disclosure of interests

All authors declare that they have no conflicts of interest. Completed disclosure of interest forms are available to view online as supporting information.

Contribution to Authorship

All authors (CvD, GdB, MS and MM) were involved in the design and execution of the trial, analysis of the data and writing of the paper.

Details of ethics approval

The study protocol was approved by the Medical Ethical Committee of the University Medical Center Groningen on November 14, 2014 (registration number NL46796.042.14).

Funding

The C&W de Boer Foundation provided funding for the research. The funding source had no role in the study design, collection, analysis, or interpretation of data, or in the writing of the manuscript or in the decision to submit it for publication. The corresponding author had full access to all study data and has final responsibility for the decision to submit for publication.

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Table 1. Baseline characteristics

Variable	Total (N = 65)	MBSR (N = 34)	CAU (N = 31)
Age, mean (SD)	47.7 (5.2)	47.0 (5.0)	48.5 (5.4)
BMI, mean (SD)	26.4 (4.9)	26.6 (4.0)	26.2 (5.8)
Married or cohabiting, n (%)			
No	7 (10.8)	1 (2.9)	6 (19.4)
Yes	58 (89.2)	33 (97.1)	25 (80.6)
Children, n (%)			
No	10 (15.4)	2 (5.9)	8 (25.8)
Yes	55 (84.6)	32 (94.1)	23 (74.2)
Children at home, n (%)			
No	16 (24.6)	4 (11.8)	12 (38.7)
Yes	49 (75.4)	30 (88.2)	19 (61.3)
Higher education[#], n (%)			
No	37 (56.9)	23 (67.6)	14 (45.2)
Yes	28 (43.1)	11 (32.4)	17 (54.8)
Employment status, n (%)			
Unemployed	10 (15.4)	6 (17.6)	4 (12.9)
Part-time	39 (60.0)	19 (55.9)	20 (64.5)
Full-time	16 (24.6)	9 (26.5)	7 (22.6)
Smoker, n (%)			
No	56 (86.2)	31 (91.2)	25 (80.6)
Yes	9 (13.8)	3 (8.8)	6 (19.4)
Alcohol consumption, n (%)			
0-1 unit / wk	36 (55.4)	17 (50.0)	19 (61.3)
2-5 units /wk	24 (36.9)	16 (47.1)	8 (25.8)
>6 units / wk	5 (7.7)	1 (2.9)	4 (12.9)
Exercise behavior, n (%)			
< 150 min / wk	12 (18.5)	8 (23.5)	4 (12.9)

≥ 150 min / wk	53 (81.5)	26 (76.5)	27 (87.1)
Underwent RRM, n (%)			
No	34 (52.3)	15 (44.1)	19 (61.3)
Yes	31 (47.7)	19 (55.9)	12 (38.7)
Had BC, n (%)			
No	48 (73.8)	25 (73.5)	23 (74.2)
Yes	17 (26.2)	9 (26.5)	8 (25.8)
Current HRT use, n (%)			
No	46 (70.8)	23 (67.6)	23 (74.2)
Yes	19 (29.2)	11 (32.4)	8 (25.8)
PHQ-2, mean (SD)	1.3 (1.3)	1.4 (1.4)	1.1 (1.1)
GAD-7, mean (SD)	5.5 (4.5)	5.0 (3.5)	5.9 (5.3)

n = 65, One participant did not return the questionnaire at T0 or at subsequent time points, so baseline data were available for 65 participants. [#]: Higher education = (applied) university or higher. Abbreviations: SD, standard deviation; BMI, body mass index; RRM, risk-reducing mastectomy; BC, breast cancer; HRT, hormone replacement therapy; PHQ-2, Patient Health Questionnaire-2; GAD-7, Generalized Anxiety Disorder-7; MBSR, mindfulness-based stress reduction; CAU, care as usual.

