A systematic review and meta-analysis exploring the efficacy of mindfulness-based interventions on quality of life in people with multiple sclerosis

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Abstract

Background Quality of life (QoL) is commonly impaired among people with multiple sclerosis (PwMS). The aim of this study was to evaluate via meta-analysis the efficacy of Mindfulness-based interventions (MBIs) for improving QoL in PwMS.

Methods Eligible randomized controlled trials (RCTs) were identified via searching six major electronic databases (MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials, AMED, and PsycINFO) in April 2022. The primary outcome was QoL. Study quality was determined using the Cochrane Collaboration risk of bias tool. Meta-analysis using a random effects model was undertaken. Effect sizes are reported as Standardized Mean Difference (SMD).

Results From a total of 1312 individual studies, 14 RCTs were eligible for inclusion in the meta-analysis, total participant \( n = 937 \). Most studies included PwMS who remained ambulatory. Cognitively impaired PwMS were largely excluded. Comorbidities were inconsistently reported. Most MBIs were delivered face-to-face in group format, but five were online. Eight studies \(( n = 8)\) measured MS-specific QoL. In meta-analysis, overall effect size (SMD) for any QoL measure \(( n = 14)\) was 0.40 (0.18–0.61), \( p = 0.0003 \), \( I^2 = 52\% \). SMD for MS-specific QoL measures \(( n = 8)\) was 0.39 (0.21–0.57), \( p < 0.0001 \), \( I^2 = 0\% \). MBI effect was largest on subscale measures of mental QoL \(( n = 8)\), SMD 0.70 (0.33–1.06), \( p = 0.0002 \), \( I^2 = 63\% \). Adverse events were infrequently reported.

Conclusions MBIs effectively improve QoL in PwMS. The greatest benefits are on mental health-related QoL. However, more research is needed to characterize optimal formatting, mechanisms of action, and effects in PwMS with more diverse social, educational, and clinical backgrounds.

Keywords Mindfulness · Multiple sclerosis · Systematic review · Meta-analysis · Quality of life

Background

Multiple sclerosis (MS) is a chronic inflammatory neurodegenerative condition [1]. Comorbidity is highly prevalent [2]. Common symptoms include stress [3], anxiety [4], depression [5], fatigue [6], spasticity [7], pain [8], temperature sensitivity [9], cognitive difficulties [10], sleep impairment [11], bowel [12], bladder [13] and sexual dysfunction [14]. Over time, high levels of physical disability affect the majority [15]. People with MS (PwMS) face many challenges to their physical and mental well-being, identity, and social function [16], and commonly report impairment of quality of life (QoL). Fatigue, depression, cognitive difficulties, and physical disability exert the greatest detrimental effects [17, 18]. Other factors associated with lower QoL in PwMS include older age at disease onset, lower socioeconomic and educational statuses [19]. MS is expensive, both from the patient perspective and with regards to health and social care [20, 21]. ‘Intangible’ costs relating to patient suffering through symptoms contribute heavily to overall costs.

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Rehabilitative approaches target functional outcomes and, ultimately, improving QoL [23, 24].

Quality of life is a multi-faceted construct, defined by the World Health Organisation as: ‘an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns. It is a broad ranging concept affected in a complex way by the person’s physical health, psychological state, personal beliefs, social relationships, and their relationship to salient features of their environment’ [25]. Measuring QoL in PwMS is complex; generic measures may not capture issues that matter most to PwMS and MS-specific measures have been developed [26]. However, as yet, no one measure captures all aspects of QoL or health-related QoL in PwMS [26].

Factors known to be associated with better QoL in PwMS include greater self-efficacy, self-esteem, resilience, and social support [17]. In addition, a recent systematic review reported psychological interventions, such as mindfulness and cognitive behavioral therapy (CBT), in addition to self-help and self-management, can improve QoL in PwMS; however, findings were in narrative format and meta-analysis was not possible due to intervention heterogeneity [17].

Mindfulness-based interventions (MBIs) are complex interventions [27], usually delivered in groups face-to-face, or, increasingly, online [28]. MBIs teach core meditation techniques aimed at enhancing attention, self-awareness, and emotion regulatory skills [29, 30]. There is high quality evidence for MBI effectiveness in non-MS populations for the treatment of stress [31], anxiety [32], recurrent depression [33] and chronic pain [34]. How MBIs work is incompletely understood, but in non-MS populations, benefits derive largely from reductions in distress, driven by increased present-moment (‘de-centring’) and body awareness [35], self-compassion [36], mindfulness [37], and reduced cognitive reactivity [38]. These benefits correlate with greater home practice [39]. Neurobiological mechanisms also include functional [40] and structural brain plasticity [41] as well as complex changes in neurohormonal [42] and immune profiles [43].

By contrast, MBI mechanisms in PwMS are poorly characterized and may be confounded by abnormal inflammatory mediator profile, monoamine dysfunction, neuronal injury, and network dysfunction [44, 45]. Nevertheless, MBIs effectively improve stress, anxiety, depression [46], and fatigue [47] in PwMS, suggesting their potential to improve QoL. However, no previous systematic review and meta-analysis has focused specifically on MBI efficacy for improving QoL in PwMS.

**Aim**

The aim is to evaluate via meta-analysis the efficacy of MBIs for improving QoL in PwMS.

**Methods**

**Protocol and registration**

This study was registered in advance with the Centre for Reviews and Dissemination, Prospero ID: 139835.

**Study eligibility**

We included all randomized controlled trials (RCTs) testing an MBI in PwMS of any phenotype, aged ≥ 18, reporting on QoL. MBIs had to contain ‘core’ components (i.e., mindful-breath awareness, body awareness, and movement) [29, 30].

**Search strategy**

We searched six major electronic databases (MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials, AMED, and PsycINFO) in April 2022 using medical subject headings and key words relating to mindfulness and multiple sclerosis, search syntax and Boolean operators. Search delimiters included: studies in humans, published in English language, between 1980—current (April 2022). We also searched reference lists, the gray literature and contacted relevant experts in the field. Our search strategies are available in Online Appendix 1.

**Study selection**

Search results were imported into Endnote, for storage and screening. Two reviewers (“blinded for peer review”) independently assessed title/abstracts for eligibility. Three reviewers (“blinded for peer review”), then independently assessed eligibility against study, population, intervention, and outcome (SPIO) characteristics. A senior reviewer (“blinded for peer review”) was available for arbitration in the event of any disagreement over study eligibility.
Data extraction

Three reviewers (“blinded for peer review”) independently extracted study data using the CONSORT and TIDieR checklists (Appendix 2).

