



Effect and Acceptability of Mindfulness-Based Stress Reduction Program on Patients With Elevated Blood Pressure or Hypertension

A Meta-Analysis of Randomized Controlled Trials

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Abstract—The mindfulness-based stress reduction program (MBSR) may reduce blood pressure (BP) in patients with hypertension or elevated BP. However, some important parameters (such as asleep BP) have not been investigated in previous reviews, and a well-conducted meta-analysis is lacking. This meta-analysis investigates the effect and acceptability of MBSR on patients with elevated BP or hypertension. Relevant articles were searched in multiple databases, including MEDLINE, EMBASE, and APA PsycInfo. Included studies were randomized controlled trials that involved patients with an elevated BP, had a control group, and investigated the effect of MBSR. The mean office and out-of-office (including 24-hour, daytime, and asleep) systolic BP and diastolic BP, psychological outcomes (depression/anxiety/stress), and dropout rate were compared between the MBSR arm and the control arm using a random-effects model. Quality assessment was conducted based on the Cochrane risk-of-bias tool. Twelve studies were included, and only one was considered having low risk of bias. MBSR decreased the office systolic BP and diastolic BP by 6.64 and 2.47 mm Hg at postintervention, respectively; the reduction in diastolic BP was sustained until 3 to 6 months after the recruitment. Our meta-analyses did not find a significant reduction in out-of-office BP after MBSR. MBSR reduced depressive, anxiety, and stress symptoms. The dropout rate from MBSR arm was 15% and was similar to that of control arm. The current evidence is limited by lack of high-quality and adequately powered trials with long-term follow-up. Furthermore, out-of-office BP was only reported by few trials. (*Hypertension*. 2020;76:1992-2001. DOI: 10.1161/HYPERTENSIONAHA.120.16160.) • [Data Supplement](#)

Key Words: anxiety ■ blood pressure ■ blood pressure monitoring, ambulatory ■ database ■ depression ■ meta-analysis ■ mindfulness

Hypertension is the most common chronic condition, affecting 30% of the adult population worldwide.^{1,2} Globally, hypertension is the leading cause of cardiovascular diseases, chronic kidney disease, and mortality.³ Although the risk of developing these complications can be ameliorated by optimal control of blood pressure (BP) using effective nondrug and drug therapies, good BP control was only achieved in less than one-third and one-tenth of patients with hypertension in high-income and lower-income countries, respectively.⁴ Therefore, alternative effective interventions for reducing BP are needed, and when given a choice, many patients prefer nondrug or lifestyle treatments.

Mindfulness-based interventions (MBIs) can be a potential novel and nondrug treatment for BP control among patients with hypertension. It trains the participants' mindfulness ability, which is defined as the awareness that arises from paying attention on purpose, in the present moment nonjudgmentally in the service of self-understanding, wisdom,

and compassion.⁵ Clinically, the most commonly used and well-structured MBI is the mindfulness-based stress reduction program (MBSR), which consists of at least 8 weekly sessions and daily ≥ 30 minutes of meditation practices.⁶ MBIs may reduce BP in a number of ways. For instance, psychological stress and mood problems, which are associated with an increased risk of hypertension and cardiovascular disease, can be reduced by MBIs.⁷⁻¹⁰ At physiological level, MBIs may reduce levels of inflammatory markers and sympathetic activity, thereby reducing BP.^{11,12} Furthermore, by cultivating nonjudgmental attitudes or by accepting the illnesses (including hypertension) and having an awareness of all the available choices, MBIs can enhance patients' self-care abilities, such as adherence to lifestyle advice and hypertension treatments.^{13,14} In addition, the most well-studied meditation technique called the transcendental meditation was shown to decrease systolic BP (SBP) and diastolic BP (DBP) by ≈ 4.5 and 3 mm Hg, respectively.^{15,16} However, mindfulness

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meditations and transcendental meditations involve different meditation techniques. Furthermore, while transcendental meditations are usually taught in individual formats, MBSR is taught in standardized and group-based formats, which could lower the cost as well as be easily implemented in health care systems.¹⁷

Although a few systematic reviews and meta-analyses suggested that MBIs can reduce BP, these meta-analyses included randomized controlled trials (RCTs) with predominantly normotensive participants (ie, BP <130/80 mmHg), included RCTs that investigated mindfulness programs of diverse duration (ie, ranging from a 1-day workshop to >10 weeks programs), included RCTs that used nonmindfulness meditation techniques and included non-RCTs; the majority of the results were, therefore, heterogeneous and difficult to interpret.^{18–23} Furthermore, although asleep BP is a stronger predictor for cardiovascular events than awake BP, the effects of MBIs on asleep BP have not been previously summarized or discussed.²⁴ As mindfulness practices can improve sleep quality, it may reduce asleep BP.^{25,26} Moreover, the majority of previous meta-analyses' results were highly heterogeneous; however, this was not adequately explored by subgroup analysis or meta-regression, and it remains unclear whether MBIs were more effective in certain subgroups of patients.^{18,20,23} Finally, the latest systematic review that investigated the effects of MBSR on BP only included 5 studies, and no meta-analysis was conducted.²⁷

This systematic review and meta-analysis investigates if in RCTs that predominantly included people with elevated office or out-of-office BP (mean BP ≥130/80 mmHg), MBSR (and its modified programs) can (1) reduce office and out-of-office (24-hour, awake, and asleep) SBP/DBP; (2) reduce stress and mood symptoms, which are independently associated with cardiovascular events¹⁰; and (3) be acceptable and safe for participants, when compared with active/inactive control groups. The subgroup and meta-regression analyses were conducted to investigate the effect of MBSR on BP levels in different populations. To put in the Population, Intervention, Comparator, Outcome, Study design format:

P: people with elevated office or out-of-office BP (ie, ≥130/80 mmHg); I: MBSR (and its modified programs); C: active or inactive control (eg, other lifestyle interventions or usual care); O: primary outcome is office and out-of-office SBP/DBP; other outcomes included psychological outcomes (eg, depression/anxiety/stress) and acceptability (ie, dropout rate) and safety; S: randomized controlled trials.

Because the BP-lowering effect of MBIs may be minimized in normotensive participants, by limiting the analysis to RCTs that included participants with elevated BP and standardizing the dose of the MBI (only MBSR and programs modified from MBSR; see below), results may be more homogenous and clinically relevant.¹⁸ The results can guide clinicians and direct future research.

Methods

The data that support the findings of this study (data extracted from each included studies) are available from the corresponding author upon reasonable request. The current review was conducted and reported in accordance to PRISMA guideline.

Study Eligibility

RCTs in which (1) the mean SBP and DBP of participants were ≥130 or ≥80 mmHg (corresponds to at least stage I hypertension in the American guideline and prehypertension in most other international guidelines),^{28,29} respectively; (2) an active or inactive control group was included; and (3) MBSR or modified MBSR were investigated. To be included in the review, the modified programs should include at least 8 weekly classes (at least for 1 hour) with daily meditation practice. This is because MBSR was often modified for different populations; for instance, shorter lessons were taught to combat age-related fatigue in the elderly population³⁰; (4) SBP and DBP were reported; and (5) Chinese or English was used. Studies that included patients who aged ≤18 were pregnant and that allowed titration of hypertension medications during the MBSR intervention period were excluded. Observational studies, animal studies, commentaries, and reviews were excluded.

