Complementary Therapies in Medicine 34 (2017) 26–34

Contents lists available at ScienceDirect

Complementary Therapies in Medicine

journal homepage: www.elsevier.com/locate/ctim

Review

Transcendental meditation for lowering blood pressure: An overview of systematic reviews and meta-analyses

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ARTICLE INFO

Keywords:
Transcendental meditation
Blood pressure
Systematic reviews
Meta-analyses

ABSTRACT

Background: Transcendental meditation (TM) is a stress reduction technique that can potentially lower blood pressure (BP) safely. The American Heart Association recommends that TM may be considered in clinical practice.

Objective: To provide an overview of all systematic reviews and meta-analyses of TM on BP for evidence-informed clinical decision making.

Method: Systematic searches of PubMed, EBSCOhost, Cochrane Library, Web of Science, Embase, and PsycINFO for all systematic reviews and/or meta-analyses of randomized controlled trials (RCTs) with TM as an intervention, and outcome measures include systolic BP (SBP) and diastolic BP (DBP). Qualitative and quantitative data were synthesized. The methodological quality of the selected reviews was assessed using the AMSTAR checklist.

Results: Eight systematic reviews and meta-analyses are included. Among them is an Agency for Healthcare Research and Quality report, a Cochrane systematic review, 4 independent reviews, and 2 reviews from a TM related institution. The quality of most of the included reviews is fair with a mean score of 5.75/11 on the AMSTAR scale. Overall, there exists a clear trend of increasing evidence over the years supporting the efficacy of TM in lowering BP. However, some conflicting findings remain across reviews and potential risk of bias exists in many of the RCTs included in these reviews.

Conclusion: Practising TM may potentially reduce the SBP by ~4 mm Hg and DBP by ~2 mm Hg. Such effect is comparable with other lifestyle interventions such as weight-loss diet and exercise. Further evidence from long-term well-designed RCTs conducted by independent researchers is needed.

1. Background

Hypertension is a major public health issue worldwide.[1] It affects about 31.1% of the adult population worldwide, with an estimated 1.39 billion people had hypertension in 2010.[2] Infamous relationships exist between hypertension with one or more of these lifestyle conditions: chronic stress, obesity, high dietary sodium intake, excessive alcohol consumption, smoking, and minimal physical activity.[3] Psychosocial stress is also a pivotal consequential contributor to an elevated blood pressure (BP).[4] With each 2 mmHg increase in systolic BP (SBP), there is a 7% increased risk of mortality from coronary heart disease and a 10% increased risk of mortality from stroke.[5] Thus, unmanaged hypertension can cause serious harm to human health.

To prevent adverse health consequences of hypertension, there exist formal guidelines for individuals to adopt lifestyle changes to safely reduce BP.[6] Proven approaches include weight loss, reduced sodium intake, minimized alcohol consumption, and exercise. However, adherence to dietary strategies (with the focus on a diet rich in fruit and vegetables and low in saturated fat) has been shown to be difficult to maintain.[7] Beyond dietary strategies, non-pharmacological treatments, such as the transcendental meditation (TM), is readily adopted and has the capacity to safely lower BP.[7]

TM is a mantra meditation technique where consciousness is directed towards repetition of a word, or a phrase as an object of focus.[8] The process allows "the ordinary thinking process to become more quiescent and a unique psychophysiological state of 'restful alertness' to be gained".[9] It has been described as "a simple, natural, and effortless procedure, optimally practiced twice a day for twenty minutes while sitting comfortably with the eyes closed".[10] The standard TM course offered by the Maharishi Foundation (the TM organization) includes an introductory and preparatory lecture, a one-hour session of personal instruction, and consecutive follow-up sessions over the next three

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http://dx.doi.org/10.1016/j.ctim.2017.07.008
Received 5 April 2017; Received in revised form 11 July 2017; Accepted 19 July 2017
Available online 24 July 2017
0965-2299/

days. After which, students will practice on their own as a daily routine.[10]

The effect of TM on BP has been extensively studied. In the American Heart Association (AHA) scientific statement on alternative approaches to lowering BP published in 2013,[7] TM was conferred a Class IIB, Level of Evidence B recommendation on its BP-lowering efficacy; the highest among all behavioral therapies. The AHA scientific statement suggested that TM might be considered in clinical practice to lower BP, after a review of evidence from available systematic reviews, meta-analyses, as well as recent clinical trials not included in the published reviews.

Newer systematic reviews and meta-analyses on this topic have been published since the recommendation by AHA, offering new data and insights. With the speed of information production today, it has become increasingly challenging to keep up-to-date with currently available evidence.[11] Hence, there is a need for an overview of all published systematic reviews and meta-analyses on the effect of TM on BP, which synthesize and integrate information to facilitate evidence-informed decision making by clinicians, researchers and patients.

2. Methods

2.1. Literature search

We conducted a targeted keywords systematic search on PubMed, EBSCOhost (All), Cochrane Library (Issue 2 of 12, February 2017), Web of Science, Embase, and PsycINFO (1967 to February Week 4 2017) without any restriction in year of publications. Keywords used were "blood pressure" AND "transcendental meditation" AND ("meta-analysis" OR "systematic review"). We also manually searched the reference lists of selected articles to identify any additional systematic reviews and/or meta-analyses. The search was conducted between February and March 2017 by two authors (SLO and MG).