Table 2. Linear mixed modeling of the primary and secondary outcomes as a function of time, treatment, and interaction

		T0	T1	T2	T3
MENQOL	Total score				
	CAU	3.8 (3.4–4.3)	3.8 (3.3–4.3)	3.7 (3.2–4.1)	3.9 (3.5–4.4)
	MBSR	4.1 (3.7–4.5)	3.5 (3.0–3.9)	3.7 (3.2–4.1)	3.6 (3.1–4.0)
	p		0.04*	0.31	0.04*
	Vasomotor subscale				
	CAU	4.2 (3.6–4.8)	4.1 (3.5–4.8)	4.2 (3.5–4.8)	4.3 (3.7–4.9)
	MBSR	4.5 (4.0–5.1)	3.5 (2.9–4.1)	3.8 (3.1–4.4)	3.6 (3.0–4.2)
	p		0.04*	0.09	0.02*
	Psychosocial subscale				
	CAU	3.7 (3.2–4.2)	3.6 (3.0–4.1)	3.6 (3.0–4.2)	3.8 (3.3–4.4)
	MBSR	3.8 (3.3–4.3)	3.4 (2.8–3.9)	3.6 (3.0–4.2)	3.7 (3.1–4.3)
	p		0.31	0.95	0.50
	Physical subscale				
	CAU	3.5 (3.1–3.9)	3.6 (3.2–4.0)	3.5 (3.0–3.9)	3.8 (3.3–4.2)
	MBSR	3.5 (3.2–3.9)	3.0 (2.6–3.4)	3.3 (2.9–3.7)	3.2 (2.7–3.6)
	p		0.01*	0.32	0.03*
	Sexual subscale				
	CAU	4.0 (3.1–4.8)	3.9 (3.0–4.7)	3.5 (2.7–4.3)	3.7 (2.9–4.4)
	MBSR	4.4 (3.6–5.2)	4.1 (3.3–4.9)	4.2 (3.4–5.0)	4.0 (3.2–4.8)
	p		0.66	0.39	0.77
FSDS	Total score				
	CAU	14.7 (10.7–18.7)	15.6 (10.7–20.4)	12.2 (7.8–16.6)	12.4 (7.5–17.2)
	MBSR	16.9 (13.1–20.8)	16.7 (12.0–21.3)	17.2 (12.9–21.5)	17.6 (12.8–22.5)
	p		0.65	0.17	0.26
FSFI	Total score				
	CAU	15.0 (11.9–18.1)	14.6 (11.3–17.8)	14.7 (11.3–18.2)	16.3 (13.0–19.6)
	MBSR	14.8 (11.9–17.8)	15.7 (12.6–18.8)	14.4 (11.0–17.8)	16.8 (13.5–20.0)
	p		0.40	0.92	0.75
	Desire subscale				
	CAU	2.7 (2.3–3.1)	2.7 (2.3–3.1)	2.6 (2.2–3.1)	2.7 (2.2–3.1)
	MBSR	2.7 (2.3–3.1)	2.5 (2.1–3.0)	2.5 (2.0–2.9)	2.7 (2.2–3.1)

p		0.63	0.66	0.97
Arousal subscale				
CAU	2.8 (2.1–3.6)	2.8 (2.0–3.6)	2.8 (2.0–3.5)	3.2 (2.5–3.9)
MBSR	3.0 (2.3–3.7)	3.2 (2.5–3.9)	2.8 (2.1–3.6)	3.2 (2.5–4.0)
p		0.71	0.75	0.69
Lubrication subscale				
CAU	2.9 (2.1–3.7)	2.7 (1.9–3.6)	3.0 (2.1–3.9)	3.0 (2.2–3.9)
MBSR	2.8 (2.1–3.6)	3.1 (2.3–3.9)	2.9 (2.1–3.8)	3.8 (2.9–4.7)
p		0.29	0.94	0.14
Orgasm subscale				
CAU	3.0 (2.2–3.8)	2.8 (2.0–3.7)	2.8 (1.9–3.7)	3.4 (2.5–4.2)
MBSR	2.9 (2.1–3.7)	3.3 (2.5–4.1)	3.1 (2.2–4.0)	3.7 (2.8–4.6)
p		0.16	0.41	0.39
Satisfaction subscale				
CAU	3.6 (3.0–4.1)	3.6 (3.0–4.2)	3.7 (3.1–4.4)	3.9 (3.3–4.6)
MBSR	3.3 (2.7–3.8)	3.3 (2.7–3.9)	3.2 (2.6–3.9)	3.3 (2.7–3.9)
p		1.00	0.71	0.38
Pain subscale				
CAU	2.8 (1.8–3.7)	2.7 (1.7–3.7)	2.6 (1.6–3.6)	3.2 (2.3–4.1)
MBSR	2.9 (2.0–3.8)	3.1 (2.2–4.0)	2.4 (1.5–3.4)	3.2 (2.2–4.1)
p		0.51	0.53	0.75