Quality appraisal

We used the Cochrane Collaboration tool [48] for assessing risk of bias (low, unclear, high) on individual outcomes (sequence generation, allocation concealment, participant blinding, personnel blinding, assessor blinding, incomplete outcomes, selective outcome reporting, any other source of bias). Based on summed individual outcomes, each study was then assigned an overall risk of bias category (low, unclear, high). Two reviewers engaged in discussion to reach consensus on overall risk of bias, when discrepancies arose.

Primary outcome

Main outcome measures were all reported as continuous with mean, standard deviation (SD) values and the number of participants for each treatment group extracted. “Effect size” is reported as the unbiased standardized mean difference (SMD), a positive SMD indicating a finding in support of the intervention having a positive treatment effect. The SMD was calculated by difference in means between the MBI and the control group at follow-up divided by the pooled follow-up SD. Where effect estimates were reported from adjusted regression models, we extracted these as the SMD with their corresponding SD.

Synthesis

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [49] when drawing together findings for our systematic review and meta-analysis. We used a random effects meta-regression model for deriving SMD, due to expected high levels of outcome heterogeneity (generic vs MS-specific QoL measures). We report effect estimates and 95% confidence intervals (as a measure of precision) and corresponding p values. We assessed heterogeneity using the $I^2$ statistic, $I^2$ representing the percentage of total variability in effect size estimates due to heterogeneity. An $I^2$ of 0% indicates that all heterogeneity is due to sampling error, while an $I^2$ of 100% suggests all variability may be attributable to studies being truly heterogeneous.

We computed Funnel plots and Egger’s test to determine asymmetry and likelihood of publication bias, with subsequent ‘trim and fill’ to assess significance of any bias. All statistical analyses were carried out using RevMan.

Results

Our initial search identified 1,852 potential studies for inclusion. Following deduplication and the addition of four further studies identified via reference list searching there were 1,312 potential studies for inclusion. After title and abstract screening, 30 full text studies were reviewed, of which 14 were included in the final analyses [50–63] (Fig. 1).

Characteristics of included studies

Eight of the 14 studies reported carrying out power calculations to determine necessary sample size [52, 55, 56, 58–60, 62, 63]; of the remaining, five did not [51, 53, 57, 58, 61] and one provided insufficient detail [54]. Studies took place across four continents, in eight different countries: three from Iran [54, 57, 63], two from Italy [55, 56], the UK [51, 53], Australia [59, 61], the USA [50, 60], and one each from Switzerland [52], Canada [62], and France [58]. Sample size ranged from 21–150. Six studies [50, 55, 56, 58, 60, 61] compared MBI against an active treatment (psychoeducation, physical activity, adaptive cognitive training, chair yoga), five usual care [51–53, 62, 63], one waitlist control [59], and in two the control condition was unclear [54, 57]. Most studies collected outcome measures thrice (pre-, post-, follow-up), but three studies were pre-post design [54, 57, 58] (Table 1).

Characteristics of study participants

Across the 14 RCTs there were 937 participants. Five studies reported on ethnicity, which was 87.8% “white” or “anglo-saxon/anglo-celtic” [50, 51, 53, 59, 60]. One study did not report the percentage of women [59], but most studies predominantly recruited women (total women = 621; 78%). Two studies did not report mean (SD) age, but rather, an age range of 20–50 [63], and a median age of 43 [58]. Of the remainder, mean (SD) age was 44.04 (9.1). Most studies did not report on socioeconomic status (SES), but in the five that did, most participants had a college degree or higher [50, 51, 53, 57, 59]. Most participants (n = 699; 74.5%) had a relapsing MS phenotype, while 128 (13.6%) had progressive disease. MS phenotype was not reported in the remainder. Where reported, disability, as measured by the Expanded Disability Status Scale (EDSS), was mostly < 6.0, indicating participants remained ambulant without a walking aid; however, one study focused solely on progressive MS, where mean (SD) EDSS was 6.5 (1.5) indicating the ability to walk for 20 m without stopping using walking aid(s) [53]. Four studies reported on comorbidity, mainly depression [55, 59–61]. One study reported comorbidity with a mean (SD) count
of 2.4 (2.0) comorbidities [51]. In six studies, most participants were on disease-modifying drugs (DMDs) [50–52, 55, 62, 63]. One study only indicated “both groups also received their routine drug treatments” without specifying the number of participants on DMDs [63], and the remaining studies did not measure use. Antidepressant use ranged from 6 to 56%. Nine studies [50–53, 55, 56, 59–61] explicitly excluded those with cognitive impairment, while the remainder did not mention cognitive impairment as an eligibility criterion (Table 2).

**Intervention characteristics**

Seven studies used Mindfulness-based stress reduction (MBSR) [50–52, 55, 59, 60, 63], two used modified MBSR (incorporating consciousness yoga [54] or somatic psychotherapy [56]). Two studies employed Mindfulness-based cognitive therapy (MBCT) [53, 57], while another adapted MBCT to an approach titled, “Mindfulness for MS” (M4MS) [61]. One study employed an MBI with physical activity [58], another used the Mindfulness Ambassador Program.
Table 1  Study characteristics