2.2. Selection of reviews

Criteria of inclusion: (1) English language systematic reviews and/or meta-analyses of clinical trials only with at least one randomized controlled trials (RCTs), (2) TM as an intervention for review, (3) Outcome measures of review include SBP and diastolic blood pressure (DBP), (4) Any systematic review not specific to TM must provide a detail review on the effect of TM on BP, (5) Any meta-analysis not specific to TM must conduct a subgroup analysis specific to TM and BP. Selection of reviews was performed by two authors (SLO and MG) and any differences were resolved through discussion with the third author (SCP) to reach a consensus.

2.3. Data extraction

Data extracted from selected systematic reviews include authors, year of publication, overall objectives, inclusion criteria, total number of included trials, aggregated sample size of all included trials, and selected concluding quote. We also extracted the list of all included trials for comparison across reviews. For meta-analyses, sample sizes for TM and control, weighted mean difference (WMD) between TM and control for SBP and DBP, reported heterogeneity (p-values and I^2 values) were extracted for all main and subgroup analyses reported. Data extraction was conducted by SLO and the results were reviewed by SCP. Any discrepancy found was resolved through discussion to reach a consensus.

2.4. Quality assessment

We used "A MeaSurement Tool to Assess systematic Reviews" (AMSTAR) checklist to assess and report on the methodological quality of the selected systematic reviews and meta-analyses.[12] AMSTAR has been demonstrated to have good agreement, reliability, construct validity, and feasibility across a diverse range of reviews. AMSTAR is also easy to apply.[13] SLO performed the quality assessment and the results were reviewed by SCP. Disagreement was resolved through discussion.

Table 1
Full text articles excluded with reasons.

Full text articles excluded	Reasons
Eisenberg et al.[22]	Not providing sufficient information
Devine & Reifschneider[23]	Not providing sufficient information
Canter & Ernst[24]	Duplication
Barnes & Orme-Johnson[25]	Non-systematic review
Black et al.[26]	Not providing sufficient information
Brook et al.[7]	Not systematic review of RCTs
Orme-Johnson & Barnes[27]	Not providing sufficient information
Nagele et al.[28]	Not providing sufficient information
Younge et al.[29]	Not providing sufficient information

3. Results

3.1. Search results and characteristics of reviews

Sixty-seven records from database searches and nine records from manual reference lists searches were found. After removing the duplicates, screening, and assessing for eligibility, eight review articles met our inclusion criteria.[14–21] Nine articles were excluded with reasons after assessing the full text[7,22–29] (See Table 1), inclusive of the AHA scientific statement which did not meet the first selection criterion. Five of the included reviews provided meta-analyses for quantitative synthesis. [14,15,17,19,20] A summary of the search process is shown in Fig. 1. The characteristics of these reviews are summarized in Table 2. The list of all trials reviewed and meta-analyzed by the selected reviews are summarized in Table 3 with full references available in the References section.[9,30–54]

3.2. Qualitative and quantitative synthesis

Walton et al. [21] reviewed TM as a potential intervention to address psychosocial stress and reduce recurrent cardiovascular disease (CVD) events by lowering risk factors including hypertension. Five studies were included with four of them being RCTs.[43,45,47,49] and the fifth [46] being a subgroup analysis of one of four RCTs. This review found both clinically and statistically significant reductions of BP with up to 13 mm Hg in SBP and 8 mm Hg in DBP reported in each study with no meta-analysis conducted. Walton et al. noted from these studies that TM program can be effectively implemented in diverse populations with a generally high compliance; significant reduction of BP in both sexes and at both ends of the spectrum of CVD risk can be achieved; and TM was twice as effective compared to progressive muscle relaxation (PMR) in reducing the BP of hypertensive older African Americans. Relatively short time of follow-up ($<=$ 4 months) was noted as a shortcoming of all the included studies.

Canter and Ernst [16] included six RCTs [33,40,43,45,47,49] with one [33] available only as an abstract. Four of which were also reviewed by Walton et al. Canter and Ernst disputed the findings of Walton et al. on the ground of methodological weaknesses and risk of bias in all the included trials. Assessing quality based on a modified Jadad scale with a maximum of four (4) points, only half of the included trials scored three (3) and above [45,47,49] Of the two trials that scored the maximum four (4) points, only one,[47] found statistically significant difference between groups that favored TM, and the other one [49] did not. One trial, which scored three (3) on the modified Jadad scale [45] also did not show a statistical difference between the groups. Consequentially, positive outcomes were associated with trials with lower quality. Furthermore, all trials were conducted by authors that had some form of

