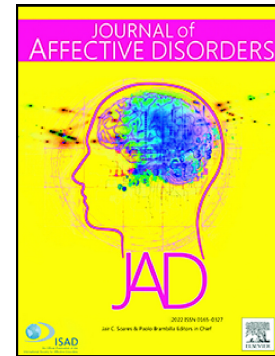


Journal Pre-proof

The effectiveness of psychosocial interventions on non-physiological symptoms of menopause: A systematic review and meta-analysis

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The effectiveness of psychosocial interventions on non-physiological symptoms of menopause: A systematic review and meta-analysis

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Abstract

Background: Menopause, a crucial transitioning stage for women, can significantly impact mood and wellbeing. We aimed to evaluate the effectiveness of psychosocial interventions on non-physiological symptoms of menopause (depression, anxiety, cognition, and quality of life) through systematic review and meta-analysis.

Methods: Five databases were searched from inception to August 2023 for randomized controlled trials. Pre- and post-test means and standard deviations for groups were extracted and used to calculate effect sizes. The effectiveness of Cognitive Behavioral Therapy (CBT) and Mindfulness-Based Interventions (MBI) on depression and anxiety were examined by subgroup analysis.

Results: Thirty studies comprising 3501 women were included. From meta-analysis, mood symptoms significantly benefited from CBT (anxiety: $d=-0.22$, 95% CI=-0.35, -0.10; depression: $d=-0.33$, 95% CI=-0.45, -0.21) and MBI (anxiety: $d=-0.56$, 95% CI=-0.74, -0.39; depression: $d=-0.27$, 95% CI=-0.45, -0.09). Psychosocial interventions were also found to significantly improve cognition ($d=-0.23$, 95% CI=-0.40, -0.06) and quality of life ($d=-0.78$, 95% CI=-0.93, -0.63). Mean total therapy hours ('dose') was lower for CBT (11.3) than MBI (18.6), indicating reduced costs and burden for women.

Limitations: Data regarding menopausal status were not collected, limiting our ability to identify the optimal timing of interventions. Potential longer-term, effects of interventions were not investigated.

Conclusion: Our review highlighted the value of psychosocial interventions in improving non-physiological symptoms (particularly depression and anxiety) during menopause, noting the heterogeneity of findings and importance of implementing effective interventions.

Keywords: menopause, Cognitive Behaviour Therapy, systematic review, meta-analysis, mindfulness-based interventions, mood

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1. Introduction

Menopause refers to the permanent end of menstruation for 12 months and beyond (Maki & Jaff, 2022). The menopause literature (STRAW+10) primarily focuses on four stages (known as the STRAW+ criteria): late reproductive stage (stage -3), early perimenopause stage (stage -2), late perimenopause stage (stage -1) and early post-menopause stage (stage +1) (Harlow et al, 2012). The menopausal transition, often lasting 5-10 years; is accompanied by multiple symptoms that vary in severity across individuals. This can include physical symptoms such as hot flushes and night sweats (Moilanen et al., 2010), cognitive decline in memory and attention (Weber et al., 2014), and psychological difficulties including depression and anxiety (Mulhall, Ansel, & Anstey, 2018). The combination of these symptoms can impact upon daily functioning, interpersonal relationships and quality of life in general. With increased life expectancy to almost 82 years, most women will spend one third of their lives in the postmenopausal stage (Welsh, Matthews and Jagger, 2021). This highlights the importance of maintaining good physical and psychological health during menopause.

As estimated by the World Health Organization (WHO, 2022), the number of postmenopausal women will reach 1.2 billion by 2030 globally, with 47 million women entering menopause every year. Nevertheless, there is a general deficiency in specialist healthcare services available for perimenopausal women (Lumsden, 2016), particularly in countries where a woman's value depends on reproductive capacity (Hoga et al., 2015). Due to a lack of information and support, women sometimes misinterpret cognitive symptoms, such as attention and memory difficulties; as dementia (Hickey et al., 2022), which may further impact wellbeing. It is thus essential to

establish appropriate public understanding around menopause and improve access to timely interventions.

The most commonly offered intervention for menopausal symptoms is hormone replacement therapy (HRT), which is the first line treatment for reducing the frequency and severity of vasomotor symptoms (NICE, 2015). However, HRT may lead to adverse effects including nausea and headaches, and it is not clinically indicated for women who have had breast cancer or other hormonally sensitive conditions (Poggio et al, 2022). Alternatively, many professional bodies (e.g., the European Menopause and Andropause Society; Stute et al., 2020) recommend psychological interventions as the frontline treatment for both physical and psychological symptoms of menopause. As an example, Cognitive Behavioural Therapy (CBT) may help women to understand the link between catastrophic thoughts (such as “hot flushes make everyone judge me”) and subsequent negative spirals of mood and behavior which can ultimately worsen symptoms (Reynolds, 2000). Mindfulness-Based Interventions (MBI) are useful in fostering a non-judgmental sense of awareness and acceptance of symptoms (Ludwig & Kabat-Zinn, 2008).

The biopsychosocial-cultural model of menopause (Hunter and Rendall, 2007) proposes that an interaction between biological (e.g. hormone changes), psychosocial (e.g. role and mood changes), and cultural (e.g. beliefs and attitudes toward menopause) factors contribute to the complex experience of menopause. It would then follow that interventions should also be holistic and support the psychosocial and cultural aspects, as well as the biological. Positive cultural

values and strong social support are crucial buffers against maladaptive behaviors such as self-harm, following common midlife stressors such as divorce (Zhao et al., 2019).

Toral et al. (2014) previously conducted a systematic review on psychosocial interventions for peri and post-menopausal women, including randomized, non-randomized and non-controlled studies. Whilst the study concluded that psychosocial interventions ‘provide multiple benefits with no side effects’, the quality of included research was variable. More recently, van Driel et al (2018) published a systematic review and meta-analysis on Mindfulness, CBT and Behavioural based therapies, including twelve RCTs. This review mainly focused on physiological symptoms, finding benefits to hot flushes and other physical symptoms. These reviews indicate the need for a systematic review and meta-analysis that is a) up-to-date, b) only includes robust research (RCTs) and c) focuses on non-physiological symptoms, something that has been neglected in previous reviews. The key research question of this current review was: ‘Are psychosocial interventions effective in reducing mood symptoms and cognitive difficulties, as well as enhancing quality of life in menopausal women?’

2. Methods

2.1 Search, Selection, and Data Extraction

The review was registered on PROSPERO in May 2023, registration number CRD42023410790; and followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). A simultaneous search was executed on EMBASE, MEDLINE, PsycINFO, CINAHL, and Cochrane Library from database inception to August 2023, limiting to peer reviewed journals on human participants and in English language. Grey

literatures were also searched on Google Scholar to gain comprehensive resources for the topic. Full search terms are listed in Appendix table A1.

