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Should acupuncture, biofeedback, massage, Qi gong, relaxation therapy, device-guided breathing, yoga and tai chi be used to reduce blood pressure?: Recommendations based on high-quality systematic reviews

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ABSTRACT

Background: This review aims to rate the quality of evidence and the strength of recommendations in high-quality systematic reviews of non-drug therapies. Hypertensive patients who are resistant or non-adherent to antihypertensive drugs may be easier to manage if they choose alternative non-drug therapies for hypertension, based on this review.

Methods: **P:** Adults (> 18 years), except pregnant women, with essential hypertension. **I:** Cupping, moxibustion, acupuncture, acupoint stimulation, yoga, meditation, tai chi, Qi gong, Chinese massage, massage, spinal manipulation, biofeedback, device-guided breathing therapy, aromatherapy, music therapy, and relaxation approaches. **C:** 1. No treatment. 2. Sham therapy. 3. Conventional treatment, including antihypertensive drugs and lifestyle modification (e.g., exercise). **O:** 1. Change in the incidence of cardiovascular death. 2. Change in the incidence of myocardial infarction. 3. Change in the incidence of stroke. 4. Change in blood pressure (BP). 5. Efficacy rate of BP lowering. 6. Adverse effects (review specific). **S:** Systematic reviews of randomized controlled trials, including meta-analyses and assessments of the methodological quality/risk of bias.

Information sources: Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane library, PubMed, Web of Science, China National Knowledge Infrastructure, and Chinese Scientific Journal Database were searched. The bibliographies of the included articles were also searched for relevant systematic reviews. GRADE criteria were used to rate the quality of evidence in systematic reviews considering 6 factors, including risk of bias.

Results: This review ultimately included 13 systematic reviews of 14 non-drug therapies (acupuncture, wet cupping, Baduanjin, blood letting, auricular acupuncture, music, massage, Qi gong, moxibustion, relaxation therapies, biofeedback, device-guided breathing, yoga and tai chi) based on the inclusion criteria. The quality of evidence was generally low, and weak recommendations were given for most therapies except massage and acupuncture plus antihypertensive drug. Based on the analyzed evidence, massage and acupuncture plus antihypertensive drug could benefit people who want to lower their BP and do not have contraindications for massage and acupuncture plus antihypertensive drug.

Discussion/Strength: The GRADE approach makes this review a unique reference for people who are considering the grade of quality of evidence in systematic reviews, the balance of desirable and undesirable consequences and the strength of recommendations to decide which intervention should be used to reduce BP.

Limitations: Many non-drug therapies were excluded due to the low methodological quality of their systematic reviews, and only 14 therapies were evaluated in this review. As no patient-important outcomes were reviewed, surrogate outcomes were used to rate the strength of recommendations. This approach may cause a decrease in evidence quality according to GRADE, but we argue that this is appropriate in the context of this review.

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1. Introduction

As one of the leading risk factors for global death and disability-adjusted life years (DALYs), hypertension caused 9.4 million deaths and 7.0% of global DALYs in 2010.[1] The global prevalence of hypertension in adults (≥18 years) was approximately 22% in 2014.[2] This number may increase to 29.2% by 2025, and almost three-quarters of the world's hypertensive population (1.15 million) will be in economically developing countries by 2025.[3] Antihypertensive drugs are typically administered for hypertension, but approximately 50% of newly diagnosed hypertensive patients are non-adherent to medication (consumption of < 80% of prescribed pill doses[4]) within the first year of treatment.[5,6] As a possible underlying cause of uncontrolled blood pressure (BP),[7] medication nonadherence can increase the risk of cardiovascular events,[6,8] stroke,[9] and hospitalization, as well as medical costs.[10] Nevertheless, there is no practical solution for medication nonadherence to date. Thus, many non-drug treatments are used as a supplement or alterative to antihypertensive drugs, such as acupuncture,[11] massage,[12] tai chi,[13] yoga[14] and meditation.[15] Their effects on BP reduction have been systematically reviewed at least once[15–23] Consequently, many systematic reviews (SRs) of randomized controlled trials (RCTs), which are considered to constitute the highest grade of evidence in evidence-based medicine, are available to health care providers, clinicians, consumers, researchers, and policy makers to support their medical decisions for unmanageable hypertensive patients

The results of SRs evaluating the same treatment may be inconsistent, such as SRs of acupuncture,[17,24] yoga [14,25] and device-guided breathing.[20,26] Thus, a reliable approach that can select and synthesize multitudinous SR evidence is crucial for health care decision-making.