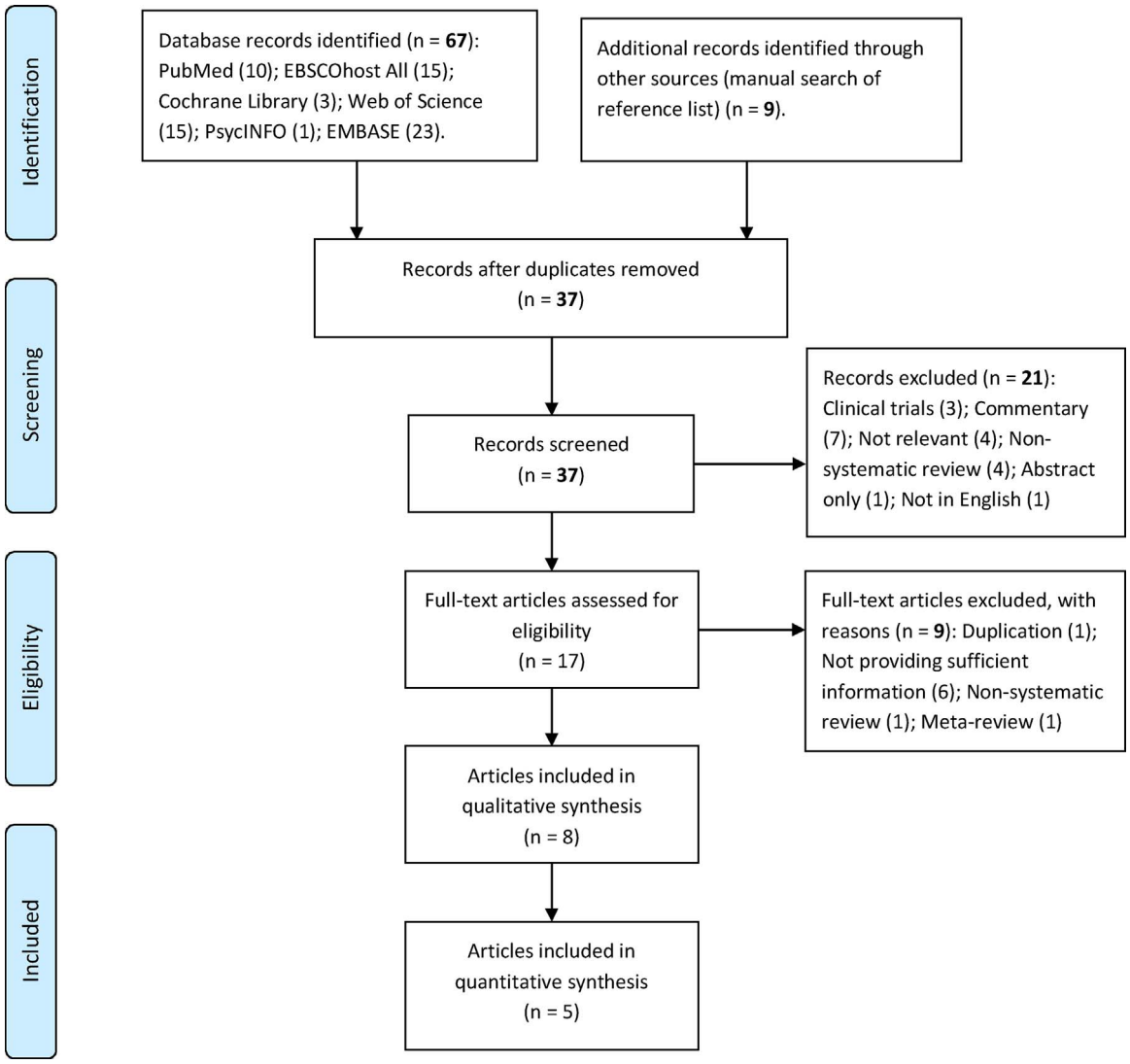

Fig. 1. Literature search flow diagram (based on PRISMA 2009).

affiliation or involvement with institutions of the TM organization, therefore there was a clear scope of bias. As such, Canter and Ernst did not find sufficient good quality evidence to conclude that TM had a cumulative positive effect on BP. Further research conducted by fully independent researchers was called for.

Ospina et al. [14] was commissioned by the Agency for Healthcare Research and Quality (AHRQ) to review the state of research on meditation practices for health. For hypertensive subjects, five TM trials, which compared TM to health education (HE), were reviewed.[33,35,39,44,47] In two of them, [39,47]TM was also compared to PMR. Only two trials [39,47] were considered as high quality (Jadad scale = 3). The results of the meta-analyses were summarized in Table 4. TM was not superior to HE in reducing BP (SBP, −1.10 mm Hg; 95% CI: −5.24, 3.04; DBP, −0.58 mm Hg; 95% CI: −4.22, 3.06) with only one short term (3 months) trial [47] reported statistically significant changes in SBP and DBP which favored TM. Compared to PMR, TM was found to have significant effects on both SBP (−4.30 mm Hg; 95% CI: −8.02, −0.57) and DBP (−3.11 mm Hg; 95% CI: −5.00, −1.22). For healthy subjects, eight trials were included [30,31,34,41,42,51,53,54] for meta-analysis. Only two were RCTs [41,42]; three were non-RCTs [31,34,51]; and another three were before-and-after trials with no control. [30,53,54] Only one trial,[42] was considered good quality (Jadad score = 3). Compared with no treatment (NT) in three trials, [31,34,42] TM was not associated with statistically significant BP reductions in both SBP (0.93 mm Hg; 95% CI: −9.53, 11.39) and DBP (−1.63 mm Hg; 95% CI: −8.01, 4.75). In the three before-and-after trials, the combined estimate of changes from baseline indicated statistically and clinically significant improvement in both SBP (-10.95 mm Hg; 95% CI: −17.52, −4.39) and DBP (-6.86 mm Hg; 95% CI: −10.54, −3.19). However, potential biases were inherent in the before-and-after design. The remaining two trials compared TM to waitlist (WL). [41,51] Small and statistically significant reductions in both SBP (-8.74 mm Hg; 95% CI: −17.47, −0.02) and DBP (-3.61 mm Hg; 95% CI: −6.62, −0.59) were observed for TM. Overall, Ospina et al. reported some evidence that TM can significantly reduce BP in both hypertensive and healthy individuals. However, the results were derived from meta-analyses of predominantly low quality trials.[14] Rainforth et al. [15] reviewed TM as one of the stress reduction programs for the management of BP in hypertensive individuals. Criteria for well-designed trials were defined to be 1) RCT in pre-hypertensive and/or hypertensive patients; 2) adequate baseline BP assessment; 3) used attention control group; 4) duration of at least 8 weeks; and 5) published in peer-reviewed journal. Six well-designed TM trials were included,[38–40,43,44,47] for meta-analysis. Statistically significant reductions in mean SBP (-5.0 mm Hg; 95% CI: −7.6, −2.3) and mean DBP (-2.8 mm Hg; 95% CI: −5.0, −0.5) were found. Subgroup analysis of single-blinded RCTs only [38,39,44,47] found similar results (SBP: −5.1 mm Hg; 95% CI: −9.4, −0.8; DBP: −2.1 mm Hg; 95% CI: −5.4, 1.4). Hence, well-designed trials on TM showed clinically and