Studies were eligible for inclusion if they 1) were RCTs; 2) recruited female participants experiencing menopausal transition; 3) primarily delivered psychological or psychosocial interventions (defined as structured treatment interventions that encompass a wide range of actions and can include multiple components which aim to modify psychological and social factors); and 4) reported at least one outcome related to mood, cognition, or quality of life using valid outcome measures. Studies were excluded if 1) interventions applied were pure education, exercise, or traditional techniques like acupuncture and aromatherapy; 2) they targeted mental health difficulties for chronic physical illnesses that were not menopause related; 3) outcomes were sleep-related only.

One reviewer (ZL) performed eligibility screening on Rayyan (<https://www.rayyan.ai>), with a second reviewer (YB) reviewing 10% of the results and a third reviewer helping to resolve disagreements. We extracted study and intervention characteristics (Table 1), as well as available mean scores and standard deviation of the intervention and control group at pretest and posttest for meta-analysis. Authors were contacted for missing data.

2.2 Data Analysis and Quality Assessment

The meta-analysis was conducted using the metafor package in R studio version 4.2.2 (v2. 4-0; Viechtbauer, 2010), with the effect size calculated for each study as recommended by Morris, (2008). This approach uses a bias-corrected estimate to calculate the pretest-posttest effect size.

A conservative value of 0.7 was imputed as most studies do not report the pretest-posttest correlation which is needed to calculate the effect size. The effect sizes were pooled in a random effects model using the inverse variance weighted method. Further subgroup analyses were conducted grouping studies by specific intervention.

Heterogeneity was assessed using the I^2 and Q statistics and interpreted as: 0%: no heterogeneity, 0%-40%: small levels, 30%-60%: moderate levels, and 75%-100%: substantial levels of heterogeneity (Higgins et al., 2022). The results from studies that did not report sufficient data to calculate the effect size were reported in a narrative synthesis.

Risk of bias was assessed using the version 2 of Cochrane risk-of-bias tool for randomized trials (RoB2; Sterne et al., 2019). We also examined publication bias via funnel plot and Egger's regression test (Egger et al., 1997) for anxiety and depression outcomes, because more than ten studies were available in the meta-analysis.

3. Results

3.1 Characteristics of Included Studies

The PRISMA flow chart presents the study selection process (Figure 1). A total of 1171 studies were initially derived from our search. The removal of 160 duplicates left 1014 studies for screening, in which 945 were excluded at title/abstract level and 22 removed after full text retrieval. Among the remaining 47 studies, 30 studies were eligible for our systematic review. Twenty-two studies provided appropriate outcome data for meta-analysis and eight studies were narratively synthesized.

As described in Table 1, participants were 3501 women undergoing gradual (n=2686) or treatment-induced (n=815) menopause, with mean age ranging from 47.0 to 59.0. The timepoint of immediate post-intervention tests ranged from one to six months. Mood, cognition, and quality of life outcomes were reported by 20, 4, and 24 studies respectively. Intervention characteristics are summarized in Table 2. Ten studies delivered CBT-based interventions that covered psychoeducation about menopausal symptoms, cognitive and behavioral strategies, relaxation techniques, and symptom monitoring. The average total dose of CBT-based interventions was 11.3 hours, ranging from 5-24 hours. Nine studies provided Mindfulness-Based Interventions that promoted focus on present experiences and non-judgmental understanding of symptoms, the average total dose being 18.6 hours (range 16-29.4 hours). The remaining eleven studies encompassed Acceptance and Commitment Therapy (ACT), group counselling, marital support, health promotion coaching, and Emotional Freedom Techniques. The doses of these interventions were less clearly specified in studies and varied substantially, ranging from 3 hours (the Couples Coping Enhancement Training; Yarelahi et al., 2021) to 3 months (the Health promotion coaching; Fujimoto, 2017). Interventions varied in terms of modality (i.e., group vs. individual, facilitated vs. self-directed, and face-to-face vs. virtual), with the vast majority (25 out of 30) being face-to-face (see appendix table A2). For CBT, all interventions were delivered within groups, apart from three which had part or all individually self-directed work. For the MBI, again all were group apart from one study using individual sessions (Garcia et al, 2018). The other psychosocial interventions were also primarily group based. The research was conducted in fourteen countries (UK, USA, Iran, Australia, The Netherlands, Germany, China, Japan, Brazil, Canada and Hong Kong).

