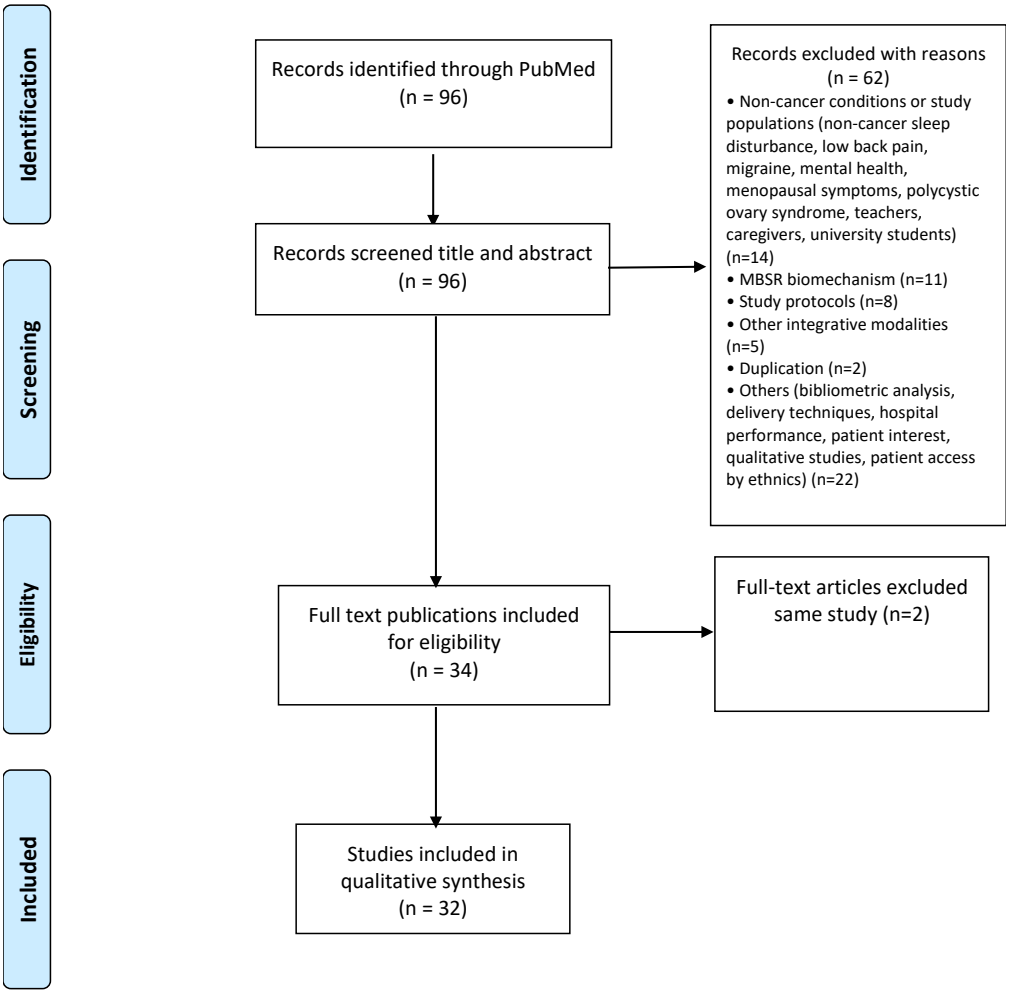
Mindfulness-based stress reduction (MBSR) for cancer – a literature review

Methodology

A literature search was conducted in the database of Medline via PubMed in June 2023. The search key words were 'mindfulness-based stress reduction' AND 'cancer'. Filters for free full text, English and human were applied. The goal of this literature review is to examine available evidence on the effect of MBSR for patients with cancer and cancer survivors. 96 entries were generated by from the database with which 62 were excluded after screening the titles and abstracts for eligibility. Reasons for exclusion are recorded in the below PRISMA diagram. 34 full text articles were retrieved and 2 excluded due to duplication. Final 32 articles were included for qualitative synthesis.

PRISMA diagram illustrating systematic search incorporated into this review.



Summary of literature

Full text articles of 11 systematic reviews and meta-analysis and 22 original studies were evaluated. Majority (>90%) of study populations were breast cancer patients and survivors. A small number of studies with small sample size included other cancer types such as colorectal cancer, osteosarcoma, lymphoma and lung cancer.