| Study | Country            | Study design | Powered | Comparator                     | Sample size (n) | Study attrition (%) | Cognitive impairment exclusion criterion | QoL measure(s)                  | Data collection                      |
|-------|--------------------|--------------|---------|--------------------------------|----------------|---------------------|------------------------------------------|-----------------------------------|---------------------------------------|
| 1.    | Grossman et al.    | Switzerland  | RCT     | Yes                            | Treatment as usual | 150                 | 5%                         | Yes                                  | HAQUAMS, PQOLC                        | Baseline, post, 6 months follow-up   |
| 2.    | Bogosian et al.    | England (UK) | RCT     | No                             | Treatment as usual | 40                  | 5%                         | Yes                                  | MSIS-29, EQ5D                          | Baseline, post, 3 months follow-up   |
| 3.    | Nejati et al.      | Iran         | RCT     | Unclear                        | Unclear          | 24                  | 0%                         | No                                   | MSQOL-54                             | Baseline, post                        |
| 4.    | Simpson et al.     | Scotland (UK)| RCT     | No                             | Treatment as usual | 50                  | 12%                        | Yes                                  | EQ5D5L                              | Baseline, post, 3 months follow-up   |
| 5.    | Carketo et al.     | Italy        | RCT     | Yes                            | Psycho-education intervention | 90                  | 21%                        | Yes                                  | FAMS                                | Baseline, post-BAM, 6 months post-BAM |
| 6.    | Cavalera et al.    | Italy        | RCT     | Yes                            | Psycho-education intervention | 139                 | 39%                        | Yes                                  | MSQOL-54                             | Baseline, post, 6 months post-MBI    |
| 7.    | Senders et al.     | USA          | RCT     | Yes                            | Educational control, matched for time and attention | 62                  | 16%                        | Yes                                  | SF-36 (EWS)                          | Baseline, mid-intervention, immediately post, 4, 8 and 12-months post-MBI |
| 8.    | Ghodspour et al.   | Iran         | RCT     | Unclear                        | Unclear (‘no treatment’) | 30                  | 23%                        | No                                   | MSQOL-54 (MHC)                       | Baseline, immediately post           |
| 9.    | Kolahkaj et al.    | Iran         | RCT     | Yes                            | Treatment as usual | 48                  | N/R                        | No                                   | QoL Questionnaire                     | Baseline, immediately post-intervention, 2 months follow up |
| 10.   | Schirra et al.     | USA          | RCT     | Yes                            | Active aCT group Waitlist control | 61                  | 18%                        | Yes                                  | World Health Organization QoL        | Baseline, immediately post-intervention, 6 months follow up |
| 11.   | Torkhani et al.    | France       | RCT     | No                             | II + PA Control group+PA | 35                  | II + PA: 0% MBI + PA: 47% Control+PA: 25% | No                                   | EQ-5D-3L                             | Baseline, immediately post           |
| 12.   | Dunne et al.       | Australia    | RCT     | No                             | Chair yoga Waitlist control | 55                  | 13%                        | Yes                                  | MSQol-54                             | Baseline, daily home practice, weekly reflective journals, post-intervention |
| 13.   | Morrow et al.      | Canada       | RCT     | Yes                            | Standard of care | 21                  | 10%                        | No                                   | SF-36                               | Baseline, immediately post-intervention, 3 months post |
| 14.   | Sessel et al.      | Australia    | RCT     | Yes                            | Waitlist control   | 132                 | 10%                        | Yes                                  | HRQoL                               | Baseline, immediately post, 3 months follow up, 6 months follow up |

**RCT** randomized controlled trial, **HAQUAMS** Hamburg quality of life questionnaire in multiple sclerosis (German), **PQOLC** Profile of health-related quality of life in chronic disorders (German), **MSIS-29** Multiple sclerosis impact scale-29, **MSQOL-54** Multiple sclerosis quality of life-54, **EQ5D5L** EuroQol, **FAMS** Functional Assessment of Multiple Sclerosis, **SF-36** Short form 36, **EWS** Emotional wellbeing subscale for SF-36, **MHC** Mental health composite for MSQOL-54, **II** Implementation Intention, **PA** physical activity, **MBI** Mindfulness Based Intervention, **HRQoL** Health Related Quality of Life, **aCT** Adaptive Cognitive Training
Table 2 Participant characteristics

| Study/Demographic | Grossman et al. (2010) [52] | Bogosian et al. (2015) [53] | Nejati et al. (2016) [54] | Simpson et al. (2017) [51] | Carletto et al. (2017) [56] | Cavalera et al. (2019) [55] | Senders et al. (2018) [50] | Ghodspour et al. (2018) [57] | Kolahkaj et al. (2019) [63] | Schirda et al. (2020) [60] | Dunne et al. (2021) [61] | Morrow et al. (2021) [62] | Torkhani et al. (2021) [58] | Sesel et al. (2022) [59] |
|------------------|-----------------------------|-----------------------------|---------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Ethnicity        | NR | 90% British white | NR | 100% British white | NR | 97% white | NR | “white”: 72% | NR | “black”: 23% | NR | NR | NR | “Anglo-Celtic/Anglo-Saxon: 80% European: 13% Asian: 2% Bicultural/Other: 5% |
| Number of        | 150 (80%) | 40 (55%) | 24 (46%) | 50 (92%) | 90 (71%) | 139 (65%) | 67 (78%) | 30 (100%) | 48 (100%) | 61 (77%) | 55 (83%) | 21 (81%) | 35 (80%) | 132 (NR) |
| participants (%) |                |                |                |                |                |                |                |                |                |                |                |                |                |                |
| Mean age (SD)    | 47.3 (10.3) | 52.2 (9.1) | 32.3 (5.1) | 45 (10.9) | 44.6 (9.4) | 42.7 (8.7) | 52.94 (11.37) | 36 (6.0) | “Ages 20–50” | 45.7 (8.2) | 48 (10.8) | 36.8 (9.35) | “Median age” = 43.8 | 44.95 (10.2) |
| Socio-economic   | NR | NR | NR | Postcode derived; controlled in analyses | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR |
| status           |                |                |                |                |                |                |                |                |                |                |                |                |                |                |
| Employment       | NR | NR | NR | 20 employed (40%) | 59 employed (65%) | NR | NR | 30% employed, 70% ‘home-makers’ | NR | NR | NR | NR | NR | Full-Time: 32% Part-time: 36% Unemployed: 11% Registered disability: 11% Retired: 8% |
| status           |                |                |                |                |                |                |                |                |                |                |                |                |                |                |
### Table 2 (continued)

| Study/Demographic | Grossman et al. (2010) [52] | Bogosian et al. (2015) [53] | Nejati et al. (2016) [54] | Simpson et al. (2017) [51] | Carletto et al. (2017) [56] | Cavalera et al. (2019) [55] | Senders et al. (2018) [50] | Ghodspour et al. (2018) [57] | Kolahkaj et al. (2019) [63] | Schirda et al. (2020) [60] | Dunne et al. (2021) [61] | Morrow et al. (2021) [62] | Torkhani et al. (2021) [58] | Sesel et al. (2022) [59] |
|-------------------|-----------------------------|----------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
| **Education status** (SD) | Mean 31 (77.5) | Mean 14.1 (1.9) | Mean 56% | Mean 11% | Mean 60% | Mean 16 (1.6) | Mean 14.5 (2.5) | Mean 17% | Mean 60% | Mean 16 (1.6) | Mean 14.5 (2.5) | Mean 17% |
| Education status | (SD) | years of education | High school diploma at least | elementary school; | college education or greater | High school: | years | High school: | years | years | years | years |
| **Disease phenotype** | RR 123 (82%) | SP 23 (57.5%) | NR | RR 40 (80%) | RR 131 (93%) | RR 41 (67%) | Multiple Sclerosis subtype | RR 59 (97%) | Multiple Sclerosis subtype | RMS 21 (100%) | RR 25 (71%) | RMS 11 (86%) |
| EDSS score | Mean 3.0 (1.1) | Mean 4.4 (1.8) | Median 3.0 | Mean 6.5 (1.5) | Mean 4.6 (1.93) | Mean 4.35 (1.29) | Multiple Sclerosis subtype | Median 3.33 | Multiple Sclerosis subtype | Multiple Sclerosis subtype | Multiple Sclerosis subtype | Multiple Sclerosis subtype |
| Comorbidity | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR |
| Disease modifying drugs | RR 27 (18%) | PP 17 (42.5%) | PP 7 (8%) | PP 2 (2%) | PP 8 (7%) | PP 15 (25%) | PP 4 (6%) | UK 2 (3%) | NR | NR | RR 25 (71%) | RR 11 (86%) |
| EDSS score | Mean 2.4 (2.0); Range 0–9 | Mean 2.3 (1.7) | Median 3.0 | Mean 6.5 (1.5) | Mean 4.6 (1.93) | Mean 4.35 (1.29) | Multiple Sclerosis subtype | Median 3.33 | Multiple Sclerosis subtype | Multiple Sclerosis subtype | Multiple Sclerosis subtype | Multiple Sclerosis subtype |
| Disease modifying drugs | 91 (60.1%) | NR | 26 (52%) | NR | 104 (85%) | 34 (55%) | Both groups also received their routine drug treatments | NR | NR | DMT 14 (66.7%) | NR | 108 (82%) |