Figure 1.
PRISMA diagram depicting the process of study selection

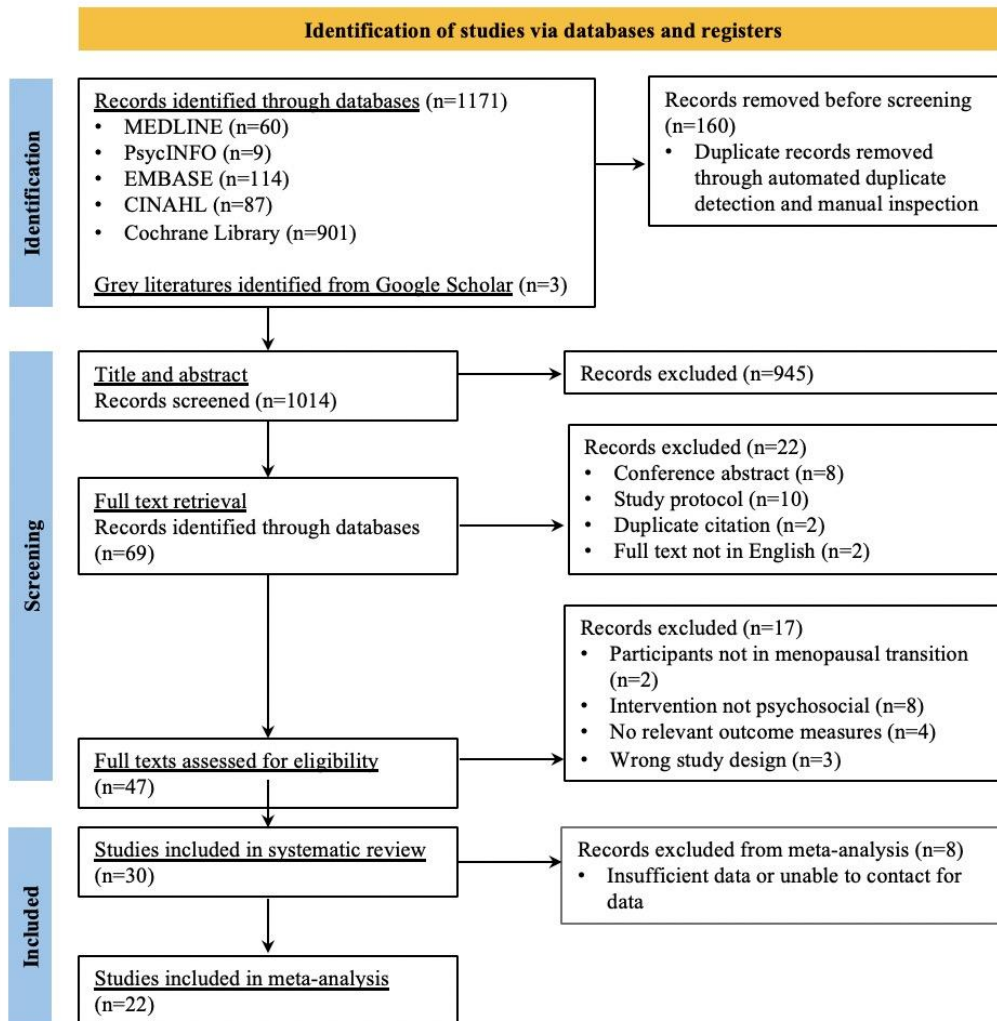


Table 1.
Characteristics of Included Studies

Author, date, country	Description of participants: Total N included, Menopause onset type, Mean age in years (SD)/age range, Demographics (E.g., Ethnicity, Education, Employment Status, Marital Status)	Control Type (excluded study arms)	Retention rate	Follow-up periods (since treatment onset)	Non-physiological measures and measurement instrument used	Intervention and outcomes	Intervention dosage (number of sessions, duration per session, total duration of intervention; otherwise specified)	Overall risk of bias ratings
Cognitive Behavioural Therapies (CBT)								
*Atema et al. (2019), Holland	254; treatment-induced (breast cancer) Int.: <i>Guided intervention group:</i> 47.5 (5.14), education (above high school 100%), employed (78.8%), married/in relationship (88.1%) <i>Self-managed intervention group:</i> 47.7 (5.73), education (above high school 97.6%), employed (72.9%), married/in relationship (83.5%) Con.: education (above high school 100%), employed (82.1%), married/in relationship (85.7%)	Non active (waitlist)	92.91%	Week 10, week 24	Anxiety, depression, distress: HADS QOL: SF-36	Guided and self-managed internet-based Cognitive Behavioral Therapy (iCBT) was not effective for mood symptoms or quality of life.	6 weekly sessions, 1.5hr (9 hours)	Some concerns
*Ayers et al. (2012), UK	140; gradual, perimenopausal Int.: <i>Group CBT:</i> 53.73 (5.9), ethnicity (White 82%), education (degree 53%), employed (76%), married/partnered (82%) <i>Self-help CBT:</i> 51.70 (4.4), ethnicity (White 87%), education (degree 55%), employed (81%), married/partnered (72%) Con.: 53.87 (5.7), ethnicity (White 78%), education (degree 62%), employed (65%), married/partnered (73%)	Non active (no intervention)	92.14%	Week 6, week 26	Depressed mood, anxiety, fears: WHQ Memory and concentration: WHQ QOL: SF-36	CBT led to significantly more reduction in mood symptoms, improvement in memory and concentration, and improvement in quality of life at week 6. Group CBT also led to significant improvement in emotional and physical functioning at week 26.	4 weekly sessions, 2hr (8 hours)	Low
Chilcot et al.	96; treatment-induced (breast cancer)	Active (TAU)	Unable to	Week 9,	Anxiety, depression:	CBT led to significantly	6 weekly	Some

(2014), UK	Int.: 53.16 (8.1); ethnicity (White 89%), education (beyond 16 years 64%), employed (64%) Con.: 54.05 (7.76); ethnicity (White 82%), education (beyond 16 years 67%), employed (35%)		calculate	week 26	WHQ	more reduction in mood symptoms at 9 weeks than control.	sessions, 1.5hr (9 hours)	concerns
*Fenlon et al (2020), UK	130; treatment-induced (breast cancer) Int.: 53.5 (9.78); ethnicity (White 96.7%), education (16+ years of age 64.4%), married/living with partner (72.9%) Con.: 55.2 (10.19); ethnicity (White 95.4%), education (16+ years of age 46.2%), married/living with partner (84.4%)	Active (TAU)	97.69%	Week 9, week 26	Depression: PHQ Anxiety: GAD-7 QOL: EQ-5D, HFRDIS	CBT led to significantly more reduction in anxiety and depressive symptom, and improvement in quality of life than control.	6 weekly sessions, 1.5hr (9 hours)	Low
*Green et al. (2019), Canada	71; gradual, perimenopausal or postmenopausal Int.: 53.27 (3.69); ethnicity (White 91.9%), married (78.4%), job (full time 64.9%) Con.: 52.88 (4.39); ethnicity (White 85.3%), married (61.8%), job (full time 38.2%)	Non active (waitlist)	69.01%	Week 12 + 3 months follow-up	Depression: BDI-II, MADRS Anxiety: HAM-A	CBT led to significantly more improvement in depressive symptoms, sleep difficulties, and sexual concerns than control. No significant effect on anxiety.	12 weekly sessions, 2hr (24 hours)	Some concerns
*Hardy et al. (2018), UK	124; gradual, perimenopausal Int.: 54.04 (3.17); ethnicity (White British 70.0%), education (degree 61.6%), married/partnered (70.0%) Con.: 54.10 (3.53); ethnicity (White British 71.4%), education (degree 65%), married/partnered (57.8%)	Non active (waitlist)	85.48%	Week 6, week 20	Memory and concentration: WHQ Anxiety/depression: WHQ QOL: WSAS	Self-help CBT led to significantly more improvement in work and social adjustment and wellbeing than control. No significant effect on anxiety/depression and memory and concentration.	4 weeks, 4 hr (16 hours)	High
*Kalmbach et al. (2019), USA	150; gradual, perimenopausal or postmenopausal Int.: 55.32 (5.39); ethnicity (White 47%) Con.: 57.24 (5.55); ethnicity (White 52%)	Active (Sleep Hygiene Education)	84%	Week 6 + 6 months	QOL: SF-36	CBT for insomnia (CBTI) led to significantly more improvement in quality of life (i.e., emotional wellbeing and resiliency to physical and emotional problems) than control.	6 weekly sessions	High
Keefer and Blanchard (2005), USA	29; gradual, perimenopausal Total age: 51.0 (4.7) Demographics not available	Non active (waitlist)	100%	Week 8	Anxiety/depression: WHQ QOL: MSQOL	No significantly effect of Cognitive Behavioral Group Therapy (CBGT) on mood	8 weekly sessions, 1.5hr (12 hours)	High