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach is a system for rating the quality of a body of evidence and grading the strength of recommendations in systematic reviews as well as other evidence syntheses addressing alternative management options.[27] To examine alternative interventions, the GRADE approach offers a systematic and transparent process for judging and presenting the quality of evidence of outcomes impacted by alternative management approaches across trials, as well as incorporating the balance of desirable and undesirable consequences of alternative management options to arrive at recommendations.[28]

Many publications[29–31] have reviewed the evidence on the effects of one or multiple non-drug treatments on BP reduction, but the evidence in those SRs of RCTs has not been systematically evaluated by the GRADE approach.

In this review, using the GRADE approach, we rated the quality of evidence of outcomes for non-drug therapies and graded the strength of recommendations for their usage in reducing BP. This approach may help determine the extent to which hypertensive patients who want to reduce their BP could benefit from non-drug therapies.

2. Methods

2.1. Inclusion criteria

2.1.1. Review

This review consisted of systematic reviews of RCTs that contained meta-analyses and assessments of the methodological quality/risk of bias. A SR was defined as a review that has the key characteristics summarized in Chapter 1.2.2 of the Cochrane handbook version 5.1.0.[32]

2.1.2. Population

Adults (> 18 years), excluding pregnant women, with essential hypertension (systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg with no primary causes).

2.1.3. Interventions

Cupping, moxibustion, acupuncture, acupoint stimulation, yoga, meditation, tai chi, Qi gong, Chinese massage, massage, spinal manipulation, biofeedback, device-guided breathing therapy, aromatherapy, music therapy, and relaxation approaches.

2.1.4. Comparisons

1 No treatment; or
2 Sham therapy; or
3 Conventional treatment, which includes: antihypertensive drugs and lifestyle modifications (e.g., exercise)

2.1.5. Outcomes

Effects of intervention:

1 Change in the incidence of cardiovascular death
2 Change in the incidence of myocardial infarction
3 Change in the incidence of stroke
4 Change in BP: Final value of SBP/DBP
5 Change in the magnitude of SBP/DBP between baseline and post-intervention
6 Efficacy rate of BP lowering.

Safety of intervention:

1 Adverse effects (review-specific)

We classified changes in the incidences of cardiovascular death, myocardial infarction, adverse effects and stroke as patient-important outcomes and change in BP as a surrogate outcome according to the GRADE approach.[33] In general, patient-important outcomes were used for grading the strength of recommendations. Surrogate outcomes were used to grade the strength of recommendations if no patient-important outcomes were found.

2.2. Literature search

The Cochrane Database of Systematic Reviews (Issue 2 of 4, April 2015), Database of Abstracts of Reviews of Effects (The Cochrane Library, Issue 2 of 4, April 2015),

Cochrane library (from Apr 2015 to Sep 2018), PubMed (from 1960/01/01 to 2018/9/8), Web of Science (from inception to 2018), China National Knowledge Infrastructure (CNKI) (1979.1.1-2018.9.15), and the Chinese Scientific Journal Database (VIP database) (1989–2018) were searched using the strategies detailed in **Online AppendixI**. Bibliographies of the included articles were also searched for relevant systematic reviews.

2.3. SR selection

According to the inclusion criteria, two reviewers independently selected titles and abstracts to decide which full articles were needed and further selected. Reviewers consulted a third person to resolve any discrepancies between them during the selection of SRs. We contacted the corresponding authors of references for full articles that we were unable to obtain by ourselves.