Search Strategy

Databases including Ovid MEDLINE, EMBASE, APA PsycINFO, Allied and Complementary Medicine, CINAHL Complete, Cochrane Library, PubMed, Scopus, Web of Science, and China Academic Journal Network Publishing Database were searched for literature published before June 9, 2020. A combination of search terms and subject headings was used, including “hypertension,” “mindfulness,” “blood pressure,” and “controlled trial.” Details of the search strategy are listed in Table S1 in the [Data Supplement](#). The search was limited to studies with adults only, and the publication languages were restricted to English and Chinese. As many previous meta-analyses only included studies published in the English language, we deliberately included Chinese databases in the literature search.

In addition, the reference lists of previously published systematic reviews were searched.^{18,20,23,31} We also searched clinicaltrial.gov for unpublished trials, and the respective authors were contacted whenever possible.

Study Screening and Data Extraction

Studies found from the search were all inputted into the Covidence program (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia; available at <https://www.covidence.org>). Two independent reviewers (E.K.P. Lee/N.C.Y. Yeung/Z. Xu) assessed the eligibility of the studies by title/abstract screening followed by full-text screening in the Covidence. Data were extracted independently by 2 reviewers (E.K.P. Lee/Z. Xu). Discrepancies were compared and resolved by the reviewers.

The extracted data included details of the RCT (eg, sample size, if included only patients with hypertension, and country information), details of the participants (eg, cardiovascular/psychiatric morbidities and age/sex), and details of the intervention/control group. When office BP was reported, the use of automated office BP (AOBP) was also extracted, because AOBP (which automatically measures BP 3 to 5 times at 1-minute intervals, typically in the absence of health care professionals) was shown to provide closer mean BP to ABPM than other office BP methods.³² Outcome measures included mean and SD of different types of BP data (out-of-office BP [including awake/asleep BP] or office BP), and scores of depression/anxiety/stress/quality of life (QOL) scales at immediately postintervention, short-term after intervention (<6 months after recruitment), and long-term after intervention (≥6 months after recruitment). When several types of QOL were presented in the same RCT, physical QOL was extracted. Furthermore, the data pertaining to the number of participants with adverse effects and all-cause dropout from the intervention/control immediately postintervention were collected.

When only abstracts were found, the authors of those records were contacted for any published report/article.

Quality Assessment

The quality assessment was based on the latest Cochrane risk-of-bias tool³³; however, since blinding of participants was not possible

for MBSR, only adequate blinding to investigators was assessed. Furthermore, the quality of BP measurements was rated. The study was at low risk of bias only when all the signaling questions were not of concern, while all other studies were categorized under unknown risk/high risk of bias. Quality assessments were conducted by 2 independent reviewers (E.K.P. Lee/Z. Xu). All discrepancies were resolved through discussion.

Statistical Analysis

All meta-analyses were conducted using Stata statistical software version 15 (StataCorp, TX). The primary outcomes were the weighted mean differences of office SBP/DBP and 24-hour/awake/asleep SBP and DBP for out-of-office BP (using home BP monitoring [HBPM] or 24-hour ambulatory BP monitoring [ABPM]) and office SBP/DBP between MBSR and the control arm at immediately postintervention, short-term after the intervention (<6 months after recruitment) and long-term after the intervention (≥6 months after recruitment). Other secondary outcomes included the weighted mean difference of depression/anxiety/stress/QOL scores. Because participants from different RCTs were diverse in comorbidities and ethnicity, a random-effects model was used for pooling these weighted mean differences. As the RCTs used different scales to measure psychological outcomes (depression/anxiety/stress/QOL scores), standardized mean differences were used for the corresponding meta-analyses. The proportion of dropout in the MBSR arm was summarized using the metaprop function and was compared with that in the control arm by the random-effects model. Heterogeneity across the studies was assessed using I^2 statistics, while publication bias was assessed using the funnel plot and Egger test. P values were 2-tailed, and P values of <0.05 were considered statistically significant.

When there were enough studies on BP outcomes (ie, ≥5 studies), subgroup and meta-regression analyses were conducted to investigate the differential effects of MBSR on different populations and to explore heterogeneity. These factors included age/sex/ethnicity/comorbidities (only hypertension, cardiovascular disease, or mental illness) of participants, the use of antihypertensives, type of MBSR (MBSR versus modified MBSR), and characteristics of the control group (active versus inactive control). Sensitivity analysis was conducted for including only relatively larger trials ($n \geq 50$) and for excluding one RCT at a time.

One study did not report the SD of BP measured using ABPM at end points; the SD at the end points was substituted with the corresponding baseline SD of that study.³⁴ This was because the SD at end points did not significantly change compared with the SD at baseline of the same BP variables in the other included studies.^{35,36}

Results

Search Results and Characteristics of the Included Studies

Of 1172 studies found in our search, 12 studies (including 872 participants) were eligible and were included in the meta-analysis (Figure 1).^{34–45} The included RCTs had a sample size ranging from 20 to 278; only 6 RCTs and 3 RCTs had a sample size of ≥50 and ≥100, respectively. Studies were conducted in the United States ($n=2$), the United Kingdom ($n=1$), Canada ($n=1$), Germany ($n=1$), Spain ($n=1$), China ($n=2$), Iran ($n=2$), and India ($n=2$). The characteristics of participants were diverse among the included studies; some RCTs included only patients with hypertension ($n=6$), with different mental illnesses (depression/anxiety; $n=3$), with diabetes or cardiovascular diseases ($n=6$), and with antihypertensive drug use ($n=8$). Most RCTs reported using the generic MBSR ($n=10$); the length of each MBSR lesson ranged from 1.25 to 2.5 hours,

and the hours of homework practice ranged from 3 to 4.5 hours per week. Most RCTs used inactive control ($n=7$) and 5 RCTs had an active control group: social support group ($n=1$), progressive muscle relaxation ($n=1$), and health education ($n=3$; Table S2). Although most included RCTs reported office BP ($n=8$), only 2 RCT involving totally 80 participants used AOBP.^{38,45}

Only one RCT was rated high quality, and most included studies did not adequately describe their randomization processes (Figure 2). Therefore, subgroup analysis according to RCT quality was not conducted.

Effects on BP

At postintervention, MBSR decreased office SBP and DBP by 6.64 mmHg (95% CI, 1.53–11.74 mmHg; $P=86.7\%$, $P<0.001$) and 2.47 mmHg (95% CI, 0.89–4.06 mmHg; $P=14.8\%$, $P=0.317$), respectively; at 3 to 6 months after recruitment, reduction in DBP was sustained (mean DBP reduction =5.82 mmHg, 95% CI, 2.54–9.1 mmHg; $P=0\%$, $P=0.726$) but was statistically insignificant for SBP (mean SBP reduction =10.17 mmHg, 95% CI, –1.68 to 22.03; $P=81.4\%$, $P=0.005$; Figure 3).