**Notes:**
- RR: Relapsing-remitting
- SP: Secondary-progressive
- PP: Primary-progressive
- PR: Progressive-relapsing
- NR: Not reported
(MAP) [62]. All but two studies [54, 57] provided details on MBI instructor characteristics, which included certified MBSR teachers and clinical psychologists. Eleven studies delivered the MBI over 8 weeks [50, 51, 53–59, 61, 63] while others delivered over four [60], nine [52] and 10 weeks [62]. Three included a day retreat [50, 52, 56].

Four studies described detailed session content [50, 51, 53, 62]. Six provided week-by-week outlines [52, 54, 57, 60, 61, 63]. Two provided a general description [52, 58], one via study protocol [64]. Ten specified home practice [50–53, 56, 58–62]. Ten delivered group MBIs [50–57, 60, 62]. Five interventions were delivered in person [51, 52, 60, 62, 63], and five virtually, of which three [53, 55, 61] were live and two were asynchronous [58, 59]. The remainder of the studies were unclear in their intervention delivery modality (Table 3).

### Treatment adherence, intervention fidelity, and study attrition

Among those studies reporting on MBI session attendance (seven studies [50–53, 55, 60, 61]), this ranged from 60 to 95%. Others reported on virtual session completion [59, 61], one reporting 90% of participants completed at least 4/5 modules [59], another stating 57% of participants attended live virtual sessions over the 8-week MBI [61]. Those reporting on home practice completion (six studies [50–52, 59–61]) reported a range of 29.2–38 min/day [50–52, 61], 136 min per week [59], or 817 min over the intervention period [60]. Six studies considered intervention fidelity [51, 53, 55, 58–60]. Study attrition ranged from 0 to 39%. One study did not report on intervention adherence, fidelity, or study attrition [63]. In one study, 33% (4/12) participants assigned to the MBI withdrew and were not included in the 6-month follow-up analysis [62].

### Outcome characteristics

The majority of included studies (n = 8) used MS-specific QoL measures. Four studies used the Multiple Sclerosis Quality of Life-54 (MSQOL-54) [54, 55, 57, 61], one the Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS) [52], two the Multiple Sclerosis Impact Scale-29 (MSIS-29) [53, 59], one the Functional Assessment of Multiple Sclerosis (FAMS) [56]. Those employing generic measures used health-related QoL measures such as the EuroQol (EQ-SD) [51, 58], Short Form-36 (SF-36) [50, 62], and Profile of health-related Quality Of Life in Chronic disorders (PQOLC) [52], as well as general QoL measures such as the World Health Organization Quality of Life (WHOQoL) [60], Satisfaction With Life Scale (SWS) [60], and the Quality of Life Scale (QoLS) [63].
| Study/checklist item | Grossman et al. (2010) [52] | Bogosian et al. (2015) [53] | Nejati et al. (2016) [54] | Simpson et al. (2017) [51] | Carletto et al. (2017) [56] | Cavalera et al. (2019) [55] | Senders et al. (2018) [50] |
|---------------------|-----------------------------|-----------------------------|-----------------------------|----------------------------|-----------------------------|-----------------------------|----------------------------|
| **1. Brief name**   | MBSR                        | MBCT                        | MBSR and Conscious Yoga     | MBSR                       | Modified MBSR—Body Affective Mindfulness | MBSR                        | MBSR                       |
| **2. Why? (rationale/ theory/goal)** | Cultivate interested, accepting, non-judgmental attitude to experience, including difficult sensations, emotions, thoughts, and behavior | Adaptation of MBSR. Focus on negative thinking, engaging low mood, changing relationship with thoughts, feelings, sensations, no longer avoiding/exerting to them automatically | Facilitate the compliance with and adaptation to medical conditions. Pay attention to being present in a non-judgmental manner | Cultivate interested, accepting, non-judgmental attitude to experience, including difficult sensations, emotions, thoughts, and behavior | Cultivation of mindful awareness, loving kindness, enrichment of listening, self-compassion, sensorimotor psychotherapy principles ‘window of tolerance’ | Cultivate interested, accepting, non-judgmental attitude to experience, including difficult sensations, emotions, thoughts, and behavior |
| **3. What—Materials provided to participants** | NR | Headset, webcam, Audio CDs for home practice | Leaflets for each session and home practice CDs | Course manual, home practice CDs, Book—Full Catastrophe Living | NR | Dedicated website with online multimedia for home practices | NR |
| **4. What—Procedures pre session** | Personal intake interview; goal planning | Screened for evidence of distress on GHQ | Personal intake interview | Session content reported in paper—Raisin exercise, Mindful awareness, body scan, sitting practice, 3-min breathing space, psychoeducation, cognitive exercises | Session content reported in paper—Body awareness, raisin exercise, 3-min breathing, yoga, sitting meditation, psychoeducation on stress, mountain meditation | General description in trial protocol—Emphasis on sensorimotor resources: grounding, centering, self-soothing, psychoeducation on stress, self-compassion, body scan, breath meditation, walking meditation, yoga exercises | General description only—Based on original MBSR protocol |
| **4. What—Procedures – in session** | General description on—Observation of sensory, cognitive, and affective experience in lying, sitting, and dynamic yoga postures | Session content reported in paper—Raisin exercise, Mindful awareness, body scan, sitting practice, 3-min breathing space, psychoeducation, cognitive exercises | Session outline reported in paper—Mindful breathing, body scan, mindful movement, psychoeducation | Session content reported in paper—Mindful breathing, body scan, mindful movement, psychoeducation | General description in trial protocol—Emphasis on sensorimotor resources: grounding, centering, self-soothing, psychoeducation on stress, self-compassion, body scan, breath meditation, walking meditation, yoga exercises | General description only—Based on original MBSR protocol |
| **4. What—Procedures for home practice** | 40 min daily | 10–20 min daily | NR | 45 min daily | 45 min daily | NR | 45 min daily |
| **4. What—Procedures – post course** | Post course interviews for all participants | Post course interviews for some participants | NR | Post course interviews for some participants | NR | NR | NR |
| **5. Who provided** | Two experienced (> 9 years), certified teachers | Study author. Had completed MBI teacher training | NR | Two experienced (7–5 years), certified physician teachers | NR | Certified MBSR teacher with 10 years of experience | NR |
| **6. How—Mode of delivery** | Group, face-to-face, 10–15 people per group | Group, via Skype, max 5 people per group | Group, 12 people per group | Group, face-to-face, 2.5 people per group | Group, number per group NR | Group, via Skype, average of 5 people per group | Group, number per group NR |
| **7. Where—Intervention location** | Clear | Participant’s own homes | Clea | NHS Centre for Integrative Care | NR | In patients own homes | NR |
| **8. When and how much** | 9 weekly 2.5 h sessions | 8 weekly hour sessions | 8 weekly 2 h sessions | 8 weekly 2.5 h sessions | 8 weekly 3 h sessions | 8 weekly sessions (7 duration) | 8 weekly 2 h sessions |
| **9. Tailoring** | Exercises did not exceed level of function | Developed with PwMS, MBCT manual adapted for Progressive MS issues | Mindful movement removed | Developed with PwMS, informed MBSR optimization for future iteration | Protocol reports tailoring to needs of participants, but not reported in paper | Music meditations and acceptance of MS symptoms introduced | NR |
### Table 3 (continued)