						or quality of life.		
*Mann et al. (2012), UK	96; treatment-induced (breast cancer) Int.: 53.16 (8.10); ethnicity (White 89%), educated beyond 16 years of age (64%), employed (64%), married/living with partner (62%) Con.: 54.05 (7.76); ethnicity (White 82%), educated beyond 16 years of age (67%), employed (65%), married/living with partner (57%)	Active (TAU)	91.67%	Week 9, week 26	Memory and concentration: WHQ Anxiety/depression: WHQ QOL: SF-36	CBT led to significantly more reduction in depressed mood at week 9 and week 26; more reduction in anxiety symptoms at week 9 but not week 26; more improvement in quality of life at week 9 and week 26, as compared to control.	6 weekly sessions, 1.5hr (9 hours)	Some concerns
Reddy and Omkarappa (2019), India	80; gradual, perimenopausal Int.: 48.63 (0.55); education (no formal education 50%), job (housewife 57.5%) Con.: 49.16 (0.8); education (no formal education 45%), job (housewife 62.5%)	Non active	78.43%	1 month, 6 months	Depression: CES-D	CBT led to significantly more reduction in depression than control at 6 months follow-up.	6 weekly sessions, 0.83-1hr (5-6 hours)	Some concerns
Mindfulness Based Interventions (MBI)								
*Aliabadi et al. (2021), Iran	66; gradual, postmenopausal Int.: 52.93 (3.29); ethnicity (persian 46.7%, Arab 26.7%, Lor 26.6%), education (above diploma 69.9%), job (housewife 80%) Con.: 53.20 (2.84); ethnicity (persian 46.7%, Arab 26.7%, Lor 23.3%, Turkish 3.3%), education (above diploma 40%), job (housewife 83.3%)	Non active	90.91%	Week 8 + 3 months follow-up	QOL: MENQOL	Mindfulness-Based Stress Reduction (MBSR) led to significantly more improvement in psychosocial, physical, and sexual dimensions of quality of life than control, immediately and three months after the intervention.	8 weekly sessions, 2hr (16 hours)	Some concerns
Carmody et al. (2011), USA	110; perimenopausal or postmenopausal Int.: 52.93 (3.29); ethnicity (Persian 46.7%, Arab 26.7%, Lur 26.6%), education (above diploma 69.9%), job (housewife 80%) Con.: 53.20 (2.84); ethnicity (Persian 46.7%, Arab 26.7%, Lur 23.3%, Turkish 3.3%), education (above diploma 40%), job (housewife 83.3%)	Non active (waitlist)	90.90%	Week 8 + 3 months follow-up	Anxiety: HADS-A QOL: MENQOL	MBSR led to significantly more improvement in quality of life and reduction in anxiety than control.	8 weekly sessions, 2.5hr (20 hours; plus an all-day class at the sixth week)	Some concerns
*Cramer et al. (2015), Germany	40; treatment-induced (breast cancer) Int.: 48.3 (4.8); education (above A-level, 68.4%), job (part time 52.6%), married (68.4%) Con.: 50.0 (6.7); education (above A-level, 42.9%), job (full time 28.6%, part	Active (TAU)	100%	Week 12, week 24	anxiety, depression: HADS QOL: FACT-B	Mindful yoga and meditation led to significantly more improvement in depression and quality of life than control. No significant effect	12 weekly sessions, 1.5hr (18 hours; plus 5-10mins of lecture per session)	Some concerns

	time 23.8%), married (81%)					on anxiety.		
*Enjezab et al. (2019), Iran	73; gradual, perimenopausal Int.: 50.89 (2.53); education (under the diploma and diploma 89%), job (housewife (92%)) Con.: 49.67 (2.73); education (under the diploma and diploma 92%), job (housewife (84%))	Non active (no intervention)	87.95%	Week 8 + 1 month follow-up	QOL: MENQOL	Mindfulness-Based Cognitive Therapy (MBCT) led to significantly more improvement in quality of life (except for the sexual dimension) than control, both immediately post intervention and at follow-up.	8 weekly sessions, 2hr (16 hours)	Some concerns
*Garcia et al. (2018), Brazil	30; gradual, postmenopausal Int.: 55.16 (6.05); education (11.25 years) Con.: 56.68 (4.01); education (12.62 years)	Non active	85.71%	Week 8	Attention: MAAS QOL: MSQOL	Mindfulness and Relaxation training for Insomnia (MRTI) led to significantly more improvement in quality of life and attention levels than control.	Daily sessions for 8 weeks, 0.4-0.67hr (29.4 hours)	High
*Gordon et al. (2021), USA	104; gradual, perimenopausal Int.: 48.7 (3.0); ethnicity (Caucasian 90%, Indigenous 2%, Other 8%), education (5.6 years) Con.: 48.7 (3.0); ethnicity (Caucasian 89%, Indigenous 4%, Other 9%), education (5.4 years)	Non active (waitlist)	91%	Week 8 + every 2 weeks for 6 months	Depression: CES-D Anxiety: STAI	MBSR led to significantly more reduction in depressive symptoms, anxiety, and improvement in resilience than control.	8 weekly sessions, 2.5hr (20 hours; plus a 7-hour intensive silent retreat)	High
*Huang et al. (2023), China	489; gradual, menopausal syndrome Int.: 59.04 (6.17); university educated (40.32%), employed (70.97%), have a spouse (66.13%) Con.: 58.73 (6.21); univervisty educated (39.66%), employed (65.52%), have a spouse (68.97%)	Active (routine care)	100%	Week 8	Anxiety: GAD-7	MBSR led to significantly more reduction in anxiety symptoms than control.	8 weekly sessions, 1hr (8 hours)	Some concerns
*van Driel et al. (2019), Holland	66; treatment-induced (risk-reducing salpingo-oophorectomy) Int.: 47.0 (5.0); no higher education (67.6%), part-time job (55.9%), married (97.1%) Con.: 48.5 (5.4); no higher education (45.2%), part-time job (64.5%), married (80.6%)	Active (TAU)	72.73%	3 months, 6 months, and 12 months	QOL: MENQOL	MBSR led to significantly more improvement in quality of life in both short- and long-term than control.	8 weekly sessions, 2.5hr (20 hours; plus a 4hr silent retreat evening and a daily 0.5-0.75hr mindfulness exercises for 6 days)	Low
*Wong et al.	197; peri- or postmenopausal	Active	Unable to	Week 8, 8	Anxiety, depression:	MBSR led to significantly	8 weekly	Some