The subgroup and meta-regression analyses were conducted for SBP/DBP immediately postintervention, and it showed that MBSR was more effective in reducing SBP in the RCTs among younger populations ($P=0.047$; Figures S1 and S2). Although MBSR appeared more effective in reducing SBP/DBP in RCTs that only included patients with hypertension and participants from the Eastern countries, these were not statistically significant (Figures S1 and S2). Other RCTs' and participants' characteristics, including the body mass index, sex, smoking status, hours of meditation practice per week, and presence of cardiovascular and mental illnesses, were not associated with changes in SBP/DBP in the meta-regression analysis (data not shown). Sensitivity analysis of removing one RCT at a time showed that the results of office DBP was unaffected, while the reduction in SBP increased when the study by Kumar et al⁴¹ was removed (mean: 7.34 mmHg [95% CI, 1.28–13.4 mmHg]; $P=85\%$, $P<0.001$) and decreased when the study by Nejati et al⁴² was removed (mean: 4.83 mmHg [95% CI, 1.15–8.51 mmHg]; $P=67.7\%$, $P<0.001$; Figure S3).

Immediately after the intervention, MBSR did not significantly reduce out-of-office BP (including 24-hour/daytime/asleep SBP and DBP); in particular, the under-reported asleep BP was only investigated by 2 RCTs involving 129 participants (asleep mean SBP reduction: 1.37 mmHg [95% CI, –4.3 to 7.05 mmHg]; $P=40\%$, $P=0.197$ and asleep mean DBP reduction: 0.22 mmHg [95% CI, –6.55 to 6.98]; $P=79.3\%$, $P=0.028$; Figure S4). Only Hartmann et al³⁵ ($n=103$) reported a long-term follow-up on ABPM data, which demonstrated a 4.9 mmHg reduction for both SBP ($P=0.116$) and DBP ($P=0.004$) at 1 year.

Psychological Outcomes

MBSR reduced depressive symptoms immediately after the intervention (SMD: 0.51 [95% CI, 0.17–0.85]; $P=54.6\%$, $P=0.066$) and its effects were sustained up to 1 year; MBSR

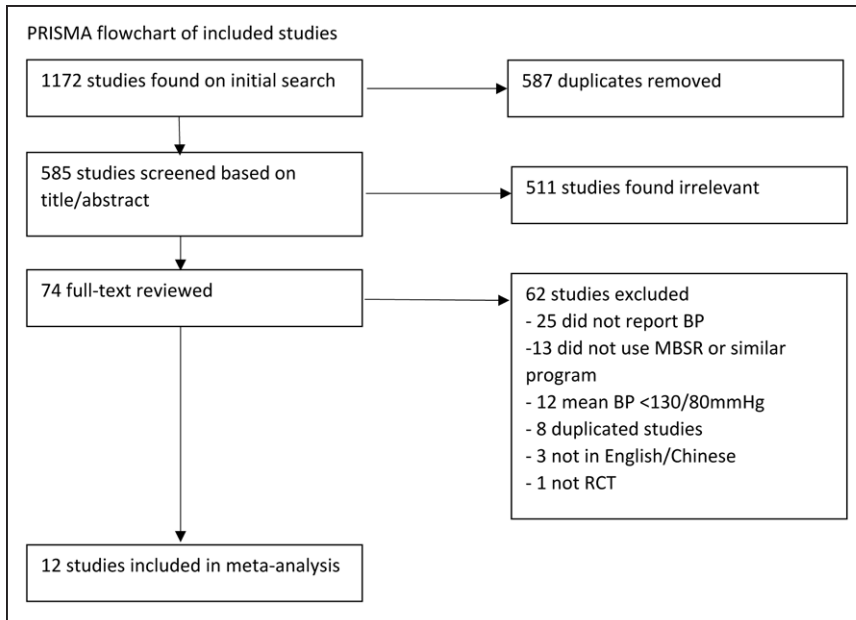


Figure 1. PRISMA flowchart of the included studies. BP indicates blood pressure; MBSR, mindfulness-based stress reduction program; and RCT, randomized controlled trial.

also reduced anxiety symptoms (SMD: 0.71 [95% CI, 0.11–1.32]; $I^2=72.7\%$, $P=0.012$) immediately postintervention and stress (SMD: 0.4 [95% CI, 0.05–0.74]; $I^2=0\%$, $P=0.662$) at 3 to 12 months after recruitment. MBSR did not improve QOL in the current analysis, but this only involved 2 studies (Figure 4).

Safety and Acceptability

Safety data were only discussed in one RCT, which reported one serious adverse event in the control group.³⁴ No RCTs discussed any side effects experienced by the participants in the MBSR arm. Meta-analysis of the dropout rates showed that

Quality assessment of included studies								
Study	Sequence generation	Allocation concealment	Blinding of investigators	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	BP collection method	Overall
Palta 2012	●	●	●	●	●	●	●	●
Momeni 2016	●	●	●	●	●	●	●	●
Kumar 2017	●	●	●	●	●	●	●	●
Nejati 2015	●	●	●	●	●	●	●	●
Augstein 2012	●	●	●	●	●	●	●	●
Hughes 2013	●	●	●	●	●	●	●	●
Blom 2014	●	●	●	●	●	●	●	●
Modi 2020	●	●	●	●	●	●	●	●
PonteMarquez 2019	●	●	●	●	●	●	●	●
Iyengar 2013	●	●	●	●	●	●	●	●
Ting 2018	●	●	●	●	●	●	●	●
Lau 2019	●	●	●	●	●	●	●	●

● high risk; ● unknown risk; ● low risk

Figure 2. Quality assessment of the included studies.