Table 2
Characteristics of the included systematic reviews and meta-analyses.

#	Review ID	Overall objectives	Inclusion Criteria	No. Trials (Sample N) Trials' Length	Quality Assessed?	Meta-analysis?	Selected concluding quote
1	Walton et al.[21]	Review of TM controlled studies on CVD risk factors, morbidity, and mortality between 1987–2002	Restricted to only quantitative meta-analyses and RCTs.	5 (N = 274) 2 to 4 Months	None	No	*"The TM program's effects on BP were also clinically significant, … produced substantial reductions in cardiovascular morbidity and mortality."*
2	Canter & Ernst[16]	Independent SR of RCTs of TM for cumulative effects on blood pressure.	Standard TM program as sole intervention; Randomisation of participants between TM and a control treatment; Measurement of the cumulative effects of TM on BP after an extended period of practice.	6 (N = 491) 2 months to 1 year	Modified Jadad Score	No	*"Insufficient good quality evidence to conclude whether or not TM has a cumulative positive effect on BP."*
3	Ospina et al.[14]	Review and synthesize the state of research on a variety of meditation practices and the effects of meditation on physiological and neuropsychological outcomes	Primary research report published in English; subjects were adults with no previous meditation; N > 10; Studies including a comparison control group or control period in the methodological design with measurable data for health-related outcomes	15 (N = 1061) 6 weeks to 18 months	Jadad Score	Yes	*"Meta-analyses based on low-quality studies and small numbers of hypertensive participants showed that TM … significantly reduced blood pressure."*
4	Rainforth et al.[15]	Summarize the existing meta-analyses on stress reduction and elevated blood pressure; critique, update, and re-analysis of the data.	RCTs with > 8 weeks' duration. Compared BP changes of a stress reduction program vs minimally treated attention-control group. Assessed baseline BP over multiple clinic visits or uses 24-h ABPR. Published in English peer-reviewed journal.	6 (N = 449) 2 Months to 1 year	None	Yes	*"…among stress reduction approaches, the TM program is associated with significant reductions in BP. Related data suggest improvements in other CVD risk factors and clinical outcomes."*
5	Anderson et al.[19]	Meta-analyses of RCTs assessing the effects of TM related to BP	RCTs that used TM as a primary intervention and evaluated BP changes as a primary or secondary outcome measure.	9 (N = 711) 2 months to 1 year	Specific rating system	Yes	*"The regular practice of TM may have the potential to reduce SBP and DBP by ~4.7 and 3.2 mm Hg, respectively. These are clinically meaningful changes."*
6	Hartley et al.[18]	To determine the effectiveness of TM for the primary prevention of CVD.	RCTs with > 3 months' duration; Healthy adults or adults at high risk of CVD; Examined TM only; Comparison group was no intervention or minimal intervention. Outcomes of interest were clinical CVD events and major CVD risk factors.	4 (N = 382) 3 months	Cochrane quality assessment tool	No	*"…very limited evidence currently available, we are unable to determine the effects of TM for the primary prevention of CVD."*
7	Bai et al.[20]	Investigate the effect of TM on BP. Use Cochrane Collaboration's RCT quality assessment tool to perform subgroup analyses among different patient groups by decreasing the heterogeneity and potential biases of primary studies	RCTs or quasi-randomized trials; TM was the primary intervention; No other meditation as a cointervention; Subjects practiced TM for at least 2 weeks; Control groups included health education, no treatment and waiting list; Baseline and endpoint values for SBP, DBP and mean BP or MDs with either 95% confidence intervals, standard error or SD values were shown in the studies.	12 (N = 996) 2 to 12 months	Cochrane quality assessment tool	Yes	*"TM may effectively decrease BP compared with a control group. TM had a greater effect on SBP among older participants, those with higher initial BP levels, and women."*
8	Shi et al.[17]	SR and meta-analysis to evaluate the effect of meditation intervention on BP, based on more comprehensive and updated data with ABPM and non-ABPM that included both TM and non-TM interventions.	RCTs using meditation as a primary intervention, using BP changes as primary or secondary outcomes, and published in English.	12 (N = 1193) 2 months to 1 year	None	Yes	*"Our results, in combination of previous findings, support the consideration of meditation as a lifestyle approach to control BP, particularly among the elderly."*

Abbreviations: Ambulatory blood pressure monitoring (ABPM); Blood pressure (BP); Cardiovascular diseases (CVD); Diastolic blood pressure (DBP); Mean difference (MD); Randomized-controlled trial (RCT); Standard deviation (SD); Systolic blood pressure (SBP); Systematic review (SR); Transcendental meditation (TM).

Table 3
List of clinical trials included in the selected systematic reviews and meta-analyses.