(2018), Hongkong	Int.: 51.9 (3.0); education (secondary school 70.4%), job (housewife 46.9%), married (73.5%) Con.: 52.1 (3.2); education (secondary school 67.7%), job (housewife 45.5%), married (73.5%)	(menopause education)	calculate	months	GCS QOL: SF-12 (validated Chinese version)	more reduction in anxiety and depression than control. No significant effect on health-related quality of life.	sessions, 2.5hr (20 hours)	concerns
Other types of interventions								
*Anderson et al. (2015), Australia	55; treatment-induced (breast cancer) Int.: 48.5 (5.9); education (above university 73.1%), job (full time 66.7%), household income (63%), married (74.1%) Con.: 49.8 (6.5); education (above university 57.7%), job (full time 65.4%), household income (60%), married (69.2%)	Active (TAU)	92.73%	Week 12	Anxiety, depression: GCS QOL: FACT-B, SF-12	The Pink Women's Wellness Program led to significantly more reduction in mood symptoms and improvement in quality of life than control.	12 weekly sessions	Some concerns
Augoulea et al. (2021), Greece	61; gradual, perimenopausal or postmenopausal Int.: 57.70 (6.89); education (4.67 years), menopause duration (6.80 years) Con.: 56.52 (4.73); education (4.52 years), menopause duration (6.94 years)	Active (audio CDs and instructions on relaxation techniques)	Unable to calculate	Week 8	Anxiety, depression, stress: DASS-21	Structured education program on stress management led to significantly more reduction in mood symptoms than control, but within-subject differences were insignificant.	8 weekly sessions	Some concerns
Fujimoto (2017), Japan	83; gradual, perimenopausal Int.: 49.13 (4.30); job (housewives 40%), household (nuclear family 83.3%) Con.: 50.93 (4.05); job (full-time job, 33.3%, housewives 30%), household (nuclear family 60%)	Active (routine care)	72.29%	Week 12 + 3 months follow-up	QOL: SF-36, SE	Health promotion coaching led to significantly more improvement in quality of life and self-efficacy than control.	3-month coaching (plus 0.67hr of telephone coaching per month)	High
Karimi et al. (2022), Iran	70; gradual, postmenopausal Int.: 53.87 (4.50); education (diploma 69.7%), job (housewives 63.6%) Con.: 55.11 (4.34); education (diploma 52.9%), job (housewives 67.6%)	Non active	95.71%	Week 5	Quality of marital life: RDAS	Self-care education program led to significantly more improvement in quality of marital life than control.	5 sessions within one week, 0.75-2hr (3.75-10 hours)	Some concerns
*Mehdipour et al. (2021), Iran	88; gradual, postmenopausal Int.: 51.77 (3.5); education (university 31.8%), job (employee 50%, housewife 38.6%), economic status (good 40.9%) Con.: 52.4 (2.85); education (university 43.2%), job (employee 43.2%, housewife	Active	100%	Week 8	Depression: BDI-II	Emotional Freedom Techniques (EFT) led to significantly more reduction in depressive symptoms than control.	2 training sessions and 8-weekly video training	Some concerns

	43.2%), economic status (good 54.5%)							
Mehrabi et al. (2021), Iran	75; gradual, postmenopausal Int.: 55.8 (3.1) Con.: 54.5 (3.3) Demographics not available	Active (routine care)	Unable to calculate	Week 6	QOL: Oxford Happiness Questionnaire	Solution-focused group counseling led to significantly more improvement in mean happiness than control.	6 weekly sessions, 1.5hr (9 hours)	Some concerns
*Moghadam et al. (2019), Iran	78; treatment-induced (bilateral salpingo oophorectomy) Unable to calculate mean age. Int.: 42-46 (15.4%), 47-51 (51.3%), 52-56 (33.3%); socioeconomic status (moderate 53.8%), education (high school diploma 56.4%) Con.: 42-46 (12.8%), 47-51 (43.6%), 52-56 (43.6%); socioeconomic status (moderate 53.8%), education (high school diploma 61.5%)	Non active (no intervention)	96.15%	Week 6 + 1 month + 3 months follow-up	QOL: MENQOL	Multi-dimensional group counseling led to significantly more improvement in overall quality of life and vasomotor, psychosocial, physical, and sexual dimensions than control.	6 weekly sessions, 1.5hr (9 hours)	Some concerns
*Monfaredi et al. (2022), Iran	86; gradual, postmenopausal Int.: 54.87 (4.49); university educated (4.7%), housewife (88.4%), relatively sufficient family income (93%), satisfied with life (95.3%) Con.: 54.75 (4.56); university educated (14%), housewife (83.7%), relatively sufficient family income (93%), satisfied with life (93%)	Active (routine care)	100%	Week 8	Anxiety, depression: GCS subscale Depression, anxiety, stress: DASS-21 QOL: MENQOL	Acceptance and Commitment Therapy led to significantly more reduction in depression, anxiety, and stress than control. No significant effect on quality of life.	8 weekly sessions, 1-1.5hr (8-12 hours)	Some concerns
Rindner et al. (2023), Sweden	370; gradual, perimenopausal Int.: <i>Group education (GE):</i> 53 (4.2); education < 12 years (51%), currently working (85%) <i>Person-centered support (PCS):</i> 53 (4.2); education < 12 years (52%), currently working (81%) <i>GE + PCS:</i> 53 (3.7); education < 12 years (54%), currently working (88%) Con.: 51 (3.9); education < 12 years (39%), > 12 years (62%); currently working (89%)	Non active	99.46%	6 months, 12 months	Anxiety and depression: HADS Depression: MADRS-S Memory and concentration: WHQ QOL: WSAS Wellbeing: WHQ	Both GE and PCS led to significantly more improvement in quality of life and physical, psychological, and urogenital symptoms than control.	GE: 4 weekly sessions, 1.5hr (6 hours) PCS: 5 sessions	Some concerns
*Yarelahi et al. (2021), Iran	80; gradual, postmenopausal Int.: 53.7 (3.4); education (elementary education 41.2%), job (35 women were housewives)	Active	93.75%	Week 8	QOL: MENQOL	Couples Coping Enhancement Training led to significantly more improvement in quality of life than control.	4 sessions, 0.75hr (3 hours)	Some concerns