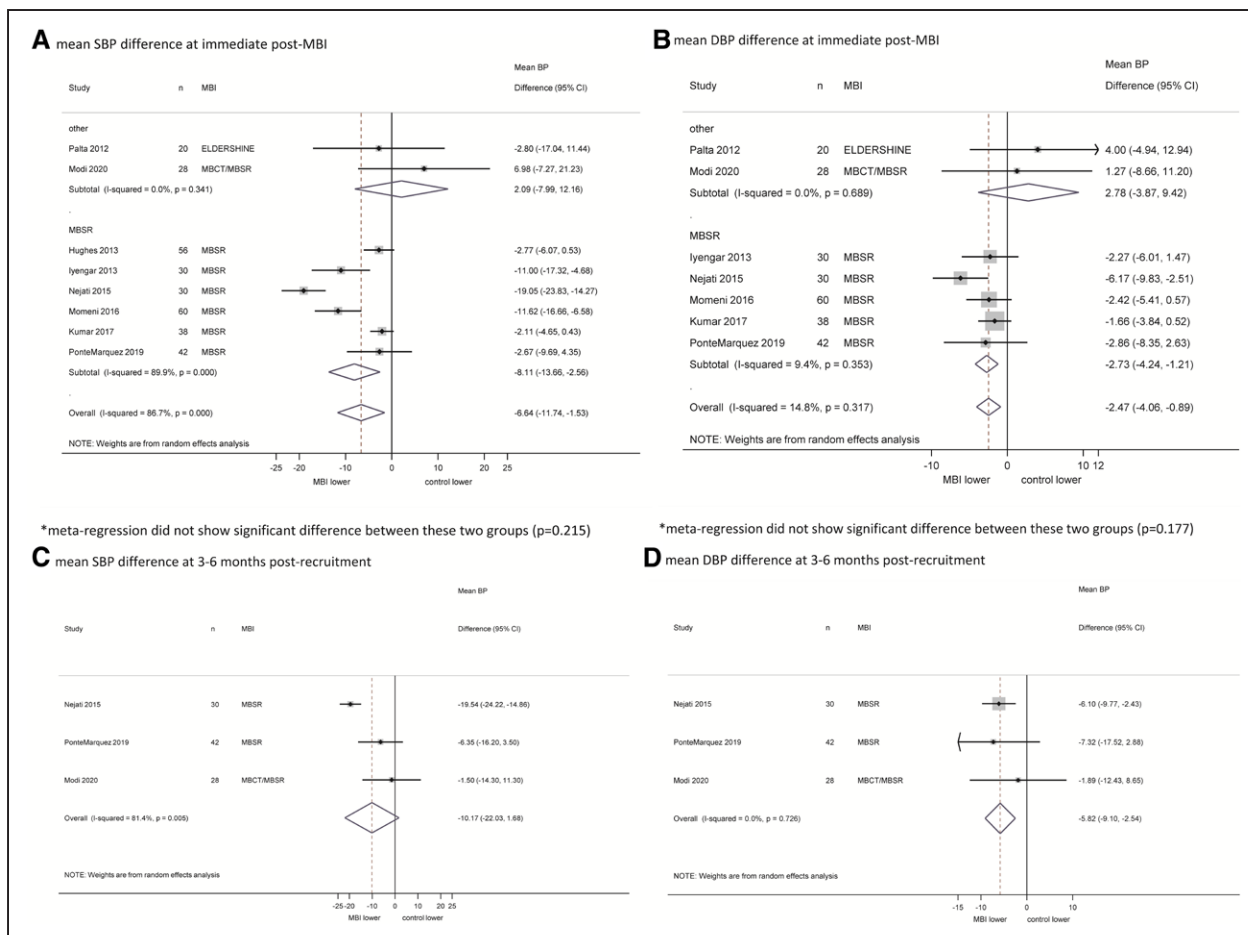


Figure 3. Mean blood pressure (BP) difference during mindfulness-based intervention (MBI). **A**, Mean systolic BP (SBP) difference immediately post-MBI. **B**, Mean diastolic BP (DBP) difference immediately post-MBI. **C**, Mean SBP difference at 3–6 mo post-recruitment. **D**, Mean DBP difference at 3–6 mo post-recruitment. MBCT indicates mindfulness-based cognitive therapy; and MBSR, mindfulness-based stress reduction.

15% of the participants dropped out from the MBSR programs (95% CI, 9%–22%; $I^2=57.52\%$, $P=0.02$). A similar dropout rate was observed in the control arm (relative risk: 1.2 [95% CI, 0.63–2.29]; $I^2=35.9\%$, $P=0.142$; Figure S5).

Publication Bias

The Egger test and funnel plot did not find a significant small study bias for office SBP (Egger $P=0.622$) and DBP (Egger $P=0.580$) immediately postintervention (Figure 5).

Discussion

Main Findings

The current meta-analysis provided evidence that a standard 8-week MBSR program can reduce office SBP/DBP in patients with an elevated BP and hypertension. Despite differences in the MBIs and populations included, reduction in office BP by MBIs was also reported by other systematic reviews.^{18–23} Except for age (which is only weakly and inversely correlated to BP reduction effect in our meta-regression), the reduction in office BP was relatively uniform across different subgroups. Although office BP was considered least accurate among BP measurement methods, results from office BP are clinically important because most therapeutic trials used office BP as outcome and office BP remains the primary treatment target

in latest international treatment guidelines.^{29,46} To date, it is uncertain if ABPM- or HBPM-guided treatments are superior than that guided by office BP.²⁹

On the contrary, the lack of significant reduction in out-of-office BP (daytime/asleep/24-hour BP) after MBSR could not be explained using the current data. Since mindfulness practices can reduce emotional reactivity, patients may be less anxious and have reduced white-coat effect during office BP measurements⁴⁷; this could explain the discrepancies between the improvements in out-of-office BP and office BP. However, it is also possible that MBSR can improve out-of-office BP but cannot be detected by the current meta-analysis because of the limited sample sizes and studies; for instance, asleep SBP which is the strongest predictor to cardiovascular events and death, was only investigated by 2 RCTs compromising totally only 129 patients and this weakened our conclusion.^{48,49} Furthermore, all of the relevant included studies reported SBP/DBP reduction on ABPM/HBPM, except the study by Blom et al³⁴ (Figure S4). Similarly, the 2 larger Chinese RCTs that used HBPM found a homogeneous SBP reduction of -13.4 mmHg, and the overall out-of-office daytime SBP only just missed statistical significance (mean BP reduction: 7.47 mmHg [95% CI, 0–14.94]; $I^2=92.8\%$, $P<0.001$; Figure S4C). Moreover, the only included study assessing the long-term

