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Menopause

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

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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 Randomised controlled trial.

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

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

Methods Women were randomised to an 8-week MBSR training programme or to 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 modelling 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.

Conclusion Mindfulness-based stress reduction 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 an improvement in sexual functioning or distress.

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

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

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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 35–40 years for *BRCA1* mutation carriers and at 40–45 years for *BRCA2* mutation carriers, provided that 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 the use of HRT.[29,30] Therefore, non-hormonal methods are needed to alleviate the 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 achieves this through a well-described, protocol-based training programme over an 8-week period. The programme 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] These studies were not carried out in women with RRSO-induced menopause, however, 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 with 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 randomised 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 14 November 2014 (registration no. 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 1 year after randomisation. 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 for being at increased risk of developing breast or ovarian cancer, including *BRCA1/2* mutation carriers, have been prospectively recorded in a database since 1994.[12] 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 (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: women who were undergoing cancer treatment at the time of inclusion, apart from those receiving adjuvant hormonal or immune therapy; women who were receiving psychiatric care; and women who had an insufficient understanding of the Dutch language to complete the questionnaires. We did not exclude women using HRT, non-hormonal medications (e.g. clonidine), or dietary or herbal remedies (e.g. soy or black cohosh), or women with a history of breast cancer. All eligible women were invited for an intake visit, and after giving written informed consent, were randomised to an intervention or to a control group. The intervention group received an 8-week MBSR training course, plus CAU, whereas the control group only received CAU.

Interventions

Participants in the MBSR group received an 8-week MBSR training course (Appendix S2). This comprised weekly sessions of 2.5 hours each, a silent retreat evening lasting 4 hours, and a commitment to performing mindfulness exercises at home for 30–45 minutes for 6 days of the week using instructions provided on an MP3 player.[31] The MBSR training was a standard training programme and was not specifically adapted to focus on menopausal symptoms. In total, six MBSR training classes were organised, each with between four and seven study participants only. Training classes took place at three locations in the north

of the Netherlands to reduce the travel time for participants, and all were led by one of three certified and experienced MBSR trainers.

Care as usual

Care as usual 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 randomisation, all participants were offered a repeat appointment with the nurse to address any remaining issues.

Randomisation

We used block randomization, stratified by HRT use. Randomisation was performed by the independent trial coordination centre of the University Medical Center Groningen via a web application, using a computerised random number generator. After randomisation, an email 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 randomisation (T0, baseline), and at 3 (T1), 6 (T2), and 12 months (T3) thereafter. If participants did not respond, a second request was sent after 4 weeks and a third request was sent after 8 weeks. If no response was received after 12 weeks, or the data were unclear, the participant was contacted by email 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 level, employment, smoking history, alcohol consumption, exercise behaviour, breast cancer history, mastectomy history, and HRT use. In addition, anxiety and depression were screened using the Generalized Anxiety Disorder 7 (GAD-7) questionnaire,[36] and the Patient Health Questionnaire 2 (PHQ-2),[37] 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 the quality of life of menopausal women over the preceding 4 weeks.[38] It records the presence and the severity of menopausal symptoms as the degree of perceived burden (or bother) that women experience from menopausal symptoms, using a seven-point scale for each 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 (FSFI) questionnaire consists of 19 items on six subdomains: desire, arousal, lubrication, orgasm, satisfaction, and pain.[39] Each domain is scored on a Likert-type scale from zero to five. Higher scores indicate better sexual functioning in the prior 4 weeks, and a score <26.55 indicates sexual dysfunction.[40]

Sexual distress was determined using the Female Sexual Distress Scale (FSDS) questionnaire for the preceding 4 weeks. The FSDS consists of 12 items scored on a five-point Likert scale from zero (no distress) to four (always experiencing distress).[41] A score of 11 or higher indicates sexual distress.[42]

Sample size calculation

The minimum sample size was calculated as 64 with, and 60 without, correcting for a 10% rate of attrition, based on a minimal clinically relevant difference of 1.0 on the MENQOL, a standard deviation of 1.36 based on a previous randomised controlled trial (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 organised 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 duration of the exercise. Participant attendance was recorded by trainers at the 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 analysed by linear mixed modelling to allow for the inclusion of women with missing time points for longitudinal data. The scores on the MENQOL, FSDS, FSFI, and their subdomains at T0, T1, T2, and T3 were modelled as a function of the treatment arm, the moment in time, and the interaction between the treatment arm and the moment in time. 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 quantile–quantile (Q–Q) plot. We used SPSS 23 (IBM Corp., Armonk, NY, USA) for all analyses. All P values were two-tailed and considered significant if $P < 0.05$.