2.3.1. Selection of SRs of high methodological quality

To ensure that only high-quality evidence was included, the two reviewers independently used the AMSTAR scale,[34,35] which is composed of 11 questions that have four types of answers, to rate the methodological quality of selected SRs. For each intervention, we only included SRs with the highest AMSTAR score, which means that only SRs with the highest methodological quality among others that examined the same intervention were included. The detailed AMSTAR

scale scoring method is presented in Supplemental Table 1. If disagreements occurred in scoring, reviewers consulted a third person to reach a consensus when they could not agree with each other through discussion.

2.4. Data extraction

Two authors independently extracted predetermined types of data from the included SRs. Items included title ID (first author and year), date of search, number of included studies, sample size, population, comparisons, treatment duration, follow-up and regimens, methodological information on the included studies and outcome measurements. If necessary, we contacted the authors of the original studies in cases of missing or ambiguous data in the SRs.

2.5. GRADE approach

2.5.1. rating the quality of evidence of outcomes

Two reviewers independently rated the quality of evidence of outcomes across trials using GRADE-provided criteria, including study design, risk of bias, precision, consistency, directness and publication bias. GRADE categorized the quality of evidence into 4 grades (Table 1). According to the GRADE approach, we rated RCTs without important limitations in the criteria that are described in Table 2 as high-quality evidence and observational studies without special strengths as low-quality evidence.

2.5.2. From systematic review evidence to recommendations

In the GRADE approach, the optimal usage of SR evidence is the grading of the strength of recommendations as weak or strong when addressing the alternative management options. The strength of recommendation reflects the extent to which we are confident that the desirable effects of an intervention outweigh the undesirable effects, or vice versa. Our recommendations regarding individual non-drug interventions were determined by estimates of the intervention effects on both desirable and undesirable outcomes, importance of outcomes and overall quality of evidence for critical outcomes.

2.6. Statistical analysis

Data were uploaded into GRADEpro[36] to rate the quality of evidence and the strength of recommendations. Dichotomous data, such as rates and proportions, and continuous data, such as means with standard deviations (SDs), were used for descriptive statistics.

3. Results

3.1. Inclusion of systematic reviews

After review, only 13 SRs[12,20,23,37–46] out of 3816 records were included in this review. Each of them had the highest AMSTAR score among the SRs examining the same intervention. The scores are presented in Table 3. A total of 3554 records were excluded during the selection of titles and abstracts because they did not meet the inclusion criteria. The characteristics, AMSTAR scores and summary of findings of the 22[21,24,26,47–65] reviews excluded due to low AMSTAR scores are presented in Supplemental Tables 2,3 and 4.

A flow diagram of study selection is presented in Fig. 1.

3.2. Characteristics of the included SRs and RCTs

The 13 included SRs included 1 SRs of tai chi[40] (Ziyu Lian 2017) with 20 RCTs, 1 SR of yoga[44] (Hongchang Yang 2017) with 19 RCTs, 1 SR of massage (XJ Xiong 2015)[12] with 24 RCTs, 1 SR of acupuncture[37] (Hao Chen 2018) with 23 RCTs, 1 SR of Qi gong (Xingjiag Xiong 2015)[23] with 20 RCTs, 1 SR of relaxation therapy (H.O Dickinson 2008)[66] and biofeedback (H.O Dickinson 2008)[66] with 29 RCTs, 1 SR of device-guided breathing (Gijs W. D. Landman 2014)[20] with 5 RCTs, 1 SR of blood letting[43] (XIONG Xing-jiang 2018) with 7 RCTs, 1 SR of music[39] (do Amaral Mayra Alves Soares 2016) with 2 RCTs, 1 SR of wet cupping[41] (Shuting Lu,2018) with 7 RCTs, 1 SR of auricular acupuncture[46] (Shi Yanan2017) with 10 RCTs, 1 SR of moxibustion[42](Xiong xinjiang 2014) and 1 SR of Baduanjin[45] (Chen Zuseng 2018) with 13 RCTs

The characteristics of the included SRs are presented in Supplemental Table 5.