#	Study ID of Clinical Trials Reviewed and Analysed	Review ID of Selected Systematic Reviews & Meta-Analyses								No. of times included
		Walton et al. (2002)	Canter & Ernst (2004)	Ospina et al. (2007)	Rainforth et al. (2007)	Anderson et al. (2008)	Hartley et al. (2014)	Bai et al. (2015)	Shi et al. (2017)	
1	Benson et al.[54]			√						1
2	Pollack et al.[53]			√						1
3	Abrams & Siegel[51]			√						1
4	Seer & Raeburn[52]						√			1
5	Bagga & Gandhi[50]					√	√		√	3
6	Alexander et al.[49]	√	√			√	√	√	√	6
7	Cooper & Aygen[34]			√						1
8	Travis[32]			√						1
9	Reddy[41]			√						1
10	Agarwal & Kharbanda[30]			√						1
11	Alexander et al.[48]			√						1
12	Schneider et al.[47]	√	√	√	√	√		√	√	7
13	Alexander et al.[46]	√						√	√	3
14	De Armond[31]			√						1
15	Wenneberg et al.[45]	√	√			√		√	√	5
16	Kondwani[33]		√	√						2
17	Calderon[35]			√						1
18	Castillo-Richmond et al.[44]			√	√	√		√	√	5
19	Barnes et al.[43]	√	√		√	√		√	√	6
20	Fields et al.[42]			√						1
21	Barnes et al.[40]		√		√	√		√	√	5
22	Schneider et al.[39]			√	√	√		√	√	5
23	Paul-Labrador[38]				√	√		√	√	4
24	Nidich et al.[9]						√	√	√	3
25	Barnes et al.[37]							√		1
26	Schneider et al.[36]							√	√	2
	Total studies included	5	6	15	6	9	4	12	12	

statistically significant BP lowering effects (See Table 4 for all meta-analysis results).

Anderson et al. [19] included nine RCTs [38–40,43–45,47,49,50] that used TM as a primary intervention and assessed BP alterations in a meta-analysis. The quality of the included trials was evaluated with an 11-element checklist with three trials being considered high quality (scores > = 75%) [38,39,47] three were of acceptable quality (scores > = 50%),[44,45,49] and the rest were sub-optimal quality.[40,43,50] TM was associated with significant reductions in SBP (-4.7 mm Hg; 95% CI: −7.4, −1.9) and DBP (-3.2 mm Hg; 95% CI: −5.1, −1.3) compared to control groups. Subgroup analysis of the three high quality trials showed even greater reductions of BP (SBP: −6.4 mm Hg; 95% CI: −11.2, −1.6; DBP: −3.4 mm Hg; 95% CI: −6.2, −0.7). For trials with hypertensive subjects, the mean reductions in SBP and DBP were −5.1 mm Hg (95% CI: −9.4, −0.8) and −2.1 mm Hg (95% CI: −5.4, 1.3), respectively (See Table 4).

Hartley el at.[18] was a Cochrane systematic review that evaluated the effectiveness of TM as the primary intervention for CVD. Only four RCTs [9,49,50,52] were identified based on the stated inclusion criteria (See Table 1). Risk of bias of the trials was assessed. Although all four trials had low selected reporting risk, risk of bias in other areas (selection, blinding, attrition and other bias) was largely unclear. While BP was measured in all included trials, only two trials [9,50] reported useable data for meta-analysis. Meta-analyses of combined data from the remaining two trials were not carried out due to considerable heterogeneity between trials (I^2 = 72%). The authors could not draw any conclusions as to the effectiveness of TM for the primary prevention of CVD and suggested that more high-quality trials with longer follow-up periods and larger sample sizes were needed.

Bai et al. [20] meta-analyzed twelve studies [9,36–40,43–46,47,49] of either RCTs or quasi-randomized trials to assess the effects that TM has on BP as a primary intervention compared to control groups of HE, NT, or WL. Risk of bias of the studies was assessed using the Cochrane quality assessment tool. The overall quality was deemed acceptable. The pooled effect of TM on BP was significant: −4.26 mm Hg (95% CI: −6.09, −2.43) for SBP and −2.33 mm Hg (95% CI: −3.70, −0.97) for DBP. Subgroup analyses were conducted based on age, initial BP level, intervention duration, and gender. It was suggested that TM had a greater effect on SBP among older subjects (-8.57 mm Hg, 95% CI: −12.40, −4.73), those with higher initial BP levels (-7.20 mm Hg, 95% CI: −14.70, −0.22 for initial SBP > 140), and women (-8.18 mm Hg, 95% CI: −13.39, −2.97). For DBP, TM might be more effective as a short-term intervention (-4.44 mmHg, 95% CI: −6.69, −2.19 for 2 months vs −1.56 mmHg, 95% CI: −3.21, 0.10 for 12 months) and with individuals experiencing higher DBP levels (-5.55 mm Hg, 95% CI: −8.46, −2.46). More trials with better study designs were required to confirm these results (See Table 4).