| Study/checklist item | Grossman et al. (2010) [52] | Bogosian et al. (2015) [53] | Nejati et al. (2016) [54] | Simpson et al. (2017) [51] | Carletto et al. (2017) [56] | Cavalera et al. (2019) [55] | Senders et al. (2018) [50] |
|----------------------|-----------------------------|-----------------------------|---------------------------|-----------------------------|-----------------------------|----------------------------|-----------------------------|
| 10. In study modifications | NR | NR | NR | Mindful movement simplified | NR | NR | NR |
| 11. How well—Treatment adherence | 92% session attendance; Average 29.2 min home practice/day | 18/19 (95%) completed > / = 4 sessions, home practice NR | 60% session attendance; Average 3.25 min home practice/day | NR | 79% session attendance | 85% attended > / = 6/8 sessions; median home practices 38 min day range 14–80 min; only 55% practiced as assigned |
| Actual/Estimated dose = actual class time (h) + actual home practice (h) | Actual/Estimated dose: 27.1 + 24.4 = 51.4 h | Actual/Estimated dose: 12 + 21.3 = 33.3 h | Actual/Estimated dose: 18.7 + 27.2 = 45.9 h |
| 12. How well—Fidelity assessment | NR | Senior clinical psychologist listened to session recordings for every session | NR | As per NIH guidance (2004) minus session observation/ recording | NR | Treatment integrity monitored, but NR how |

| Study/Checklist item | Ghodspour et al. (2018) [57] | Kolahkaj et al. (2019) [63] | Schirda et al. (2020) [60] | Morrow et al. (2021) [62] | Torkhani et al. (2021) [58] | Dunne et al. (2021) [61] | Sesel et al. (2022) [59] |
|----------------------|-----------------------------|-----------------------------|---------------------------|-----------------------------|-----------------------------|----------------------------|-----------------------------|
| 1. Brief name | MBCT | MBSR | MBT | MBI | MBI + PA | M4MS; Chair yoga | MBI |
| 2. Why? (rationale/theory/goal) | Focus on negative thinking, engaging low mood, changing relationship with thoughts, feelings, sensations, no longer avoiding/reacting to them automatically | Practices targeting both focused attention and open monitoring | To assess whether an MBI would lessen the negative consequences of stress, mood symptoms and QOL, as well as objective markers of inflammation | Aimed at developing awareness of emotions and sensations | To work skillfully with pain, discomfort, and emotions | Aimed at reducing depressive symptoms, anxiety, fatigue, pain and HRQoL |
| 3. What—Materials provided to participants | NR | NR | Homework and written study materials | Take-away assignment, designed to help reinforce the specific learnings, was assigned at the end of each session | Pre-recorded mindfulness sessions using TailorBuilder | ‘Home practice materials’ (i.e., diaries, journals) | Meditation audio guides, interactive virtual modules |
| 4. What—Procedures pre session | Interview to diagnose anxiety, depression, stress | Attend briefing session, demographic questionnaire at baseline | Pre-training assessment; daily; diary; self-report questionnaires; neuropsychological sessions | Demographic and clinical evaluation, primary, secondary, and exploratory outcomes at baseline | Neurological exam; demographic and clinical evaluation; intake screening and baseline questionnaires | If necessary, screened by clinical psychologist for suicidality; Baseline questionnaire | Pre-trial eligibility assessment; primary, secondary and process outcomes at baseline |
### Table 3 (continued)