	Con.: 53.3 (3.5); education (elementary education 48.8%), job (37 women were housewives)							
*Yazdkhasti et al. (2012), Iran	110; gradual, postmenopausal Int.: 53.13 (5.86); job (housewives 78.8%), SES (moderate 65.4%), education (elementary 36.5%) Con.: 53 (6.07); job (housewives 81.1%), SES (moderate 50.9%), education (elementary 49.1%)	Non active	95.45%	Week 10	QOL: MENQOL	Support group led to significantly more improvement in vasomotor, psychosocial, physical, and sexual dimensions of quality of life than control.	10 weekly sessions 2hr (20 hours)	High
<p>* = included in meta-analysis</p> <p>Note: BDI-II=Beck Depression Inventory-Second Edition, CES-D=Center for Epidemiologic Studies Depression Scale, DASS-21=Depression, Anxiety, and Stress Scale-21 Items, EQ-5D=European Quality of Life Five Dimensions, FACT-B=the Functional Assessment of Cancer Therapy-Breast, GAD-7=General Anxiety Disorder-7 Items, GCS=Green Climacteric Scale, HADS=Hospital Anxiety and Depression Scale, HAM-A=Hamilton Anxiety Rating Scale, HFRDIS=Hot Flash Related Daily Interference Scale, MAAS=Mindfulness Awareness Attention Scale, MADRS=Montgomery-Asberg Depression Rating Scale, MENQOL=Menopause Quality of Life, MSQOL=Menopause Specific Quality of Life, PHQ=Patient Health Questionnaire, QOL=quality of life, RDAS=Revised Adjustment Scale, SE=General Self-Efficacy Scale, SF-12=12 Item Short Form Health Survey, SF-36=36 Item Short Form Health Survey, STAI=State-Trait Anxiety Inventory, WHQ=Women's Health Questionnaire, WSAS=Work and Social Adjustment Scale</p>								

3.2 Risk of bias

The distribution of risk-of-bias judgments by percentage within each bias domain is provided in Table A1 (supplementary materials). Overall, the quality of studies was moderate and did not appear to differ markedly by interventions. 66.7% of included studies were judged to have “some concerns” in risks of bias including five CBT studies, six MBI studies and nine other studies. 23.3% of studies were classified as having “high” risks of bias with two from MBI studies, two from other studies and three from CBT studies. 10% of studies were “low” in risks of bias, including two CBT studies and one MBI study. Risks of bias was mainly due to unblinded intervention assignment, participants’ self-reported symptoms, and not explicitly stating that data were collected after determining a statistical analysis plan. From the inspection of funnel plots and the Egger’s test, there was significant evidence of asymmetry for both anxiety ($z=-2.98$, $p<.01$) and depression ($z=-3.87$, $p<.01$) outcomes, suggesting potential publication bias that may affect the validity of our findings.

3.3 Meta-analytic findings

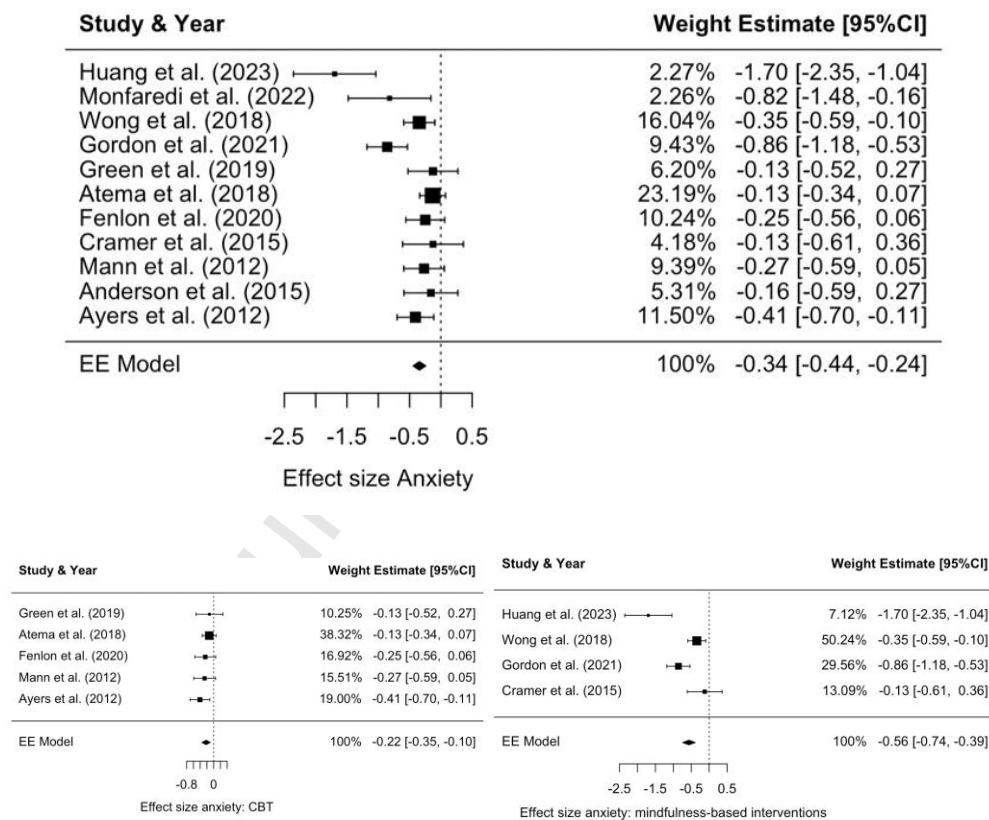
We performed meta-analysis for mood symptoms (anxiety and depression), cognition (memory and attention), and quality of life outcomes based on the Menopause-Specific Quality of life (MENQOL).

3.3.1 Mood

Anxiety (Figure 2): Data from eleven studies ($n=1662$) were available to be pooled for meta-analysis. There was a significant reduction in anxiety symptoms in the intervention group compared to control with small to medium effect size ($d=-0.34$, 95% CI=-0.44, -0.24). The

heterogeneity in the model was significant and high ($X^2=35.34$, $df=10$, $p < .01$, $I^2=71.7\%$). Subgroup analysis revealed significant but small effect of CBT ($d=-0.22$, 95% CI=-0.35, -0.10), in which heterogeneity of data was non significant ($p = .63$). Mindfulness-based interventions were observed with significant, medium to large effect size ($d=-0.56$, 95% CI=-0.74, -0.39) and considerable heterogeneity of data ($X^2=20.66$, $df=3$, $p < .01$, $I^2=85.48\%$).