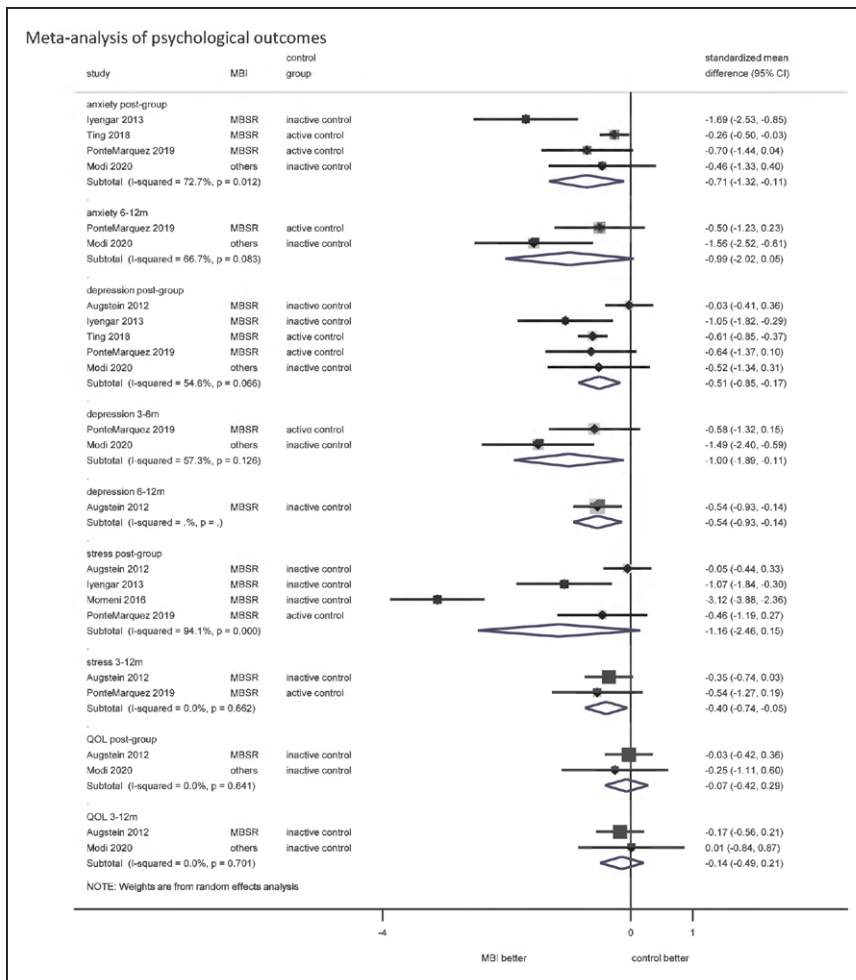


Figure 4. Meta-analysis of the psychological outcomes. MBI indicates mindfulness-based interventions; MBSR, mindfulness-based stress reduction program; and QOL, quality of life.

BP outcome also reported a significant reduction in DBP at the 1-year follow-up.³⁵ Finally, a previous meta-analysis found an improvement of SBP/DBP measured by ABPM by both transcendental and nontranscendental meditations (including mindfulness meditations).²²

There is a lack of safety data for MBSR from the included studies because only one adverse event in the control group was reported. However, MBSR was acceptable to patients, and the rate of dropout from MBSR was similar to that observed in the control group. A previous review suggested that safety data of MBSR was underreported in RCTs, but it also suggested that MBSR was safe.⁵⁰ Furthermore, our analysis confirmed that MBSR could reduce stress and mood symptoms.

Strength and Limitations

Since our search included a more homogeneous population and had standardized the dose of the MBI, our results were relatively homogeneous (eg, office DBP) and may be more clinically relevant because MBSR was the most commonly used MBI clinically.¹⁷ Furthermore, our extensive search yielded more studies (n=12) than the previous review with a similar scope in 2018 (n=5). Moreover, no significant small study bias was detected. To the best of our knowledge, this is the first review that included Chinese populations (the 2 larger studies) and summarized the effect of

MBSR on asleep BP. The subgroup analysis (eg, trials that only included patients with hypertension) was conducted to investigate the differential effects and heterogeneity of MBSR on BP.

However, our results and conclusion were weakened by the choice of BP measurement method by the included studies. Although office BP was the most commonly used method by the included RCTs and in clinical practice, it is consistently least predictive of cardiovascular outcomes among BP measurement methods due to both white-coat and masked effects^{51,52}; further measurement bias can be introduced to office BP if the person doing the measurement had poor adherence to measurement recommendations.⁵³ In the current study, the paucity of studies using ABPM/HBPM has, therefore, prevented a definite conclusion about the effect of MBSR on out-of-office BP. Measurement bias on office BP may be overcome by the use of AOBP, which automatically measures BP a few times in the absence of health care professionals and may eliminate white-coat effects.³² However, AOBP remains uncommonly used by clinicians and in research; and in the current review, only 2 RCTs comprising of 80 participants used AOBP.^{54,55} Although our post hoc subgroup analysis did not show a mean office BP difference between studies that used AOBP or not (Figures S1H and S2H), this is likely due to small sample sizes.

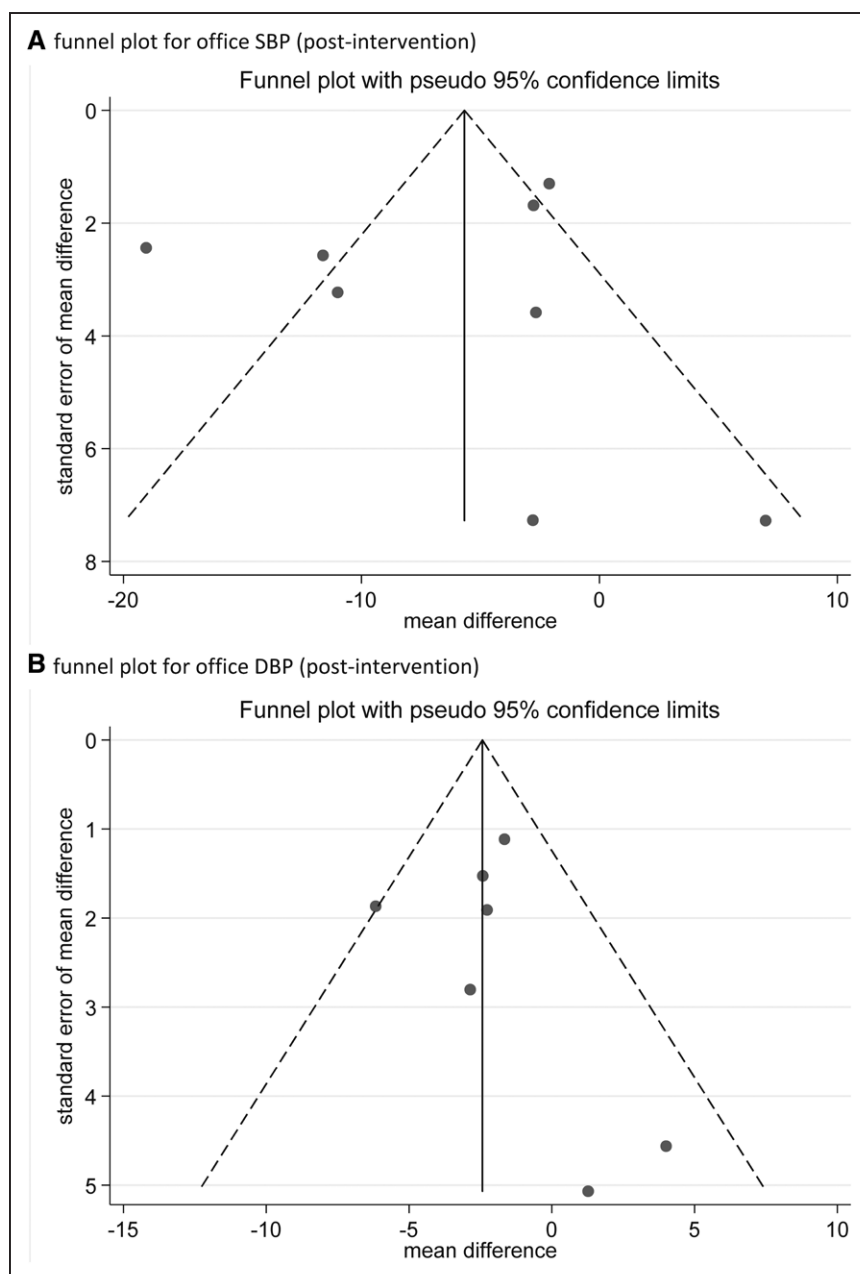


Figure 5. Funnel plots for the office blood pressure (BP). **A**, Funnel plot for office systolic BP (SBP; postintervention) and **B**) funnel plot for office diastolic BP (DBP; postintervention).