| Study/Checklist item | Ghodspour et al. (2018) [57] | Kohakj et al. (2019) [63] | Schirda et al. (2020) [60] | Morrow et al. (2021) [62] | Torkhani et al. (2021) [58] | Dunne et al. (2021) [61] | Sesel et al. (2022) [59] |
|----------------------|-------------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
| **4. What—Procedures—in session** | Session outline reported in paper—Autopilot, coping with obstacles, mindful breathing, living in the moment, authorized presence, thoughts are not facts, self-care, application in negative mood states | Session content reported in paper—Raisin exercise, body-inspection, facing obstacle, yoga, mastering STOP technique, identifying and accepting unpleasant experiences, moving from the intrapersonal to the interpersonal world, conflict management, managing outrage or conscious anger, planning for personal care, alleviating pain, writing autobiography | Session content reported in paper—Introduced to the construct of mindfulness, extended body scan meditative practice, mindful eating exercise, breath awareness, gentle standing/standing yoga, and mindful listening etc. | Session content reported in paper—Each week with a unique focus (e.g., paying attention; practicing gratitude; noticing emotional triggers; handling conflict; nurturing compassion), in-session guided mindfulness skills (e.g., mindful breathing, mindful listening, body scan practices). A take-away assignment, designed to help reinforce the specific learnings, was assigned at the end of each session | General description only—All practice was home practice (see below) | Session content reported in paper—M4MS: Taught participants to work skillfully with pain, discomfort, and emotions | Session content reported in paper—All practice was home practice |
| **4. What—Procedures for home practice** | NR | NR | Engaging in the respective practices for 40 min each day for the remaining 6 days of each week | A take-away assignment, designed to help reinforce the specific learnings, was assigned at the end of each session | All baseline measures repeated at post-intervention (or equivalent) and 6 months later | Questionnaire 8 weeks after randomization | Five interactive modules, Five meditation audio-guides, tele-coaching |
| **4. What—Procedures—post course** | NR | The quality-of-life questionnaire post-test and 2 months follow up | Post-training assessment session | Questionnaire 8 weeks after randomization | Post-intervention questionnaire | Post-intervention questionnaires at week 9, 3 months and 6 months post-intervention |
| **5. Who provided** | NR | Trained psychologist | Doctoral students in clinical psychology | RN with clinical and research experience with PwMS who was trained to be a MAP facilitator | M4MS: Clinical psychologist who is certified mindfulness practitioner | Internet adaptation created by psychologists; brief ‘tele-coaching’ calls with psychologists |
| **6. How—Mode of delivery** | Group, method of delivery unclear | In person | Group- In person (group sizes ranged from 2 to 5) | In person- group | Virtual | Virtual- via live web sessions, but sessions also recorded |
| **7. Where—Intervention location** | NR | All the MBRS sessions were held in Ahvaz MS Society | Department of Psychology at The Ohio State University | NR | Home, place of participants choosing | Home, place of participants choosing |
| **8. When and how much** | 8 weekly 2 h sessions | 4 weekly sessions; 2 h + 40 min a day for the remaining 6 days of the week | 2 h; weekly; 10 weeks; take away assignment NR | 10 min; 6 days a week; 8 weeks | 1 h; weekly; 8 weeks; + 10 min of home practice per day | 5 modules– 15 min each; 8 weeks + 5-8 brief telephone calls, 10 min each + 5 meditation guides; 30 min each; daily |
| Study/Checklist item | Ghodspour et al. (2018) [57] | Kolahkaj et al. (2019) [63] | Schirida et al. (2020) [60] | Morrow et al. (2021) [62] | Torkhani et al. (2021) [58] | Dunne et al. (2021) [61] | Sesel et al. (2022) [59] |
|----------------------|-------------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| **Recommended**      | Total dose: at least 16 h     | Total ‘dose’ = 16 h         | Total ‘dose’ = at least 8 h + 16 h = 24 h | Total ‘dose’ = 10 h         | Total ‘dose’ = 8 h + 9.33 h home practice = 17.33 h total | Total ‘dose’ = 210 min per week × 8 weeks = 28 h total |
| **Tailoring**        | Original MBCT protocol translated into Persian | NR                           | Adapted to be 4 weeks rather than 8 | The research team, in partnership with MBW, adapted the Mindfulness ambassador Program for use in the PwMS (i.e., 10 weeks instead of 12 weeks) | “Adapted if required” | M4MS adapted from Mindfulness-based cognitive therapy; sessions 1 h rather than 2 Chair yoga adapted from traditional Hatha yoga | Yes—internet version adapted based on interviews with PwMS and experts in the field using co-design methodology; |
| **In study modifications** | NR                           | NR                          | NR                          | NR                          | NR                          | NR                          | Hatha yoga component of MBSR was omitted |
| **How well—Treatment adherence** | NR                           | 2 MBSR participants lost to follow up | 75% of the MBT participants attended all four weekly sessions and did homework on an average of 20.8 days | Three subjects randomized to the MBI group in the spring session missed > 2 sessions and removed from study. One subject in the MBI spring session withdrew consent | Actual/estimated dose = 4.24 h | M4MS: Actual/estimated dose = 57% of 8 h (4.56 h) + 20 (7) home practice minutes | Actual/estimated dose = 136 min |
| **Actual/estimated dose** | = actual class time (h) + home practice (h) | Actual/estimated dose = 8 + 13.86 = 21.86 h | Actual/estimated dose = 5.13 h + 20 (7) home practice minutes | Actual/estimated dose = 13% of 8 h (1.04 h) + 24 (4) home practice minutes | Actual/estimated dose = 5% adherence for MBI | Chair Yoga actual/estimated dose = 13% of 8 h (1.04 h) + 24 (4) home practice minutes | 54 participants (87%) completed at least 4/5 modules |
| **How well—Fidelity assessment** | NR                           | Attendance, completion of homework and practice time monitored | NR                          | Weekly telephone call—detailed report concerning the session(s) was reviewed | NR                          | A meditation adherence questionnaire |

NR not reported, MBI mindfulness-based intervention, PA physical activity, M4MS Mindfulness for Multiple Sclerosis, MBSR Mindfulness-Based Stress Reduction
Overall effect size (SMD) in the meta-analysis for any QoL measure ($n = 14$) was $0.40$ (0.18–0.61), $p = 0.0003$; heterogeneity was moderate ($I^2 = 52\%$) (Fig. 2). When examining only those studies which included an active comparator ($n = 6$), the SMD was $0.28$ (95% CI 0.06–0.49), $p = 0.01$, $I^2 = 0\%$ (Fig. 3). SMD for MS-specific QoL measures ($n = 8$) was $0.39$ (0.21–0.57), $p < 0.0001$, $I^2 = 0\%$. (Fig. 4). Among those studies using generic QoL measures ($n = 6$), SMD was $0.61$ (95% CI: 0.05–1.16), $p = 0.03$, $I^2 = 25\%$ (Fig. 5). MBI effect was largest on subscale measures of mental QoL ($n = 8$), where SMD was $0.70$ (0.33–1.06), $p = 0.0002$, though heterogeneity was substantial ($I^2 = 63\%$). (Fig. 6). Face-to-face MBIs ($n = 9$) had a larger SMD $0.44$ (0.17–0.71), $p = 0.001$, but with moderate heterogeneity ($I^2 = 51\%$), when compared with online MBIs ($n = 5$), SMD was $0.29$ (0.06–0.53), $p = 0.01$, $I^2 = 0\%$, but these differences were not statistically significant ($p = 0.38$) (Fig. 7).

**Heterogeneity and publication bias**

Across the 14 studies heterogeneity was moderate (52%) and there was no evidence of publication bias ($p = 0.7589$) (Fig. 8).

**Study quality**

There was no evidence of selective outcome reporting in any of the included studies. Most ($n = 12$ out of 14) described sequence generation, the majority ($n = 9$ out of 14) described allocation concealment, blinding procedures ($n = 9$ out of 14), and most ($n = 9$ out of 14) accounted for incomplete outcome reporting. Overall, half of included studies ($n = 7$ out of 14) were adjudged low risk of bias (Fig. 9).

**Adverse events**

In one study, a participant undertaking MBSR reported an increase in neuropathic pain following the ‘raisin exercise’—an introductory MBI exercise, which involves exploring sensory experiences associated with seeing, touching, and tasting a raisin using mindful awareness [51]. In another study, a participant felt more anxious after a MBSR day retreat and a participant experienced muscle spasticity during a muscular relaxation activity [50]. Lastly, in one study, four participants experienced an MS relapse or hospitalization, however these events were deemed unrelated to the MBI [59].