Shi et al. [17] meta-analyzed the effect of meditation on BP. Studies were categorized by type of interventions (TM and non-TM) and type of BP measurement (Ambulatory BP monitoring [ABPM] and non-ABPM). Twelve TM studies [9,36,38–40,43–47,49,50] were included with only three of them [40,43,45] using ABPM measurement. The pooled effect estimates among TM studies using ABPM measurement were −2.49 mm Hg (95% CI: −7.51, 2.53) and −4.26 mm Hg (95% CI: −6.21, −2.31) for SBP and DBP, respectively. For TM studies with non-ABPM measurement, the pooled effect estimates were −5.57 mmHg (95% CI: −7.41, −3.73) for SBP and −2.86 mmHg (95% CI: −4.27, −1.44) for DBP (Table 4). Consistent DBP change in favor of TM was confirmed regardless of BP measurement type. However, the pooled estimate of SBP change for the three ABPM trials with TM was not significantly different from the null effect. Hence, more TM trials with ABPM measurement might be needed to better understand the impact of TM on ABPM-measured SBP outcome.

3.3. Methodological quality of the included reviews

The assessment with AMSTAR (See Table 5) found two high quality reviews (Score = 10) [14,18] four medium quality reviews (Scores

Table 4
Summary of results from all meta-analyses of clinical trials of TM on BP.

#	Review ID	Comparison	N (TM) /N (Control)	WMD SBP (95% C.I.)	Heterogeneity p-value; I^2	WMD DBP (95% C.I.)	Heterogeneity p-value; I^2
1	Ospina et al. (2007)	TM vs HE (Hypertensive)	175/162	−1.10 (-5.24, 3.04)	p = 0.05; I^2 = 56.9%	−0.58 (-4.22, 3.06)	P = 0.75; I^2 = 74.8%
		TM vs HE (Hypertensive, 3 MO)	36/38	−8.90 (-15.05, −2.75)	P = 0.005	−6.30 (-9.91, −2.69)	P = 0.0006
		TM vs HE (Hypertensive, > 3 MO)	139/124	0.70 (−2.29, 3.68)	P = 0.65; I^2 = 0%	1.02 (1.41, 3.44)	P = 0.41; I^2 = 25.2%
		TM vs PMR (Hypertensive)	90/89	−4.30 (-8.02, −0.57)	P = 0.25; I^2 = 25.6%	−3.11 (-5.0, −1.22)	P = 0.67; I^2 = 0%
		TM vs NT (Healthy)	67/65	0.93 (−9.53, 13.39)	p = 0.04; I^2 = 69.7%	−1.63 (-8.01, 4.75)	P = 0.04; I^2 = 68.8%
		TM vs NT (Healthy, 3 MO)	38/38	7.41 (0.85, 13.97)	p = 0.03	2.77 (−1.36, 6.90)	P = 0.19
		TM vs NT (Healthy, > 3 MO)	29/27	−5.24 (-12.85, 2.37)	P = 0.48; I^2 = 0%	−5.19 (-10.24, −0.13)	P = 0.4; I^2 = 68.8%
		TM (no control, Healthy, before-and-after)	58/0	−10.95 (-17.5, −4.39)*	P = 0.16; I^2 = 64.1%	−6.86 (-10.54, −3.19)*	P = 0.16; I^2 = 46.3%
		TM vs WL (Healthy)	41/29	-8.74 (-17.47 to −0.02)	P = 0.15; I^2 = 52.6%	-3.61 (-6.62 to −0.59)	P = 0.31; I^2 = 4.6%
2	Rainforth et al. (2007)	TM vs HE	223/226	−5.0 (-7.6, −2.3)	P = 0.0002 **	−2.8 (-5.0, −0.5)	P = 0.02 **
		TM vs HE (SB-RCT)	158/158	-5.1 (-9.4 to −0.8)	P = 0.02 **	−2.1 (-5.4, +1.4)	P = 0.22 **
3	Anderson et al. (2008)	TM vs Control (Combined)	344/367	−4.7 (-7.4, −1.9)	N/A	−3.2 (-5.1, −1.3)	N/A
		TM vs Control (Hypertension)	202/211	−5.1 (-9.4, −0.8)	N/A	−2.1 (-5.4, 1.3)	N/A
		TM vs Control (High quality)	131/144	−6.4 (-11.2, −1.6)	N/A	−3.4 (-6.2, −0.7)	N/A
4	Bai et al. (2015)	TM vs Control	495/501	−4.26 (-6.09, −2.43)	P = 0.11; I^2 = 36.1%	−2.33 (-3.70, −0.97)	P = 0.107; I^2 = 37.8%
		TM vs Control (Age < 25)	109/112	−3.48 (-6.91, −0.04)	P = 0.086; I^2 = 54.5%	−3.09 (-5.03, −1.16)	P = 0.568; I^2 = 0.0%
		TM vs Control (Age 25–65)	278/289	−3.26 (-5.31, −1.22)	P = 0.637; I^2 = 0.0%	−1.45 (-3.43, 0.54)	P = 0.122; I^2 = 48.2%
		TM vs Control (Age > 65)	108/100	−8.57 (-12.40. −4.73)	P = 0.527; I^2 = 0.0%	−3.46 (-9.05, 2.12)	P = 0.107; I^2 = 37.8%
		TM vs Control (Normal BP)	SBP < 120 (94/114) DBP < 80 (329/332)	−2.4 (-5.58, 0.78)	N/A	−1.99 (-3.09, −0.88)	P = 0.664; I^2 = 0.0%
		TM vs Control (Pre-hypertensive)	SBP 120–139 (311/305) DBP 80 − 89 (31/29)	−4.09 (-6.16, −2.03)	P = 0.188; I^2 = 30.0%	2.40 (−1.72. 6.5)	N/A
		TM vs Control (Hypertensive)	SBP > 140 (90/82) DBP > 90 (135/140)	−7.20 (-14.17, −0.22)	P = 0.112; I^2 = 60.4%	−5.55 (-8.46, −2.46)	P = 0.566; I^2 = 0.0%
		TM vs Control (2 MO)	101/106	−4.57 (-7.22, −1.92)	P = 0.505; I^2 = 0.0%	−4.44 (-6.69, −2.19)	P = 0.896; I^2 = 0.0%
		TM vs Control (3 MO)	204/207	−5.87 (-10.31, −1.43)	P = 0.069; I^2 = 57.7%	−3.86 (-6.82, −0.89)	P = 0.110; I^2 = 54.7%
		TM vs Control (4 MO)	146/145	−3.32 (-6.50, −0.15)	P = 0.115; I^2 = 49.4%	−2.30 (-4.11, −0.49)	P = 0.459; I^2 = 0.0%
		TM vs Control (6 MO)	85/73	−2.29 (-6.89, 2.31)	P = 0.514; I^2 = 0.0%	−1.13 (-8.09, 5.83)	P = 0.018; I^2 = 82.0%
		TM vs Control (12 MO)	153/146	−3.61 (-7.14, −0.07)	P = 0.246; I^2 = 25.7%	−1.56 (-3.21, 0.10)	P = 0.889; I^2 = 0.0%
		TM vs Control (Male)	Unclear	−2.37 (-9.68. 4.95)	P = 0.042;	−4.72 (-7.86, −1.59)	P = 0.355;