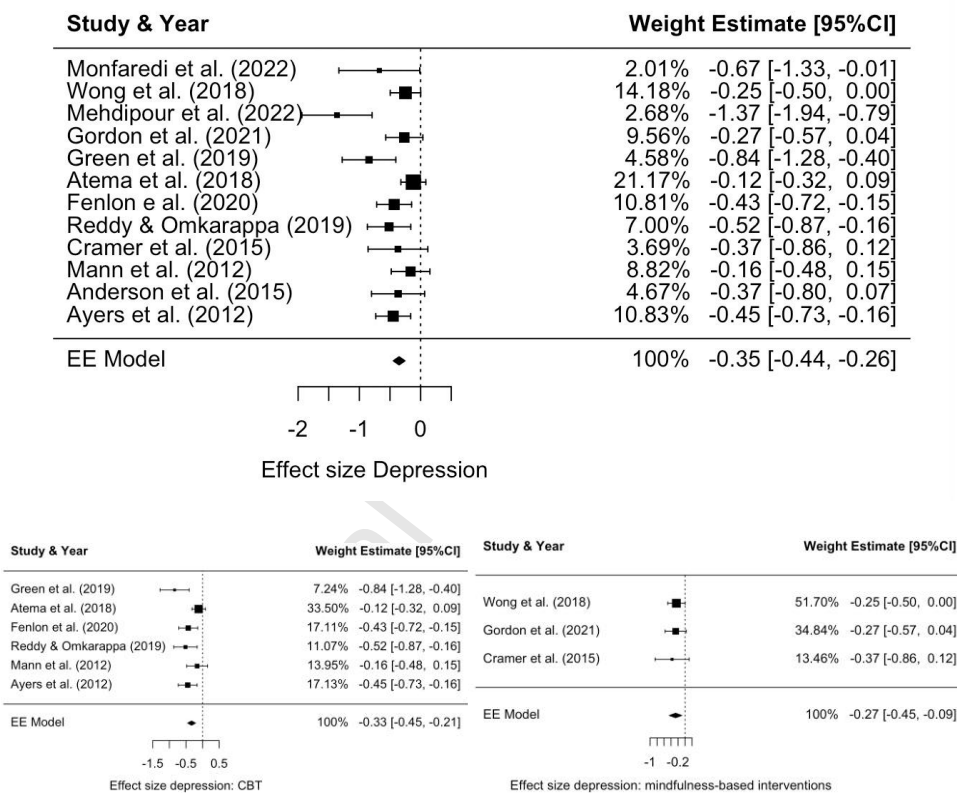
Figure 2.
Forest plot of meta-analytic anxiety outcomes



Depression (Figure 3): Pooling effect sizes from twelve studies ($n=1341$), there was a significant reduction in depressive symptoms in the intervention group ($d=-0.35$, 95% CI=-0.44, -0.26). There was significant and moderate heterogeneity ($X^2=26.72$, $df=11$, $p < .01$, $I^2=58.83\%$) in the model. After subgroup analysis, significant but small effect sizes were maintained for CBT

($d=-0.33$, 95% CI= -0.45 , -0.21) and mindfulness-based interventions ($d=-0.27$, 95% CI= -0.45 , -0.09) respectively. Heterogeneity of data was significant and substantial for CBT ($X^2=12.67$, $df=5$, $p=.03$, $I^2=60.52\%$) and non-significant for mindfulness-based interventions ($p=.91$).

Figure 3.
Forest plot of meta-analytic depression outcomes

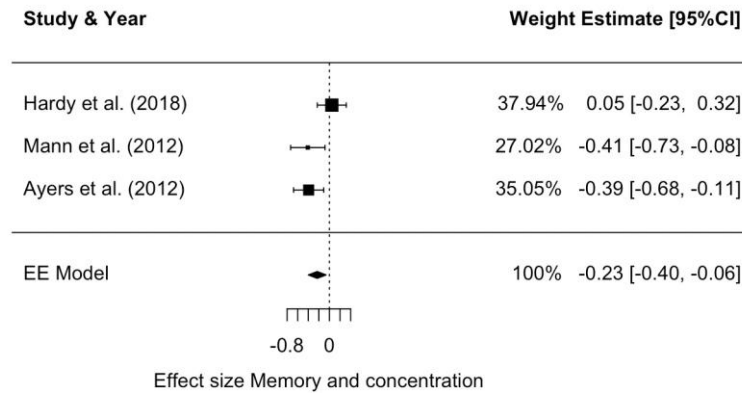


3.3.2 Cognition: Memory and Concentration (Figure 4)

Three CBT-based studies ($n=360$) examined the effectiveness of psychosocial interventions on participants' memory and concentration using the Women's Health Questionnaire (WHQ). CBT led to a significant reduction in participants' memory and concentration difficulties with a small effect size ($d=-0.23$, 95% CI= -0.40 , -0.06). The heterogeneity for the pooled data was significant and substantial ($X^2=6.30$, $df=2$, $p=.04$, $I^2=68.28\%$).

Figure 4.

Forest plot of meta-analytic memory and concentration outcomes

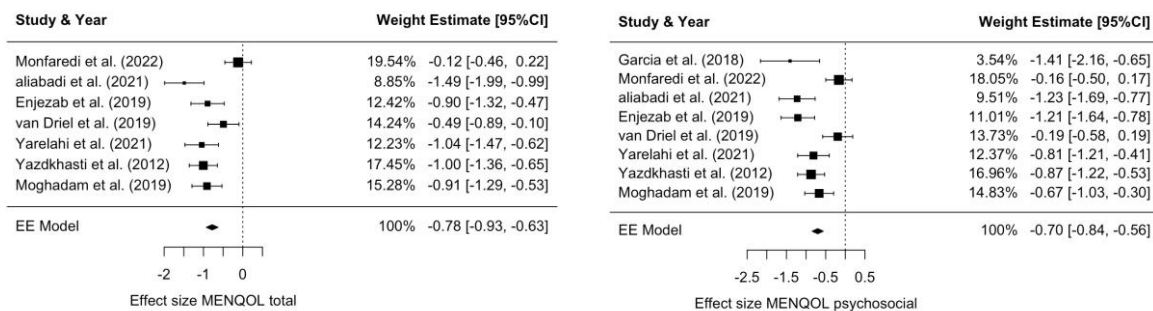


3.3.3 Quality of Life (Figure 5)

Psychosocial interventions were found to be effective in improving women's quality of life, as measured by the MENQOL. We focused the analyses on MENQOL total score and the Psychosocial subscale. Both were found with medium to large effect sizes (Total: $d=-0.78$, 95% CI=-0.93, -0.63; Psychosocial: $d=-0.70$, 95% CI=-0.84, -0.56) and considerable heterogeneity (Total: $X^2=28.22$, $df=6$, $p<.01$, $I^2=78.74\%$; Psychosocial: $X^2=31.86$, $df=7$, $p<.01$, $I^2=78.03\%$).

Figure 5.

Forest plot of meta-analytic MENQOL quality of life outcomes



3.4 Narrative findings

Eight studies (Augoulea et al., 2021; Carmody et al., 2011; Chilcot et al., 2014; Fujimoto, 2017; Karimi et al., 2022; Keefer & Blanchard, 2005; Mehrabi et al., 2021; Rindner et al., 2023) were not included in the meta-analysis due to insufficient data.