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 randomised 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 any benefit. At each time point, at least 70% of the 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 practising for 33 minutes on average per day.

Primary and secondary outcomes

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

At randomisation (T0), 63% (41/65) of participants reported five or more complaints with a bothersome score of six or higher (scale ranged from 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 for 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 3 and 12 months after the start of the intervention (Table 2). At 6 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 randomisation (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 MENQOL 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 randomised 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 randomised 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.

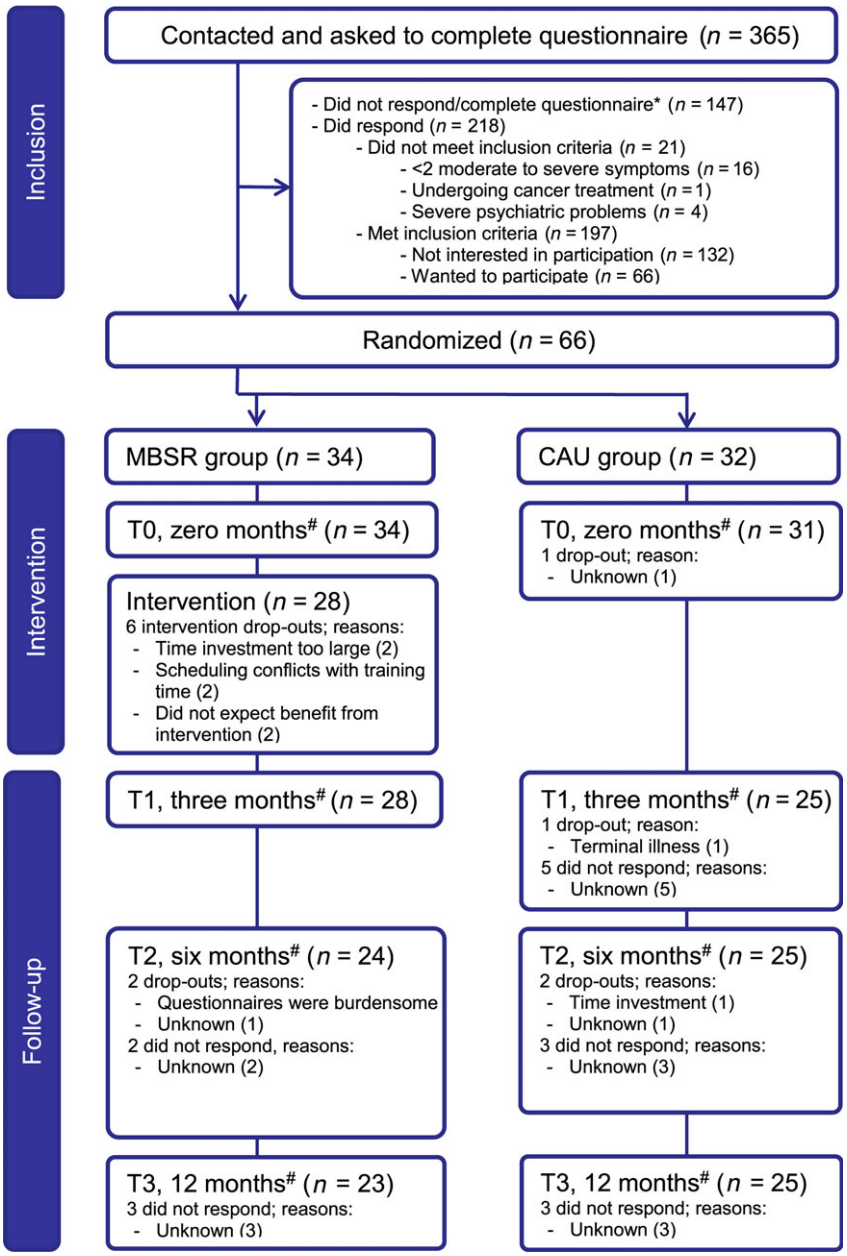

Figure 1. Population flowchart. *A total of 39 women responded that they had no interest in participating in the study without filling in the rest of the questionnaire. #The T0, T1, T2, and T3 questionnaires were sent out at 0, 3, 6, and 12 months after randomisation, respectively.