Study outcomes focused on psychological outcomes (such as anxiety, depression, and stress), quality of life, cancer-related fatigue, as well as biological outcomes (e.g., biomarkers for inflammatory and immune response). The follow-up time ranged between 2 and 24 months, 6 being the most common. A consistent and significant small to medium effect of MBIs on decreasing anxiety, depression, stress, rumination, fear and emotional control was found. However, the results are inconsistent on QoL, pain relief, cancer-related fatigue and sleep quality with small number of studies presenting positive effect whereas other studies showed no effects. Small biological effects were shown with increased immune or inflammatory related markers in some studies. These beneficial effects were maintained in short term up to 6 months, but tend to disappear with longer follow-ups.

Further larger and more rigorous studies are required to establish conclusive evidence about the efficacy and effectiveness of MBSR in oncology cares. High quality evidence is needed to establish if MBIs effects are clinically relevant and to identify for whom MBIs may work best.

Definition of MBSR

Mindfulness-based stress reduction is a program that aims to reduce stress by developing mindfulness, meaning a non-judgmental, accepting moment-by-moment awareness. (Schell et al., 2019) MBSR program is based on intensive training in mindfulness that preconizes present-centered non-judgmental acceptance, awareness, and attentiveness compassion. MBSR is based on four foundations: awareness of the body, feeling tone, mental states, and mental contents. The term Mindfulness-Based Interventions (MBIs) has emerged to include interventions with mindfulness components in conjunction with other interventions or theoretical approaches. The gold-standard model which is in the base of other two main programs broadly used in clinical settings, namely the Mindfulness-Based Cognitive Therapy (MBCT) and the Mindfulness-Based Cancer Recovery (MBCR), is the MBSR 8-week course, involving 20–26 h of formal meditation in group classes of 1.5–2.5 h each, one all-day (6 h) class, and home practice (about 45 min/day, 6 days/week). (Pedro et al., 2021)

However, a universal technical definition of *mindfulness* has not yet been found. There are diverse ways to carry out teaching and practicing mindfulness. There are yet standardized MBI protocols, which can hinder clinical research on effectiveness of MBSR in terms of its replicability and the quality of evidence.

Systematic reviews and meta-analyses

Eleven systematic reviews and meta-analysis were evaluated. Majority (>90%) of study populations were breast cancer patients and survivors. Study outcomes focused on psychological outcomes (such as anxiety, depression, and stress), quality of life, cancer-related fatigue, as well as biological outcomes (e.g., inflammatory response). The follow-up time ranged between 2 and 24 months, 6 being the most common. A consistent and significant small to medium effect of MBIs on decreasing anxiety, depression, and stress was found. However, the results are inconsistent on QoL with small number of studies presenting positive effect whereas other studies showed no effects. Small biological effects were shown with increased immune or inflammatory related markers in some studies. These beneficial effects were maintained in short term up to 6 months but tend to disappear with longer follow-ups. Further larger and more rigorous studies are required to establish conclusive evidence about the efficacy and effectiveness of MBSR in oncology cares. High quality evidence is needed to establish if MBIs effects are clinically relevant and to identify for whom MBIs may work best.

Synopsis of each systematic review

McCloy et al. (McCloy et al., 2022) conducted a systematic review and meta-analysis of randomized control trials (RCTs) that studied the effects of MBIs on fatigue and psychological wellbeing in women with cancer. Based on twenty-one studies with a total of 2326 participants (97% breast cancer). MBSR showed significant effects in improving cancer-related fatigue (CRF), depression and anxiety, but no effect was observed for QoL and sleep.

Ladenbauer and Singer (Ladenbauer & Singer, 2022) published a systematic review on evidence of MBSR that can influence the QoL, anxiety, and depression of women diagnosed with breast cancer. With six studies included, two studies found positive impacts on QoL, whereas three did not find a positive correlation. Four out of six studies found a positive relation between MBSR and anxiety scores, but only half of the included studies found positive results for the interaction between MBSR and depression scores.