(continued on next page)

Table 4 *(continued)*

#	Review ID	Comparison	N (TM) /N (Control)	WMD SBP (95% C.I.)	Heterogeneity p-value; I^2	WMD DBP (95% C.I.)	Heterogeneity p-value; I^2
					I^2 = 68.6%		I^2 = 3.3%
		TM vs Control (Female)	Unclear	−8.18 (-13.39, −2.97)	P = 0.481;	−4.68 (-7.43, −1.93)	P = 0.473;
					I^2 = 0.0%		I^2 = 0.0%
5	Shi et al. (2017)	TM vs Control (ABPM)	128/127	−2.49 (-7.51, 2.53)	P = 0.003;	−4.26 (-6.21, −2.31)	P = 0.813;
					I^2 = 82.5%		I^2 = 0.0%
		TM vs Control (non-ABPM)	470/468	−5.57 (-7.41, −3.73)	P = 0.000;	−2.86 (-4.27, −1.44)	P = 0.000;
					I^2 = 97.0%		I^2 = 97.9%

Abbreviations: Ambulatory blood pressure monitoring (ABPM); Blood pressure (BP); Confidence interval (C.I.); Diastolic blood pressure (DBP); Health education (HE); Not treatment (NT); Month (MO); Progressive muscle relaxation (PMR); Single-blinded RCT (SB-RCT); Systolic blood pressure (SBP); Transcendental meditation (TM); Wait-list (WL); Weighted mean difference (WMD).
*Combined estimated BP measurement change from baseline.
**p-value for significant test instead of test of heterogeneity.

Table 5
AMSTAR quality assessment of the selected systematic reviews and meta-analyses.

AMSTAR Checklist:	Review ID of Selected Systematic Reviews & Meta-Analyses							
	Walton et al. (2002)	Canter & Ernst (2004)	Ospina et al. (2007)	Rainforth et al. (2007)	Anderson et al. (2008)	Hartley et al. (2014)	Bai et al. (2015)	Shi et al. (2016)
1. Was an 'a priori' design provided?	N	N	Y	N	N	Y	N	N
2. Was there duplicate study selection and data extraction?	CA	Y	Y	N	N	Y	Y	Y
3. Was a comprehensive literature search performed?	N	Y	Y	N	Y	Y	N	Y
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	N	Y	N	N	Y	Y	N	N
5. Was a list of studies (included and excluded) provided?	CA	N	Y	N	Y	Y	N	N
6. Were the characteristics of the included studies provided?	Y	Y	Y	Y	Y	Y	Y	Y
7. Was the scientific quality of the included studies assessed and documented?	N	Y	Y	N	Y	Y	Y	N
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	N	Y	Y	N	Y	Y	Y	N
9. Were the methods used to combine the findings of studies appropriate?	N	N	Y	Y	Y	Y	Y	Y
10. Was the likelihood of publication bias assessed?	NA	NA	Y	N	N	Y	N	Y
11. Was the conflict of interest included?	N	N	Y	N	N	N	N	N
AMSTAR Score:	**1**	**6**	**10**	**2**	**7**	**10**	**5**	**5**
Overall assessment	**Low**	**Med**	**High**	**Low**	**Med**	**High**	**Med**	**Med**

Table 6
Effects of different lifestyle interventions on blood pressure.

Lifestyle Interventions	Effect on SBP (mm Hg, 95% CI)	Effect on DBP (mm Hg, 95% CI)
Diet (weight loss)	-6.0 (-8.6 to −3.4)	-4.8 (-6.9 to −2.7)
Transcendental meditation	-4.26 (-6.09 to −2.43)	-2.33 (-3.70 to −0.97)
Relaxation therapies	-3.7 (-6.0 to −1.3)	-3.5 (-5.1 to −1.9)
Alcohol reduction	-3.7 (-6.1 to −1.3)	-3.2 (-5.0 to −1.4)
Reducing sodium intake	-3.4 (-4.5 to −2.3)	-2.2 (-3.0 to −1.5)
Exercise	-3.1 (-5.5 to −0.7)	-1.8 (-3.5 to −0.2)
Coffee reduction	-2.4 (-3.7 to −1.0)	-1.2 (-2.1 to −0.4)

Abbreviations: Diastolic blood pressure (DBP); Systolic blood pressure (SBP).
All data extracted from NCGC Clinical Guideline 127 on Hypertension (2011)[56] except data on transcendental meditation which is from Bai et al.[20]

range = 5 to 7) [16,17,19,20] and two low quality reviews (Score < = 2) [15,21]. The mean score for all reviews is 5.75.