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. As the FSFI was not found to be statistically significantly improved in the MBSR arm compared with 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, and therefore a self-selection bias is plausible that could have caused an overestimation of the intervention effect.

Table 1. Baseline characteristics

Variable	Total (n = 65)	MBSR (n = 34)	CAU (n = 31)
Age (years), mean (SD)	47.7 (5.2)	47.0 (5.0)	48.5 (5.4)
BMI (kg/m^2), 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 units/week	36 (55.4)	17 (50.0)	19 (61.3)
2–5 units/week	24 (36.9)	16 (47.1)	8 (25.8)
>6 units/week	5 (7.7)	1 (2.9)	4 (12.9)
Exercise behaviour, *n* (%)			
<150 minutes/week	12 (18.5)	8 (23.5)	4 (12.9)
≥150 minutes/week	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 breast cancer, *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.

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 1 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 6 months (T2), this was not statistically significant. Given that the change in effect at 6 months (T2) is small but in the same direction as the short- and long-term significant effect, it is likely that this is merely 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 a 0.5-point change.[38] This suggestion was based on previous publications that compared patient-rated relevant changes in symptoms with the corresponding change on a seven-point scale in other disease-specific quality-of-life questionnaires (similar to the MENQOL questionnaire).[43,44] 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.[43,44]

In the current study the improvement in the total MENQOL score was mainly the result of an 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, and urination frequency). The average difference on a seven-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 a reduction in the frequency of symptoms. 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 the frequency of hot flushes and the change in the MENQOL score, an improvement of approximately one point in the MENQOL score was found together with a 45% reduction in the frequency of hot flushes (representing an estimated reduction of approximately four hot flushes per day); however, the conclusion that a one point change in the MENQOL score represents the aforementioned reduction in hot flushes is an oversimplification. Changes in the other symptom domains or other (unknown) factors influence the total MENQOL score as well, and therefore, the relationship between MENQOL score and hot flush frequency could be different in other circumstances.

Table 2. Linear mixed modelling 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

The baseline level of sexual dysfunction was very high in this study, comparable with that reported after RRSO in other research, but much higher than that reported in the general population.[27,45] 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.[46,47] Differences in study populations could explain the results, because the sexual problems in previous

Table 2. (Continued)

	T0	T1	T2	T3
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. *P* values are reported for the group × time interactions in contrast with T0 in a linear mixed model. $*P < 0.05$ corresponds to a statistically significant difference in the outcome measure between the MBSR and CAU groups from T0.

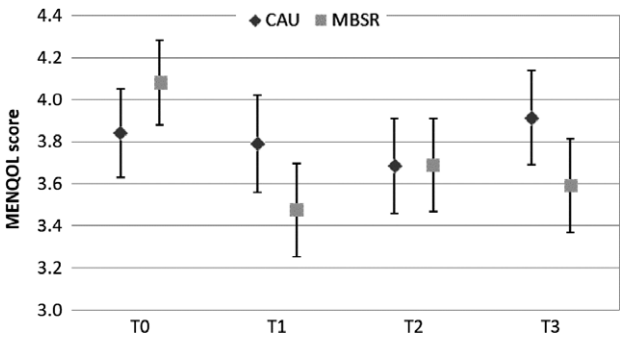

Figure 2. MENQOL score estimates per time point and treatment arm. The error bars represent standard errors.

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 mixed psychological and physiological nature (e.g. vaginal discomfort and loss of desire as a result of estrogen deprivation).[46,47] Consistent with our study, however, the earlier research also failed to show any improvement in sexual distress.[46,47] 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.[48]

It has been proposed that mindfulness facilitates a more accepting, even-tempered state of being that helps to decrease reactivity to stimuli.[49] 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.[50] Indeed, it might be that MBSR also primarily affects the psychological aspects of sexual problems by improving cognitive appraisal rather than 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 any improvement.[46] Another hypothesis, however, 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.[50,51] 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.[52,53]

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.

Disclosure of interests

None declared. Completed disclosure of interests form 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 the 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 14 November 2014 (registration no. NL46796.042.14).

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Q–Q plots for the MENQOL, FSFI, and FSDS outcome measures.

Appendix S1. Translated questionnaire on the presence and severity of menopausal symptoms.

Appendix S2. Translated MBSR training protocol summary.

Video S1. Author insights. ■

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