Chayadi et al. (Chayadi et al., 2022) conducted a systematic review and meta-analysis about the effects of MBI on symptoms of depression, anxiety, and CRF in oncology patients. 36 independent studies (n = 1677), including non-randomized (K = 20, n = 784) and randomized controlled trials (K = 16, n = 893), were evaluated for their overall effect sizes, subgroup analyses, and quality appraisals. Participants were patients with mixed cancers (K = 17), breast cancer (K = 16) lung cancer (K = 1), prostate cancer (K = 1), and thyroid cancer (K = 1). The majority of participants were females (82.66%). The findings include that MBIs have significant medium effects in reducing symptoms of depression, anxiety and CRF, which were maintained at least three months post-intervention. MBIs were also superior in reducing symptoms of anxiety, depression and CRF in oncology samples relative to control groups. The superiority of MBIs to control groups was also maintained at least three months post-intervention for anxiety and CRF symptoms, but not for depressive symptoms.

A meta-review was conducted by Pedro et al. (Pedro et al., 2021) based on previous systematic reviews on evidence of psychological and biological effects of MBI for cancer patients and survivors, measured by psychological outcomes (such as anxiety, depression, and stress), quality of life (QoL), as well as biological outcomes (e.g., inflammatory response). Ten previous reviews were inncluded with 80-90% study population

being breast cancer patients and survivors. The main findings were beneficial small to medium effect of MBI on psychological health, such as anxiety, depression, stress, and quality of life. Some studies demonstrated a small beneficial effect for biological outcomes. Results on long-term follow-up seem to indicate that the effects tend not to be maintained, namely in shorter follow-ups (6 months).

A systematic review and meta-analysis on MBSR for improving sleep quality in cancer survivors was conducted by Suh et al. (Suh et al., 2021) Based on the nine studies analyzed, MBSR significantly improved sleep quality compared to usual care. However, there were no favorable results with sleep parameters. Compared to active controls (e.g. psycho-education, stress management techniques), the pooled result indicated that MBSR improved sleep quality less than active controls. The efficacy and effectiveness of MBI in improving sleep quality and sleep parameters are inconclusive.

The systematic review and meta-analysis published by Cillessen et al. (Cillessen et al., 2019) on MBI for psychological and physical health outcomes in cancer patients and survivors analyzed 29 independent RCTs (reported in 38 papers) with 3274 participants. The findings include that small significant pooled effects of MBIs on psychological distress, significant effects for a range of self-reported secondary outcomes such as anxiety, depression, fear of cancer recurrence, fatigue, sleep disturbances, and pain. Improvements in mindfulness skills were associated with greater reductions in psychological distress at post-intervention. MBIs appear efficacious in reducing psychological distress and other symptoms in cancer patients and survivors. However, many of the effects were of small magnitude.

Zhang et al. (2019) conducted a systematic review on effects of MBIs on quality of life of women with breast cancer. The MBSR intervention on quality of life among women with breast cancer was effective and safe. Adverse events were inadequately reported.

A Cochrane database systematic review by Schell et al. (Schell et al., 2019) on MBSR for women diagnosed with breast cancer included ten RCTs involving 1571 participants for meta-analysis. This review suggests that MBSR may improve quality of life slightly at the end of the intervention but may result in little to no difference later on. MBSR probably slightly reduces anxiety, depression and slightly improves quality of sleep at both the end of the intervention and up to six months later. A beneficial effect on fatigue was apparent at the end of the intervention but not up to six months later. Up to two years after the intervention, MBSR probably results in little to no difference in anxiety and depression.

Cifu et al. (Cifu et al., 2018) conducted a systematic review on MBIs for cognitive function among breast cancer survivors. Based on six studies included for analysis, two found no association between mindfulness interventions and cognitive function, two found improvement that was not sustained at the follow-up, and another two found sustained improvement at 2 or 6 months.

Hulett et al. (Hulett & Armer, 2016) conducted a systematic review on MBIs for psychoneuroimmunological (PNI) outcomes in breast cancer survivors. Based on twenty-two articles reviewed, cortisol was the most common PNI biomarker outcome studied. Compared with control groups, intervention groups demonstrated

positive mental health outcomes and improved or stable neuroendocrine-immune profiles, although limitations exist.

Zhang et al. (Zhang et al., 2015) published their meta-analysis on effectiveness of MBIs for reducing anxiety and depression in patients with cancer. Based on seven studies, involving 469 participants, the pooled standardized mean difference (SMD) of the change in anxiety and depression significantly favored mindfulness-based therapy over control treatment. This improvement was for follow-up ≤12 weeks after the start of therapy, but not >12 weeks. There was a lack of consistency between the studies in the type of mindfulness-based/control intervention implemented.