The strength of the current evidence was further weakened by the lack of high-quality and adequately powered studies (Figure 2). Furthermore, only studies published in Chinese and English were included because the reviewers could only read these 2 languages. Moreover, although we had preset the search strategies and analysis, the current review was not preregistered in database such as PROSPERO. This may raise concerns such as multiple statistical testing; therefore, we also presented all our statistical results in the [Data Supplement](#) materials to enhance credibility. Finally, the baseline imbalances of office DBP and ABPM BP between the 2 arms were reported by Palta et al⁴⁵ and Hughes et al.³⁷ The effects of this imbalance was investigated using sensitivity analysis by excluding one RCT at a time when there were sufficient number of studies. Another alternative would include extracting means and SDs of BP changes for each arm (instead of extracting means and SDs

of BP at end points), but most included studies did not provide relevant information. The calculation of SDs of BP changes would, therefore, require assumptions and imputations, which might result in inaccuracies. As commented in the Cochrane handbook, these techniques should be used sparingly.⁵⁶

Clinical and Research Implications

Given our results and the other proven health benefits of MBSR, we agree with international guidelines that MBSR can be recommended to patients with elevated BP and hypertension, preferably in conjunction with other lifestyle and drug treatments^{57–59}; MBSR may be especially beneficial for patients with white-coat effect and symptoms of psychological stress and mood problems. However, given the modest reduction of BP and limited quality of RCTs, the effect of MBSR on BP in individual patients should be monitored, and

other interventions should be considered if BP remains suboptimal. Furthermore, there is a lack of RCTs, including patients with grade II hypertension (BP $\geq 160/100$ mmHg as defined by the International Society of Hypertension). Therefore, the generalizability of our results to these patients was not known, although our office BP results were uniform across different baseline BP levels.

For researchers, our study provided important dropout and outcome data for trial design and sample size calculations. For example, using a type I and type II error of 5% and 20%, a reduction of office SBP of 6.64 mmHg (from our results) and a typical office SBP SD of 15 mmHg, 160 participants were needed; however, only one of the included studies had a sample size larger than 160. Furthermore, there was a lack of RCTs that (1) measured out-of-office BP (especially asleep BP), (2) adequately described their randomization process, (3) were adequately powered, (4) reported long-term follow-up data (most RCTs ended at postintervention), and (5) reported safety data of MBSR. These limitations should be addressed in future RCTs. Previously, measurement of asleep BP can only be achieved using ABPM, which can be expensive and is poorly tolerated by patients.⁶⁰ However, the measurement of asleep BP is made possible by a few models of HBPM, which is better tolerated and provides nocturnal BP readings and predicts cardiovascular events similar to those observed using ABPM.^{48,61}

Perspectives

In conclusion, MBSR is acceptable to patients and can reduce office BP, stress level, and mood symptoms. More long-term, adequately powered, and high-quality RCTs are needed. Such RCTs should consider out-of-office BP measurements.

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References

1. Sarafidis PA, Li S, Chen SC, Collins AJ, Brown WW, Klag MJ, Bakris GL. Hypertension awareness, treatment, and control in chronic kidney disease. *Am J Med*. 2008;121:332–340. doi: 10.1016/j.amjmed.2007.11.025
2. Moran AE, Odden MC, Thanataveerat A, Tzong KY, Rasmussen PW, Guzman D, Williams L, Bibbins-Domingo K, Coxson PG, Goldman L. Cost-effectiveness of hypertension therapy according to 2014 guidelines. *N Engl J Med*. 2015;372:447–455. doi: 10.1056/NEJMs1406751
3. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Delling FN, et al; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2020 update: a report from the American Heart Association. *Circulation*. 2020;141:e139–e596. doi: 10.1161/CIR.0000000000000757
4. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, Chen J, He J. Global disparities of hypertension prevalence and control: a systematic analysis of population-based studies from 90 countries. *Circulation*. 2016;134:441–450. doi: 10.1161/CIRCULATIONAHA.115.018912
5. Kabat-Zinn J. *Wherever You Go, There You Are: Mindfulness Meditation in Every-Day Life*. New York: Hyperion, 1994.
6. Gu J, Strauss C, Bond R, Cavanagh K. How do mindfulness-based cognitive therapy and mindfulness-based stress reduction improve mental health and wellbeing? A systematic review and meta-analysis of mediation studies. *Clin Psychol Rev*. 2015;37:1–12. doi: 10.1016/j.cpr.2015.01.006
7. Pan Y, Cai W, Cheng Q, Dong W, An T, Yan J. Association between anxiety and hypertension: a systematic review and meta-analysis of epidemiological studies. *Neuropsychiatr Dis Treat*. 2015;11:1121–1130. doi: 10.2147/NDT.S77710
8. Meng L, Chen D, Yang Y, Zheng Y, Hui R. Depression increases the risk of hypertension incidence: a meta-analysis of prospective cohort studies. *J Hypertens*. 2012;30:842–851. doi: 10.1097/HJH.0b013e32835080b7
9. Sparrenberger F, Cicheler FT, Ascoli AM, Fonseca FP, Weiss G, Berwanger O, Fuchs SC, Moreira LB, Fuchs FD. Does psychosocial stress cause hypertension? A systematic review of observational studies. *J Hum Hypertens*. 2009;23:12–19. doi: 10.1038/jhh.2008.74
10. Kivimäki M, Steptoe A. Effects of stress on the development and progression of cardiovascular disease. *Nat Rev Cardiol*. 2018;15:215–229. doi: 10.1038/nrcardio.2017.189
11. Curiati JA, Bocchi E, Freire JO, Arantes AC, Braga M, Garcia Y, Guimarães G, Fo WJ. Meditation reduces sympathetic activation and improves the quality of life in elderly patients with optimally treated heart failure: a prospective randomized study. *J Altern Complement Med*. 2005;11:465–472. doi: 10.1089/acm.2005.11.465
12. Fang CY, Reibel DK, Longacre ML, Rosenzweig S, Campbell DE, Douglas SD. Enhanced psychosocial well-being following participation in a mindfulness-based stress reduction program is associated with increased natural killer cell activity. *J Altern Complement Med*. 2010;16:531–538. doi: 10.1089/acm.2009.0018
13. Mikolasek M, Berg J, Witt CM, Barth J. Effectiveness of mindfulness- and relaxation-based ehealth interventions for patients with medical conditions: a systematic review and synthesis. *Int J Behav Med*. 2018;25:1–16. doi: 10.1007/s12529-017-9679-7
14. Rogers JM, Ferrari M, Mosely K, Lang CP, Brennan L. Mindfulness-based interventions for adults who are overweight or obese: a meta-analysis of physical and psychological health outcomes. *Obes Rev*. 2017;18:51–67. doi: 10.1111/obr.12461
15. Anderson JW, Liu C, Kryscio RJ. Blood pressure response to transcendental meditation: a meta-analysis. *Am J Hypertens*. 2008;21:310–316. doi: 10.1038/ajh.2007.65
16. Bai Z, Chang J, Chen C, Li P, Yang K, Chi I. Investigating the effect of transcendental meditation on blood pressure: a systematic review and meta-analysis. *J Hum Hypertens*. 2015;29:653–662. doi: 10.1038/jhh.2015.6
17. Holt A. Mindfulness-based stress reduction and transcendental meditation: current state of research. *J Patient Cent Res Rev*. 2015;2:64–68.
18. Abbott RA, Whear R, Rodgers LR, Bethel A, Thompson Coon J, Kuyken W, Stein K, Dickens C. Effectiveness of mindfulness-based stress reduction and mindfulness based cognitive therapy in vascular disease: a systematic review and meta-analysis of randomised controlled trials. *J Psychosom Res*. 2014;76:341–351. doi: 10.1016/j.jpsychores.2014.02.012
19. Park SH, Han KS. Blood pressure response to meditation and yoga: a systematic review and meta-analysis. *J Altern Complement Med*. 2017;23:685–695. doi: 10.1089/acm.2016.0234
20. Scott-Sheldon LAJ, Gathright EC, Donahue ML, Balletto B, Feulner MM, DeCosta J, Cruess DG, Wing RR, Carey MP, Salmoirago-Blotcher E. Mindfulness-based interventions for adults with cardiovascular disease: a systematic review and meta-analysis. *Ann Behav Med*. 2020;54:67–73. doi: 10.1093/abm/kaz020
21. Pascoe MC, Thompson DR, Jenkins ZM, Ski CF. Mindfulness mediates the physiological markers of stress: systematic review and meta-analysis. *J Psychiatr Res*. 2017;95:156–178. doi: 10.1016/j.jpsychores.2017.08.004
22. Shi L, Zhang D, Wang L, Zhuang J, Cook R, Chen L. Meditation and blood pressure: a meta-analysis of randomized clinical trials. *J Psychiatr Res*. 2017;95:156–178.
23. Intarakamhang U, Macaskill A, Prasittichok P. Mindfulness interventions reduce blood pressure in patients with non-communicable diseases: a systematic review and meta-analysis. *Heliyon*. 2020;6:e03834. doi: 10.1016/j.heliyon.2020.e03834
24. Roush GC, Fagard RH, Salles GF, Pierdomenico SD, Rebollo G, Verdecchia P, Eguchi K, Kario K, Hoshida S, Polonia J, et al. Prognostic impact from clinic, daytime, and night-time systolic blood pressure in nine cohorts of 13844 patients with hypertension. *J Hypertens*. 2014;32:2332–2340. doi: 10.1097/HJH.0000000000000355
25. Rusch HL, Rosario M, Levinson LM, Olivera A, Livingston WS, Wu T, Gill JM. The effect of mindfulness meditation on sleep quality: a