Results are presented as means and 95% confidence intervals. n = 65, one participant did not return the questionnaire at T0 or at subsequent time points, resulting in baseline data being available for 65 participants. Reported p-values are reported for the group x time interactions in contrast to T0 in a linear mixed model. A p-value<0.05 (*) corresponds to a statistically significantly difference in the outcome measure between the MBSR and CAU groups from T0. Abbreviations: MENQOL, Menopause-Specific Quality of Life; FSDS, Female Sexual Distress Scale; FSFI, Female Sexual Functioning Index; CAU, care as usual; MBSR, mindfulness-based stress reduction.

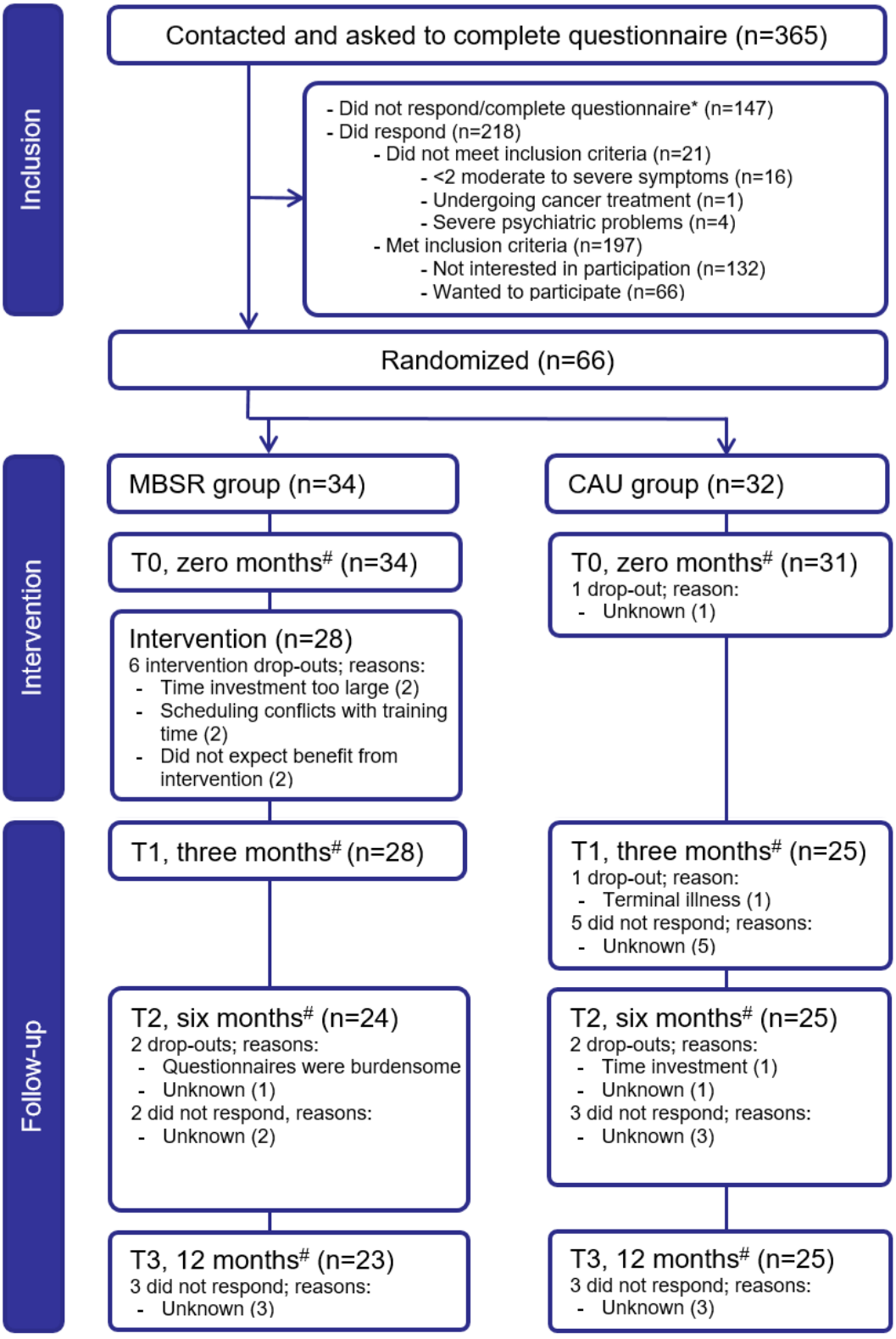

Figure 1: Population flowchart

*: 39 women responded they had no interest in participating in the study without filling in the rest of the questionnaire

#: The T0, T1, T2 and T3 questionnaires were sent zero, three, six and 12 months after randomization respectively

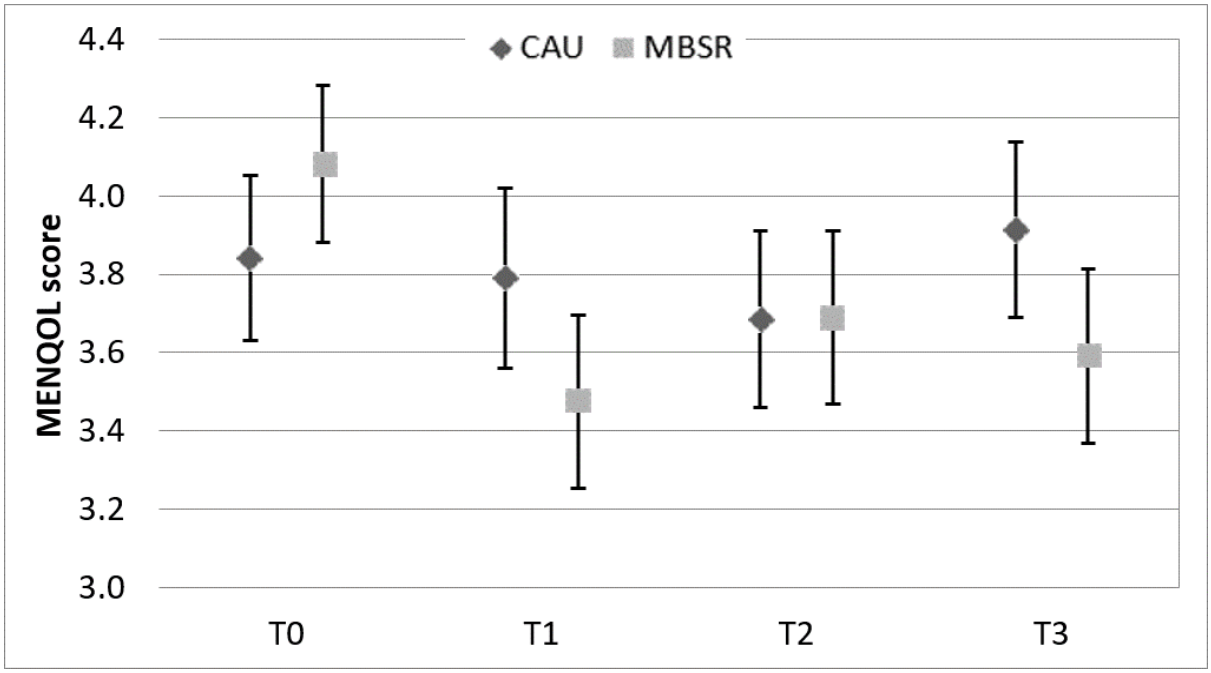

Figure 2: MENQOL score estimates per time point and arm.

The error bar represents the standard error.