Original studies

Full-text articles of 22 original studies were retrieved and reviewed. Results of these studies are in line with those presented the above systematic reviews. Over 95% of the study population is early stage breast cancer patients. A small number of studies with small sample size included other cancer types such as colorectal cancer, osteosarcoma, lymphoma and lung cancer. Most studies reported MBSR beneficial in psychological wellbeing such as anxiety, depression, rumination, fear and emotional control. Mixed results are reported on quality of life, pain relief, cancer-related fatigue and sleep quality, with some studies indicated positive impact of MBSR. However, most of the studies concur that these effects were short-term up to 3-6 months after intervention completion. A few studies investigated the possible correlation between biomarkers such NK-cell, CD4+CD8+ T cells, lymphocyte, and interleukin (IL-4, IL-6, IL-8) and MBSR effects, however, the results are not consistent.

Synopsis of each study

For breast cancer

A RCT by Bagherzadeh et al. (Bagherzadeh et al., 2022) investigated the effects of MBSR training on rumination in 46 female breast cancer survivors. There was no significant difference in the rumination scores of the experimental group at pretest, posttest, and follow-up stages, however, the experimental group was more successful in avoiding increased rumination than the control group, an ability that can be attributed to the effect of mindfulness training.

Sakki et al. (Sakki et al., 2022) tested psychological wellbeing and stress response biomarkers (cortisol, adrenocorticotropine, and high-sensitivity-CRP) of 23 breast cancer survivors with clinically significant symptoms of depression at 1-year post-operative follow-up. All measures were addressed at baseline, mid-program (4 weeks after baseline) and at the completion of the 8-week MBSR program. This study reported significant increases in resilience, and quality of life, and significant reductions in symptoms of depression, anxiety, insomnia, and marginally significant reduction in perceived stress. However, these favorably experienced changes did not transfer to the level of stress biomarkers during the 8-week program.

Shergill et al. (Shergill et al., 2022) randomized 98 breast cancer survivors into MBSR group and control group for evaluating changes in pain, emotional function, quality of life, and global impression of change. This study reported no significant differences on pain scores and no significant changes among other outcomes. The authors pointed out that nonsignificant results of MBSR are often unpublished.

Chang et al. (Chang et al., 2022) studied the effects of MBSR on female sexual function. 51 women with breast cancer were allocated into 6-week MBSR (n=26) sessions or usual care (n=25). This study reported that MBSR did not significantly improve sexual desire and depression in patients with breast cancer, but MBSR had small to medium effect on parts of female sexual function such as arousal, lubrication and satisfaction. A large effect was found on mental health such as anxiety and stress.

A randomized study by Mirmahmoodi et al. (Mirmahmoodi et al., 2020) reported that the MBSR group had significantly lower anxiety compared with the control group, however, no significant in the reduction of perceived stress and depression, and no significant difference between the two groups in C-reactive protein and cortisol levels after the intervention.

Lengacher et al. (Lengacher et al., 2019) randomized 322 breast cancer survivors to a 6-week MBSR program or to usual care. Measurements of salivary cortisol and pro-inflammatory cytokine interleukin-6 (IL-6) were then analyzed. MBSR reduced salivary cortisol and IL-6 levels in the short term.

Kenne Sarenmalm et al. (Kenne Sarenmalm et al., 2017) randomized 166 women with breast cancer to one of three groups: MBSR (8 weekly group sessions of MBSR), active controls (self-instructing MBSR) and non-MBSR. The MBSR group experienced significant improvements in scores of depression, distress, symptom burden, and mental health. There were no changes in numbers of IL-6 or IL-8, instead, changes in NK-cell activity and numbers of both NK cells and B cells within the MBSR group as well as between groups were seen.

A randomized trial by Reich et al. (Reich et al., 2017) included 322 stage 0-III post-treatment breast cancer survivors assigned to either a six-week MBSR(BC) program or usual care. This study reported MBSR effectiveness in both the psychological (anxiety, depression, perceived stress and QOL, emotional well-being) ($P = 0.007$) and fatigue (fatigue, sleep, and drowsiness) ($P < 0.001$) clusters. Results between six and 12 weeks showed sustained effects, but further improvement was not observed.

Johns et al. (Johns et al., 2016) compared MBSR to psychoeducational support (PES) for persistently fatigued breast and colorectal cancer survivors. Breast (n = 60) and colorectal (n = 11) cancer survivors were randomized to MBSR or PES group. This study reported no significant difference between-group in cancer-related fatigue at any time point, although there was a trend favoring MBSR.