Mood: MBSR was found to significantly reduce anxiety symptoms compared to waitlist control (Carmody et al., 2011). Augoulea et al. (2021) found significant between-subject differences ($p = .003$) but not significant within-subject differences in the Depression Anxiety Stress Scale (DASS), supporting some but little benefit of stress management psychoeducation over relaxation training on mood. Chilcot et al. (2014) found support for the effectiveness of CBT based on Women's Health Questionnaire (WHQ), but this contradicted the findings of Keefer and Blanchard (2005) and Hardy et al. (2018).

Cognition: Garcia et al.'s (2018) study of mindfulness and relaxation training for insomnia measured cognition through looking at participants' attention and awareness in everyday situations, finding significant improvements following the intervention.

Quality of Life: Three studies (Ayers et al., 2012; Kalmbach et al., 2019; Mann et al., 2012) found evidence for the effectiveness of CBT on the outcomes of the 36 Item Short Form Health Survey (SF-36, Ware & Sherbourne, 1992). CBT was also found to reduce hot flash daily interference, work and social adjustment and general wellbeing (Hardy et al., 2018). The effectiveness of MBSR was observed from the MENQOL (Carmody et al., 2011) but not SF-12 (12 item Short Form Health Survey; Wong et al., 2018). Karimi et al. (2022) found that quality of marital life was facilitated by a self-care education program. Further, solution-focused group counselling was effective in enhancing participants' self-rated happiness (Mehrabi et al., 2021). Interventions that were less effective include the structured education program on stress management (Augoulea et al., 2021), health promotion coaching (Fujimoto, 2017), and the Pink Women's Wellness Program (Anderson et al., 2015).

4. Discussion

4.1 Summary and discussion of results

The results of the meta-analyses indicated the overall effectiveness of psychosocial interventions in improving mood and quality of life in women experiencing menopausal symptoms. For anxiety, CBT had a small effect and MBI had a medium effect. However, there was significant heterogeneity in MBI model, making this a less robust and interpretable model. Notwithstanding this, the MBI trials on average were of a much larger 'dose' (18.6, compared to 11.3 hours), making it harder to compare the approaches and may well accounting for the stronger effect. For depression, the effect sizes for CBT and MBI were fairly similar, but with more heterogeneity (and therefore less strength) in the CBT model.

Narrative synthesis partially supported the findings. Limited studies used cognitive outcomes, but significant effects of CBT on memory and concentration was pooled from three studies. Other effective interventions included the self-care education program (Karimi et al., 2022) and solution-focused group counseling (Mehrabi et al., 2021), both which benefited quality of life. Overall, the quality of studies was moderate and did not appear to differ markedly between intervention types.

Our findings align to previous studies proving support for the effectiveness of psychosocial interventions on mood symptoms (Green et al., 2015; Holger et al., 2012; Shabani et al., 2022) and quality of life (Chen et al., 2021) in menopausal women, but have the benefit of combining data from multiple trials. A common feature of all was an interactive nature, indicating that group exercises and sharing experiences and perceptions of menopause was important (Parsa et al., 2017). More broadly, psychosocial therapies should enable women to consider the biopsychosocial nature of the menopause transition, reflecting upon common challenges at this life-stage including aging parents, children leaving home and challenges in confidence due to the physical symptoms. Empowering women to develop and apply new coping strategies and more positive thinking styles is likely to have added additional benefits beyond that from purely biological (hormonal) treatments.

The average 'dose' of CBT in terms of frequency and duration was notably lower than that of MBI, the latter which often constituted of both weekly sessions and complementary exercises (such as silent retreats; Carmondy et al., 2011; Gordon et al., 2021; van Driel et al., 2019). This difference is likely to have significant cost implications, which may as a result favour CBT as the

treatment of choice. An additional benefit to a lower dose therapy is the cost-benefit ratio to the patients, with busy women perhaps more likely to adhere to briefer interventions, which also enable reduced time away from other activities such as work. Both intervention types were predominantly group based, offering a more cost-effective solution than individual therapies. Future investigations could explore the cost-effectiveness of CBT and MBI for clinical guidelines, supporting more comprehensive and informed recommendations.

4.2 Strengths and Limitations

As the first meta-analysis on the effectiveness of psychosocial interventions on menopause, we performed a broad literature search to gain an overview. A strength was that data was included from fourteen countries, with diversity in language and culture, enabling generalizability. Of note, all were high income countries (with the exception of Brazil and China, both middle income countries). A limitation was that all participants in all studies were described as ‘women’, with an absence of considering (or defining) others such as non-binary people or trans men. Due to limited availability of studies, we did not control the context of study, stage participants’ symptom severity, and comparison format. It was not possible to look at stage of menopause without individual patient data, which limits our understanding of the optimum time to deliver interventions. Nevertheless, we minimized the heterogeneity of studies by applying stringent eligibility criteria. Another limitation was not accounting for longer follow-up symptom changes in our analysis. This is important as some interventions may require longer exposure to show more significant effects, whilst in contrast the benefits of others might not be maintained. Future research should demonstrate long-lasting effects of interventions to inform valid symptom management.

4.3 Implications

While the perceived overall quality of life in menopausal women depends on the combination of physical, psychological, and cognitive functioning (Schneider, 2002), our review identified cognition as an under-researched domain that may benefit from psychosocial interventions. Future research may introduce more localized interventions adapted for specific sociocultural backgrounds, for example CBT may address stigmatized menopausal perceptions, including loss of value due to reproductive capacity decline in low-and-middle-income countries (Hoga et al., 2015).

Our review could inform the development of menopause services, in which enhanced professional training could pave the way for integrating mindfulness and CBT as conventional healthcare service options. At the center of treatment is the understanding of menopausal symptoms and embracing sufficient social support. Therefore, we recommend better development of internet-based programs and establishing community support groups to increase women's accessibility to psychosocial resources. Future research should consider cost-benefit analysis of face-to-face versus online interventions. Efforts are also required from authorized organizations to promote public awareness of menopause and integrated approaches (both medical and psychosocial) to menopause management at a systems level .

4.4 Conclusion

The findings of this review add to existing menopause literature by supporting the effectiveness of psychosocial interventions on non-physiological symptoms of mood, cognition, and quality of

life. This review recommends the application of Mindfulness-Based Interventions, CBT, and group-based interventions in clinical management of menopause and highlights where future research is needed.

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Journal Pre-proof

**The effectiveness of psychosocial interventions on non-physiological symptoms of
menopause: A Systematic Review and Meta-analysis**

Highlights

- Menopausal transition can significantly impact depression, anxiety and cognition.
- Psychosocial interventions include Cognitive Behavioural Therapy and Mindfulness.
- Psychosocial interventions can improve anxiety and depression in menopause.
- Psychosocial interventions may help cognition in menopause. More research is needed.