- systematic review and meta-analysis of randomized controlled trials. *Ann NY Acad Sci.* 2019;1445:5–16. doi: 10.1111/nyas.13996
26. Yano Y, Kario K. Nocturnal blood pressure and cardiovascular disease: a review of recent advances. *Hypertens Res.* 2012;35:695–701. doi: 10.1038/hr.2012.26
 27. Solano López AL. Effectiveness of the mindfulness-based stress reduction program on blood pressure: a systematic review of literature. *Worldviews Evid Based Nurs.* 2018;15:344–352. doi: 10.1111/wvn.12319
 28. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension.* 2018;71:e13–e115. doi: 10.1161/HYP.0000000000000065
 29. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement D, Coca A, De Simone G, Dominiczak A, et al; List of authors/Task Force members. 2018 Practice guidelines for the management of arterial hypertension of the European Society of Hypertension and the European Society of Cardiology: ESH/ESC Task Force for the Management of Arterial Hypertension. *J Hypertens.* 2018;36:2284–2309. doi: 10.1097/HJH.0000000000001961
 30. Berk L, van Boxtel M, van Os J. Can mindfulness-based interventions influence cognitive functioning in older adults? A review and considerations for future research. *Aging Ment Health.* 2017;21:1113–1120. doi: 10.1080/13607863.2016.1247423
 31. Shi L, Zhang D, Wang L, Zhuang J, Cook R, Chen L. Meditation and blood pressure: a meta-analysis of randomized clinical trials. *J Hypertens.* 2017;35:696–706. doi: 10.1097/HJH.0000000000001217
 32. Roerecke M, Kaczorowski J, Myers MG. Comparing automated office blood pressure readings with other methods of blood pressure measurement for identifying patients with possible hypertension: a systematic review and meta-analysis. *JAMA Intern Med.* 2019;179:351–362. doi: 10.1001/jamainternmed.2018.6551
 33. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ.* 2019;366:14898. doi: 10.1136/bmj.14898
 34. Blom K, Baker B, How M, Dai M, Irvine J, Abbey S, Abramson BL, Myers MG, Kiss A, Perkins NJ, et al. Hypertension analysis of stress reduction using mindfulness meditation and yoga: results from the HARMONY randomized controlled trial. *Am J Hypertens.* 2014;27:122–129. doi: 10.1093/ajh/hpt134
 35. Hartmann M, Kopf S, Kircher C, Faude-Lang V, Djuric Z, Augstein F, Friederich HC, Kieser M, Bierhaus A, Humpert PM, et al. Sustained effects of a mindfulness-based stress-reduction intervention in type 2 diabetic patients: design and first results of a randomized controlled trial (the Heidelberg Diabetes and Stress-study). *Diabetes Care.* 2012;35:945–947. doi: 10.2337/dc11-1343
 36. Ponte Márquez PH, Feliu-Soler A, Solé-Villa MJ, Matas-Pericas L, Filella-Agullo D, Ruiz-Herrerías M, Soler-Ribaudi J, Roca-Cusachs Coll A, Arroyo-Díaz JA. Benefits of mindfulness meditation in reducing blood pressure and stress in patients with arterial hypertension. *J Hum Hypertens.* 2019;33:237–247. doi: 10.1038/s41371-018-0130-6
 37. Hughes JW, Fresco DM, Myerscough R, van Dulmen MH, Carlson LE, Josephson R. Randomized controlled trial of mindfulness-based stress reduction for prehypertension. *Psychosom Med.* 2013;75:721–728. doi: 10.1097/PSY.0b013e3182a3e4e5
 38. Momeni J, Omid A, Raygan F, Akbari H. The effects of mindfulness-based stress reduction on cardiac patients' blood pressure, perceived stress, and anger: a single-blind randomized controlled trial. *J Am Soc Hypertens.* 2016;10:763–771. doi: 10.1016/j.jash.2016.07.007
 39. Liu D, Liu Y, Liao X, Liao X. Effect of mindfulness-based stress reduction on type A personality and blood pressure in essential hypertension patients with type A personality. *Jiangxi Med J.* 2019;54:900–902.
 40. Ding H, Feng D, Guo J, Wang X. Effect of mindfulness-based stress reduction combined with supportive psychological care on older adults with hypertension in community. *J Nurs Rehabil.* 2018;2:27.
 41. Kumar S, Lathif F, Raghavan V. Effects of mindfulness-based stress reduction on blood pressure (MBSR) among patients with type-2 diabetes - a randomised pilot study. *Nurs J India.* 2017;108:61–63.
 42. Nejati S, Zahiroddin A, Afrookhteh G, Rahmani S, Hoveida S. Effect of group mindfulness-based stress-reduction program and conscious yoga on lifestyle, coping strategies, and systolic and diastolic blood pressures in patients with hypertension. *J Tehran Heart Cent.* 2015;10:140–148.
 43. Parswani MJ, Sharma MP, Iyengar S. Mindfulness-based stress reduction program in coronary heart disease: a randomized control trial. *Int J Yoga.* 2013;6:111–117. doi: 10.4103/0973-6131.113405
 44. Alsubaie M, Dickens C, Dunn BD, Gibson A, Ukoumunne OC, Evans A, Vicary R, Gandhi M, Kuyken W. Feasibility and acceptability of mindfulness-based cognitive therapy compared with mindfulness-based stress reduction and treatment as usual in people with depression and cardiovascular disorders: a three-arm randomised controlled trial. *Mindfulness.* 2020;11:30–50.
 45. Palta P, Page G, Piferi RL, Gill JM, Hayat MJ, Connolly AB, Szanton SL. Evaluation of a mindfulness-based intervention program to decrease blood pressure in low-income African-American older adults. *J Urban Health.* 2012;89:308–316. doi: 10.1007/s11524-011-9654-6
 46. NICE. Hypertension in adults: diagnosis and management: NICE guideline. 2019. <https://www.nice.org.uk/guidance/ng136>. Accessed May 26, 2020.
 47. Britton WB, Shahar B, Szepsenwol O, Jacobs WJ. Mindfulness-based cognitive therapy improves emotional reactivity to social stress: results from a randomized controlled trial. *Behav Ther.* 2012;43:365–380. doi: 10.1016/j.beth.2011.08.006
 48. Kario K, Kanegae H, Tomitani N, Okawara Y, Fujiwara T, Yano Y, Hoshide S. Nighttime blood pressure measured by home blood pressure monitoring as an independent predictor of cardiovascular events in general practice. *Hypertension.* 2019;73:1240–1248. doi: 10.1161/HYPERTENSIONAHA.118.12740
 49. Hansen TW, Li Y, Boggia J, Thijs L, Richart T, Staessen JA. Predictive role of the nighttime blood pressure. *Hypertension.* 2011;57:3–10. doi: 10.1161/HYPERTENSIONAHA.109.133900
 50. Wong SYS, Chan JYC, Zhang D, Lee EKP, Tsoi KKF. The safety of mindfulness-based interventions: a systematic review of randomized controlled trials. *Mindfulness.* 2018;9:1344–1357.
 51. Gorostidi M, Vinyoles E, Banegas JR, de la Sierra A. Prevalence of white-coat and masked hypertension in national and international registries. *Hypertens Res.* 2015;38:1–7. doi: 10.1038/hr.2014.149
 52. Banegas JR, Ruilope LM, de la Sierra A, Vinyoles E, Gorostidi M, de la Cruz JJ, Ruiz-Hurtado G, Segura J, Rodríguez-Artalejo F, Williams B. Relationship between clinic and ambulatory blood-pressure measurements and mortality. *N Engl J Med.* 2018;378:1509–1520. doi: 10.1056/NEJMoa1712231
 53. Myers MG, Godwin M, Dawes M, Kiss A, Tobe SW, Kaczorowski J. Measurement of blood pressure in the office: recognizing the problem and proposing the solution. *Hypertension.* 2010;55:195–200. doi: 10.1161/HYPERTENSIONAHA.109.141879
 54. Lee EKP, Choi RCM, Liu L, Gao T, Yip BHK, Wong SYS. Preference of blood pressure measurement methods by primary care doctors in Hong Kong: a cross-sectional survey. *BMC Fam Pract.* 2020;21:95. doi: 10.1186/s12875-020-01153-6
 55. Kaczorowski J, Myers MG, Gelfer M, Dawes M, Mang EJ, Berg A, Grande CD, Kljucic D. How do family physicians measure blood pressure in routine clinical practice? National survey of Canadian family physicians. *Can Fam Physician.* 2017;63:e193–e199.
 56. Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Handbook for Systematic Reviews of Interventions.* 2019. <https://training.cochrane.org/handbook/current/chapter-10#section-10-5>. Accessed May 26, 2020.
 57. Levine GN, Lange RA, Bairey-Merz CN, Davidson RJ, Jamerson K, Mehta PK, Michos ED, Norris K, Ray IB, Saban KL, et al. Meditation and cardiovascular risk reduction: a scientific statement from the American Heart Association. *J Am Heart Assoc.* 2017;6:e002218. doi: 10.1161/JAHA.117.002218
 58. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, Ramirez A, Schlaich M, Stergiou GS, Tomaszewski M, et al. 2020 International Society of Hypertension global hypertension practice guidelines. *Hypertension.* 2020;75:1334–1357. doi: 10.1161/HYPERTENSIONAHA.120.15026
 59. Goldberg SB, Tucker RP, Greene PA, Davidson RJ, Wampold BE, Kearney DJ, Simpson TL. Mindfulness-based interventions for psychiatric disorders: a systematic review and meta-analysis. *Clin Psychol Rev.* 2018;59:52–60. doi: 10.1016/j.cpr.2017.10.011