Bower et al. (Bower et al., 2015) published their randomized study on mindfulness meditation for young (at or before age 50) breast cancer patients. Seventy-one women who had completed cancer treatment were randomly assigned to a 6-week Mindful Awareness Practices (MAPS) intervention group (n = 39) or to a wait-list control group (n = 32). This study reported that the MAPS intervention led to significant reductions in perceived stress and marginal reductions in depressive symptoms, as well as significant reductions in proinflammatory gene

expression and inflammatory signaling at postintervention. However, these effects on psychological and behavioral measures were not maintained at the 3-month follow-up assessment.

A randomized study by Lengacher et al. (Lengacher et al., 2015) evaluated the effects of mindfulness-based stress reduction on objective and subjective sleep parameters in women with early-stage breast cancer. 79 patients were randomly assigned to either the formal (in-class) 6-week MBSR(BC) program or usual care. This study reported a positive effect of MBSR on objective sleep parameters at 12 weeks on sleep efficiency, percent of sleep time and less number waking bouts.

Eyles et al. (Eyles et al., 2015) investigated mindfulness for the self-management of fatigue, anxiety, and depression in women with metastatic breast cancer. Nineteen women took part in 3 MBSR courses. Commitment to 8 weeks was a reason for non-participation, and proved challenging to participants during the course. Some patients reported benefits including feeling less reactive to emotional distress and more accepting of the disruption to life.

Reich et al. (Reich et al., 2014) randomized 41 breast cancer patients to either a 6-week of MBSR program or usual care. This study suggested that the number of baseline CD4+CD8+ T cells and lymphocytes and interleukin (IL)-4 could be the predictors to identify the patients likely to benefit from MBSR intervention.

Lengacher et al. (Lengacher et al., 2014) randomized 82 post-treatment breast cancer survivors (stages 0-III) to a 6-week MBSR program (n = 40) or to usual care group (UC) (n = 42), and reported that MBSR reduced fear of recurrence and improved physical functioning which reduces perceived stress and anxiety.

Henderson et la. (Henderson et al., 2013) reported the results of their randomized study of 120 breast cancer patients that MBSR intervention significantly improved psychosocial variables including meaningfulness, helplessness, cognitive avoidance, depression, paranoid ideation, hostility, anxiety, global severity, anxious preoccupation, and emotional control, as compared with the nutrition education and usual care at 4 months.

Garland et al. (Garland et al., 2013) analyzed the self-report assessments of stress and mood disturbances of 268 individuals with cancer (breast cancer 58.2%, lymphoma and leukemia 7.8%, colorectal cancer 6.0%), before and after participation in an 8-week MBSR program. This study reported a significant reduction in mood disturbance (55%) and symptoms of stress (29%) by MBSR.

Hoffman et al. (Hoffman et al., 2012) randomized 229 patients to the 8-week MBSR program or standard care and reported that MBSR significantly improved POMS total mood disturbance and its subscales of anxiety, depression, anger, vigor, fatigue, and confusion. And the results persisted at three months.

Henderson et al. (Henderson et al., 2012) conducted a randomized trial of 172 breast cancer patients to compare 8-week MBSR with nutrition education program (NEP) and usual supportive care (UC). This study reportd that at 4-month, MBSR significantly improved the primary measures of QOL and coping outcomes including meaningfulness, depression, paranoid ideation, hostility, anxiety, unhappiness, and emotional control. However, results tended to decline at 12 months and even more at 24 months.

For colorectal cancer (CRC)

Sun et al. (Sun et al., 2022) studied 42 patients with CRC receiving chemotherapy and MBSR intervention compared to 46 patients without MBSR intervention. This study reported improved psychological state with decreased agitation and depression score, improved treatment compliance, strengthened self-care ability in the MBSR intervention group as compared to the control group.

For osteosarcoma

Liu et al. (Liu et al., 2019) randomized 101 patients with osteosarcoma into the intervention and control groups to investigate impacts of MBSR combined with music therapy (MT). This study reported that 8 weeks of the combined MBSR/MT intervention effectively reduced pain and anxiety scores and improved the quality of sleep in patients.

For lung cancer

van den Hurk et al. (van den Hurk et al., 2015) included 19 lung cancer patients and 16 partners in a MBSR program and reported no significant changes in psychological distress among participants, however, caregiver burden in partners decreased significantly.

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