Of the two high quality reviews, one being the AHRQ report by Ospina et al. [14], and the other being the Cochrane systematic review of Hartley et al. [18]; both types of review are known to be methodologically rigorous with low risk of bias. Incidentally, the two low quality reviews were written by authors with affiliation with an institution of the TM organization (Maharishi University of Management).

4. Discussion

The two high quality reviews, despite being methodologically sound, are not without limitations. Ospina et al. [14] was criticized for using study design factors that are not suitable for behavioral trials of hypertension, ignoring the importance of baseline BP measurement protocols, paying no attention to the quality and adequacy of controls, and excluding trials on adolescents and youth.[15] Too many poor quality trials were included in Ospina et al., and there was no subgroup analysis of good quality trials.[14] All these limitations affected the findings of the report. Hartley et al. [18] imposed a strict inclusion criteria to avoid the potential confounding effects; it required TM as the sole intervention and the comparison group with no intervention, attention control or minimal intervention. Many trials that were included in other reviews.[33,42,45,47] were rejected with the reason being "control not minimal". This severely limited the number of included trials for drawing any meaningful conclusion.

Considering the four reviews [16,17,19,20] of reasonable quality, there exists a clear trend of increasing evidence over the years. In 2004, Canter and Ernst [16] did not find sufficient good quality evidence with only six trials (N = 491). In 2008, Anderson et al. [19] meta-analyzed nine trials (N = 711), inclusive of five of the six trials previously reviewed by Canter and Ernst (excluding the one trial available as abstract only) and found good evidence to support the efficacy of TM for lowering both SBP and DBP. Anderson et al. addressed Canter and Ernst's quality of evidence concerns by assessing the included trials with a quality checklist and performed subgroup analysis of high quality trials to confirm the consistency of the findings. In 2015, Bai et al. [20] meta-analyzed twelve trials (N = 996) encompassing all but one small trial (N = 12) previously analyzed by Anderson et al. With the addition of larger and newer trials, Bai et al. could perform more extensive subgroup analyses to provide further insights. The findings were consistent with Anderson et al. that TM may effectively decrease BP compared with a control group. The latest meta-analysis by Shi et al. [17] (N = 1193) published in 2017 had eleven out of twelve trials overlapped with those included in Bai et al. (See Table 3 for a list of included clinical trials compared across reviews). Overall findings were still consistent with both Anderson et al. and Bai et al., albeit the impact of TM on ABPM-measured SBP outcome was not clear.

Hitherto, the accumulative evidence from these reviews suggests that practising TM can potentially lower SBP by ~4 mm Hg and DBP by ~2 mm Hg. Such effect is modest comparing to what can be achieved with antihypertensive drugs (SBP: ~10–15 mm Hg, DBP: ~8–10 mm Hg), but commensurate with other recommended BP-lowering lifestyle interventions (weight-loss diet, relaxation therapies, alcohol reduction, reduced sodium intake, exercise, and coffee reduction), as shown in Table 6.

Among the included reviews, three [14,15,19] were discussed in the AHA scientific statement [7] The findings of these three reviews coupled with the results of eleven RCTs formed the evidence base for AHA's recommendation on TM's BP lowering efficacy.[55] Three reviews[17,18,20] were published after the AHA's recommendation. The highest quality review (Hartley et al. [18]) did not find sufficient high quality RCTs to confirm the effectiveness of TM for primary prevention of CVD. The subgroup analysis of ABPM trials with TM as a primary intervention by Shi et al. [17] showed that the mean change in SBP was not significantly different from the null effect. Nonetheless, Bai et al. [20] showed pooled effect on BP in favor of TM that was significant and consistent across subgroup analyses, albeit a lower combined effect on BP was found compared to what was reported by Anderson et al. [19] Only one new clinical study,[37] not previously included in the earlier reviews and/or AHA scientific statement was identified: an RCT of relatively small sample size (N = 62) with TM as the primary intervention, but BP was only measured as a secondary outcome without detailed analysis. Hence, no new convincing evidence was found to warrant an upgrade to the AHA recommendation.

The issue that most of the RCTs were conducted by authors that had some form of affiliation or involvement with institutions of the TM organization, as first pointed out by Canter and Ernst [16] remains a valid concern. Most of the later meta-analyses including Anderson et al. [19], Bai et al. [20], and Shi et al. [17], continued to rely heavily on the results of trials conducted by authors who might have conflict of interest due to their affiliation with the TM organization. Hence, potential risks of bias cannot be ignored. New evidence from high quality, well-designed RCTs with large sample size conducted by independent researchers is needed. Such trials should be long term, appropriately blinded, use ABPM measurement with TM as the sole intervention, and the controls should be no treatment or minimal treatment.

5. Conclusion

Current evidence from systematic reviews and meta-analyses suggests that regular practice of TM has a BP lowering effect comparable with other well-accepted lifestyle interventions such as weight-loss diet and exercise. However, the strength of evidence is considerably weakened by conflicting findings across reviews and potential risks of bias in many of the included RCTs. Further research is still needed to validate the findings.

Author disclosure statement

No competing financial interests exist.

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