60. Wood S, Greenfield SM, Sayeed Haque M, Martin U, Gill PS, Mant J, Mohammed MA, Heer G, Johal A, Kaur R, et al. Influence of ethnicity on acceptability of method of blood pressure monitoring: a cross-sectional study in primary care. *Br J Gen Pract.* 2016;66:e577–e586. doi: 10.3399/bjgp16X685717
61. Hosohata K, Kikuya M, Asayama K, Metoki H, Imai Y, Ohkubo T. Comparison of nocturnal blood pressure based on home versus ambulatory blood pressure measurement: the Ohasama Study. *Clin Exp Hypertens.* 2020;42:685–691. doi: 10.1080/10641963.2020.1779281

Novelty and Significance

What Is New?

- A meta-analysis involving extensive literature search (including Chinese databases) and 12 randomized controlled trials was conducted.
- The standardized mindfulness-based stress reduction program can significantly reduce office blood pressure (BP), stress, and mood symptoms in patients with elevated BP and hypertension.
- Mindfulness-based stress reduction did not significantly improve out-of-office BP (daytime, asleep, 24-hour BP).

What Is Relevant?

- Mindfulness-based stress reduction can be an adjunct lifestyle treatment for patients with elevated BP and hypertension.

Summary

Mindfulness-based stress reduction is acceptable to patients and can reduce office BP, stress level, and mood symptoms. More long-term, adequately powered, and high-quality randomized controlled trials are needed. Such randomized controlled trials should consider out-of-office BP measurements.