Outcome measurements, sample sizes, intervention effect estimates and quality of evidence of each outcome for every included intervention are presented in **online appendix II GRADE evidence profiles.**

3.3. Quality rating of SR evidence of outcomes

We analyzed the evidence from 13 SRs of 14 non-drug interventions regarding the effect on hypertension. We found that no patient-important outcomes were quantitatively measured and presented in the included SRs, with the exception of 2 RCTs of massage, 4 RCTs of acupuncture and 4 RCTs of blood letting that analyzed adverse effects. Therefore, we can only rate the quality of evidence of surrogate outcomes, which were the change in the magnitude of BP, final value of BP after intervention and efficacy rate of BP lowering.[23] All of these outcomes were quantitatively measured in 35 comparisons. With the exception of auricular acupuncture vs. antihypertensive drugs (AD), efficacy rates were rated as very low or low quality for other comparisons, such as wet cupping versus AD. The rating of evidence for final values were ranged from moderate, such as in the comparison between Qi gong plus AD and AD alone for examining the effect of Qi gong on SBP, to very low, which was found when evaluating biofeedback versus sham biofeedback and other comparisons. The evidence for the magnitude of BP change was rated as low quality in two comparisonsand very low quality in six comparisons.

3.4. Study limitations (risk of bias)

Each included SR had the highest AMSTAR score among all the SRs examining the same intervention. However, the quality of evidence across outcomes was nearly all downgraded due to significant risk of bias. These limitations were mainly caused by the fact that no less than 70% of the RCTs for each included intervention were assessed as having an unclear risk of bias in one or two fields of the Cochrane risk of bias assessment tool, such as allocation concealment, blinding and sequence generation. The details regarding risk of bias information are presented in Supplemental Table 6.

Table 1
Description of grades of quality of evidence.

Grade of quality of evidence	Description
High quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low quality	We are very uncertain about the estimate

Table 2
Limitations in the risk of bias, precision, directness, consistency and publication bias resulting in the down-rating of quality of evidence.

Criteria	Limitations for rating down
Risk of bias[71]	1 Lack of allocation concealment 2 Lack of blinding 3 Incomplete accounting of patients and outcome events 4 Selective outcome reporting bias 5 Other limitations Seriousness of risk of bias was analyzed from the above five fields
Precision[72]	For binary outcomes: 1 The boundaries of the confidence interval (CI) are not on the same side of the decision-making threshold (25% relative risk reduction (RRR)) 2 Or, the optimal information size (OIS)[73] criterion is not met. 3 Or, the CI overlap has no effect (i.e., CI includes an RR of 1.0) and fails to exclude important benefits or important adverse effects (an RRR or RR increase of 25% or more) For continuous outcomes: 1 The OIS criterion is not met 2 A recommendation would be altered if the lower but not the upper boundary of the CI represented the true underlying effect. (We set -5 mmHg as a recommendation decision-making threshold, which means the quality of evidence would be downgraded for imprecision if the lower boundary of CI was located to the right of -5 mmHg.) 3 There are sample sizes that are less than 400 4 Large estimate of effect was concluded from very small sample sizes Evidence associated with one of the above limitations was considered to be imprecise
Directness[33]	1 Population, intervention, or outcomes differ from those in which we are interested 2 No head-to-head comparisons between the alternative management strategies under comparison (indirect comparison) Evidence for one of the above limitations was considered to be indirect
Consistency[74]	1 Point estimates vary widely across studies; 2 CIs show minimal or no overlap; 3 The statistical test for heterogeneity shows a low P-value ($P < 0.05$); 4 The I^2 is large (less than 40% is low, 30-60% may be moderate, 50-90% may be substantial, and 75-100% is considerable[75]) Evidence for one of the above limitations was considered to be inconsistent
Publication bias[76]	1 The evidence consists of a number of small studies, most of which are industry-sponsored or likely to be industry-sponsored 2 The funnel plot shows that the smaller studies are not symmetrically distributed around either the point estimate (dominated by the larger trials) or the results of the larger trials themselves Seriousness of the risk of bias was analyzed based on the above two fields

3.5. Consistency

The quality of evidence for the final value of BP was rated down due to inconsistency in Qi gong versus AD, biofeedback versus sham therapy, yoga versus education and relaxation therapy versus no treatment. This was primarily caused by the fact that P value of heterogeneity analysis smaller than 0.05 and $I^2 > 60\%$.