**Discussion**

**Main findings**

Overall, 14 RCTs were eligible for inclusion in this systematic review and meta-analysis. Pooled results across all studies suggest MBIs effectively improve QoL among PwMS with moderate treatment effects (SMD = 0.40). However, when considering only those six studies employing an active comparator, pooled effects on QoL were smaller (SMD = 0.28). Most studies collected data at baseline, post-MBI, and a variable follow-up point ranging from 2 to 6 months. Across studies, a total of 937 PwMS participated. All MS phenotypes were included, the majority being relapsing remitting. Most studies tested group-based MBSR, or a tailored derivative, but there was a mix of face-to-face and online delivery. Most studies assessed QoL using MS-specific measures; effects sizes were larger in studies using a generic QoL measure (SMD = 0.61 vs 0.39). The largest effects were seen on mental QoL subscales (SMD = 0.70). Face-to-face MBIs had a non-significant trend toward larger treatment effects (SMD = 0.44) than online (SMD = 0.29). Study attrition and treatment adherence varied widely.

**Comparison with extant literature**

No previous study has systematically assessed the RCT-based evidence specifically for efficacy of MBIs in PwMS for improving QoL. A previous systematic review and meta-analysis [65] of controlled trials ($n = 21$) testing MBI effects on depression, anxiety, stress, fatigue, and QoL among PwMS found a comparable effect on QoL when pooling just six studies (Hedge’s $g = 0.22$; 95% CI 0.0—0.45, $p < 0.05$), but did not examine differential effects relating to type of QoL measure or aspect of QoL under assessment. Another meta-analysis [66] of RCTs of psychosocial interventions for PwMS (total $n = 1,617$; mean age 47.18; 76% female; 71% relapsing remitting) assessing CBT [$n = 6$]; progressive muscular relaxation [$n = 2$]; self-management [$n = 2$]; mindfulness [$n = 1$]; motivational interviewing [$n = 1$]; coping skills [$n = 1$], reported significant small, but stable beneficial effects on overall (Cohen’s $d = 0.308$; 95% CI 0.143–0.473) and mental health-related QoL ($d = 0.220$; 95% CI 0.084–0.357). Treatment effects on physical health-related QoL were smaller and non-significant ($d = 0.099$; 95% CI 0.165–0.363). Intervention dose moderated outcomes, where higher therapy hours (range 3.5–50 h) increased effect sizes. This fits with data from non-MS populations, where MBI ‘dose’ (amount of home practice) mediates beneficial treatment effects, although minimum effective dose remains
Fig. 2  Overall meta-analysis (any QoL measure)

| Study or Subgroup       | Mindfulness Mean | SD  | Total | Control Mean | SD  | Total | Weight | Std. Mean Difference IV, Random, 95% CI | Std. Mean Difference IV, Random, 95% CI |
|-------------------------|------------------|-----|-------|--------------|-----|-------|--------|--------------------------------------|---------------------------------------|
| Bologian et al. 2015    | 10.67            | 23.56 | 17    | 0.8          | 25.33 | 18    | 6.1%   | 0.39 [-0.28, 1.06]                    |                                       |
| Carletto et al. 2017    | 10.1             | 23.61 | 45    | 0.2          | 24.42 | 45    | 9.5%   | 0.41 [0.01, 0.83]                     |                                       |
| Cavalera et al. 2018    | 5.23             | 15.62 | 46    | -0.94        | 14.11 | 50    | 9.8%   | 0.41 [0.00, 0.81]                     |                                       |
| Dunne et al. 2020       | 4.1              | 16    | 16    | -0.4         | 22.33 | 19    | 8.1%   | 0.22 [-0.44, 0.89]                    |                                       |
| Ghodspour et al. 2018   | 8.16             | 41.73 | 15    | -5.48        | 54.94 | 15    | 5.5%   | 0.27 [-0.45, 0.99]                    |                                       |
| Grossman et al. 2010    | 0.18             | 0.67  | 76    | -0.1         | 0.6   | 74    | 11.2%  | 0.44 [0.11, 0.76]                     |                                       |
| Kolahjai et al. 2019    | -0.25            | 7.27  | 24    | -14.2        | 5.33  | 24    | 5.5%   | 2.15 [1.43, 2.88]                     |                                       |
| Moroow et al. 2020      | 6.78             | 18.3  | 9     | 1.6          | 29.3  | 9     | 3.9%   | 0.20 [-0.72, 1.13]                    |                                       |
| Nejati et al. 2016      | 6.18             | 18.04 | 12    | -0.71        | 10.3  | 12    | 4.7%   | 0.44 [-0.37, 1.25]                    |                                       |
| Schirma et al. 2020     | 0.356            | 0.94  | 20    | 0.1          | 0.96  | 21    | 6.7%   | 0.26 [-0.35, 0.88]                    |                                       |
| Senders et al. 2018     | 17.74            | 16.69 | 31    | 9.14         | 16.25 | 28    | 8.1%   | 0.16 [-0.36, 0.67]                    |                                       |
| Sossel et al. 2022      | 17.1             | 21.75 | 62    | 8.84         | 35.36 | 63    | 10.7%  | 0.28 [-0.07, 0.63]                    |                                       |
| Simpson et al. 2017     | 0.71             | 2.25  | 12    | 0.13         | 2.94  | 25    | 7.4%   | 0.23 [-0.33, 0.76]                    |                                       |
| Torkhani et al. 2021    | 13               | 14.5  | 12    | 0.15         | 10    | 12    | 4.8%   | -0.16 [-0.96, 0.65]                   |                                       |

Total (95% CI) 410 415 100.0% 0.40 [0.18, 0.61]

Heterogeneity: Tau² = 0.06; Chi² = 26.92, df = 13 (P = 0.01); I² = 52%
Test for overall effect: Z = 3.65 (P = 0.0003)

Fig. 3  Active comparator studies only

| Study or Subgroup       | Mindfulness Mean | SD  | Total | Active Control Mean | SD  | Total | Weight | Std. Mean Difference IV, Random, 95% CI | Std. Mean Difference IV, Random, 95% CI |
|-------------------------|------------------|-----|-------|---------------------|-----|-------|--------|--------------------------------------|---------------------------------------|
| Carletto et al. 2017    | 10.1             | 23.61 | 45    | 0.2                 | 22.42 | 45    | 26.2%  | 0.41 [-0.01, 0.83]                    |                                       |
| Cavalera et al. 2018    | 5.23             | 15.62 | 46    | -0.94              | 14.11 | 50    | 27.9%  | 0.39 [-0.01, 0.79]                    |                                       |
| Dunne et al. 2020       | 4.1              | 16    | 16    | 0.1                | 21.17 | 18    | 10.0%  | -0.15 [-0.83, 0.52]                   |                                       |
| Ghodspour et al. 2018   | 0.356            | 0.94  | 20    | 0.196             | 0.94  | 20    | 11.8%  | 0.17 [-0.45, 0.79]                    |                                       |
| Senders et al. 2019     | 17.74            | 16.69 | 31    | 9.14              | 16.25 | 28    | 17.4%  | 0.16 [-0.36, 0.67]                    |                                       |
| Torkhani et al. 2021    | 13               | 19.07 | 12    | 6                   | 5.93  | 11    | 6.8%   | 0.47 [-0.36, 1.30]                    |                                       |

Total (95% CI) 170 172 100.0% 0.28 [0.06, 0.49]

Heterogeneity: Tau² = 0.00; Chi² = 2.78, df = 5 (P = 0.73); I² = 0%
Test for overall effect: Z = 2.55 (P = 0.01)

Fig. 4  MS-specific QoL measures only

| Study or Subgroup       | Experimental Mean | SD  | Total | Control Mean | SD  | Total | Weight | Std. Mean Difference IV, Random, 95% CI | Std. Mean Difference IV, Random, 95% CI |
|-------------------------|-------------------|-----|-------|--------------|-----|-------|--------|--------------------------------------|---------------------------------------|
| Bologian et al. 2015    | 6.33              | 19.8 | 17    | 0.91         | 19.74 | 19    | 7.5%   | 0.27 [-0.36, 0.93]                    |                                       |
| Carletto et al. 2017    | 10.1              | 23.61 | 45    | 0.2         | 24.42 | 45    | 18.7%  | 0.41 [-0.01, 0.83]                    |                                       |
| Cavalera et al. 2018    | 5.23              | 15.62 | 46    | -0.94       | 14.11 | 50    | 19.9%  | 0.41 [0.00, 0.81]                     |                                       |
| Dunne et al. 2020       | 4.1               | 16    | 16    | -0.4        | 23.33 | 18    | 6.6%   | 0.21 [-0.49, 0.92]                    |                                       |
| Ghodspour et al. 2018   | 8.16              | 41.73 | 15    | -5.48       | 54.94 | 15    | 6.3%   | 0.27 [-0.45, 0.99]                    |                                       |
| Grossman et al. 2010    | 0.18              | 0.67  | 76    | -0.1        | 0.6   | 74    | 31.1%  | 0.44 [0.11, 0.76]                     |                                       |
| Nejati et al. 2016      | 6.19              | 18.04 | 12    | -0.71       | 10.33 | 12    | 4.9%   | 0.44 [-0.37, 1.25]                    |                                       |
| Torkhani et al. 2021    | 6.5               | 6.7   | 12    | 3.5         | 6.3   | 12    | 4.9%   | 0.45 [-0.37, 1.26]                    |                                       |

Total (95% CI) 237 245 100.0% 0.39 [0.21, 0.57]

Heterogeneity: Tau² = 0.00; Chi² = 0.61, df = 7 (P = 1.00); I² = 0%
Test for overall effect: Z = 4.22 (P < 0.0001)
Fig. 5  Generic QoL measures only

Fig. 6  Mental QoL measures only

Fig. 7  Face-to-face vs online MBI

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obscure and likely will vary [39]. In this current study, MBI dose (session attendance + home practice) was infrequently reported, but ranged from 16 to 66 h, with session attendance ranging from 60 to 95%, and home practice 29.2–38 min/day.

**Strengths and weaknesses of this study**

We used recommended tools for carrying out our systematic review and meta-analysis, leaving our findings open to external scrutiny and audit. Our research team was multidisciplinary (nursing, rehabilitation, family medicine, psychiatry, psychology, statistics). We included solely RCTs to collate the highest quality evidence for the use of MBIs to improve QoL in PwMS.

Our study was necessarily limited to include only those articles published in English. As the concepts underpinning mindfulness originally derive from Asia, it is possible we missed relevant literature (i.e., non-English language publications) on the use of this technology in diverse contexts, where participant characteristics, intervention acceptability and effects may differ somewhat. However, we found no statistical evidence of publication bias.

**Strengths and weaknesses of studies in this review**

This study had several strengths. All studies in this systematic review and meta-analysis were RCTs. Six compared against an active comparator condition, attempting to minimize non-specific treatment effects, likely in a group-based complex intervention [67] such as MBIs [68]. An RCT is widely regarded as the best study design to minimize bias in the ‘hierarchy of evidence’ [69]. Although a wide range of participants took part in the studies in this review, mean participant age was relatively low (44.04), socioeconomic and educational statuses infrequently documented. Thus, very little is known about effects of MBIs among older PwMS, those with late onset disease, or with diverse social and educational backgrounds. Similarly, limited reporting on other factors known to impair (physical and mental health comorbidities, physical disability, cognitive impairment), stabilize or improve QoL in PwMS (e.g., ‘second generation’ DMD use [70]) limits somewhat the scope of analyses, whereas lack of biological outcome measurement (e.g., structural or functional MRI) limits somewhat interpretation of meaning in findings. In addition, regarding quality, although half of studies included in this review were deemed to have low risk of bias, reporting of study procedures, population characteristics, intervention components, and outcomes
MBIs effectively improve depression in PwMS [46], a factor strongly associated with reduced QoL in this population [18]. However, the impact of MBIs on other factors known to impair QoL in PwMS, such as cognitive impairment [17] should be assessed, as in general populations MBIs can improve aspects of cognitive function (working and autobiographical memory, cognitive flexibility, and meta-awareness) [71].

The factors that mediate or moderate effectiveness of MBIs in PwMS are not known. Feasibility work suggests important roles for acceptance, self-efficacy, and self-compassion [72]. Future research may examine the neurobiological mechanisms that underpin MBIs, as well as test a wider range of candidate factors in larger, powered samples of PwMS.

Implications for clinical practice

MBIs appear to be a safe approach to improving QoL in PwMS, with the greatest benefits seen on mental QoL. Both face-to-face and online MBIs hold potential for effectiveness, though the small number of studies in this area makes drawing firm conclusions difficult. In pragmatic terms, online or virtual MBIs may now be preferrable to PwMS, given the ongoing context created by the COVID-19 pandemic, and may also help to address some of the inequalities PwMS face in accessing mental healthcare [73].

Conclusions

MBIs effectively improve QoL in PwMS. The greatest benefits are on mental health-related QoL. However, more research is needed to characterize optimal formatting, mechanisms of action, and effects in PwMS with more diverse social, educational, and clinical backgrounds.

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Declarations

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical approval The manuscript does not contain clinical studies or patient data.

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