3.6. Directness

The GRADE approach considers evidence of surrogate outcomes to be indirect evidence for addressing alternative management options.[33] However, we did not rate down the quality of evidence for the surrogate outcomes that we analyzed, as the magnitude of BP is directly linked to the incidence of stroke, cardiovascular death and myocardial infarction, and it has been estimated that a 5-mmHg reduction of SBP in the population would result in a 14% overall reduction in mortality due to stroke, a 9% reduction in mortality due to CHD, and a 7% decrease in all-cause mortality.[67,68] Therefore, we did not rate down the quality of evidence across outcomes due to indirectness and rated the BP change magnitude and the final value of BP as critical outcomes for grading the strength of recommendations.

3.7. Precision

We set a recommendation decision-making threshold of -5 mmHg due to the clinical significance of a 5 mmHg reduction of BP,[67,68] which means the mean difference in BP change between the intervention and control groups was −5 mmHg for the final value of the continuous outcomes of BP and BP change magnitude. A 25% relative risk reduction (RRR, = [1-risk ratio]) was the decision-making threshold for efficacy rate. We only considered the final value of SBP for Qi gong plus AD versus AD alone, the efficacy rate and the change magnitude of BP of acupuncture versus AD, the efficacy rate of acupuncture plus AD vs. AD, final value of DBP of Taichi vs. No treatment and efficacy rate of auricular acupuncture vs. AD as precise evidence. We regarded evidence across outcomes in other comparisons as imprecise because either the lower boundary of the CI of effect estimates was located at the right of decision-making threshold or the sample size of comparisons were less than 400.

3.8. Publication bias

SRs of blood letting, music, wet cupping, and auricular acupuncture, qigong, massage, device guided breathing and moxibustion didn't analysis publication bias due to an insufficient number of studies. Other SRs used Egger's test to analysis the publication bias and presented the funnel plot. Among them, except Taichi, yoga, relaxation therapy and biofeedback, publication bias was strongly suspected in other SRs so that resulted in the down grade of the evidence. The SR of device-guided breathing used a commercial device to test the effect of the intervention. This review was susceptible to publication bias, which resulted in a downgrading of the quality of evidence.

3.9. Strength and direction of recommendations

The GRADE approach divided the strength of recommendation into 4 grade (Table 4). In detail, the strength and direction of recommendations were directly determined by best estimates of the magnitude of effects, importance of outcomes, overall quality of evidence of critical outcomes, and balance between desirable and undesirable effects, which are presented in Table 5. Evidence for rating the strength and direction of recommendations generally included outcomes of comparisons between non-drug therapies and antihypertensive drugs. As we wanted to know whether the non-drug therapies could be accepted by clinics, we believed that AD, as a general treatment strategy, was the best comparison to determine the answer. We did not grade the strength of recommendation for moxibustion,

Table 3
AMSTAR score of included SRs.

AMSTAR criteria	**Hongchang Yang 2017**(yoga)	Hao Chen 2018(acupuncture)	XJ Xiong, SJ L 2015(massage)	Xingjiang Xiong 2015(气功)	H.O Dickinson 2008(relaxation therapy)	Gijs W. D. Landman 2014(DGB)	Xingjiang Xiong 2014(moxibustion)	Ziyu Lian 2017(Taichi)	XIONG Xing-jiang 2018(blood letting)	do Amaral Mayra Alves Soares 2016(music)	Shuting Lu,2018(wet cupping)	Shi Yanan2017(auricular acupuncture)	Chen Zuseng 2018(Ba Duanjin)
Total score(out of maximum of 11	8	10	7	8	11	8	8	10	8	7	7	7	8

blood letting and auricular acupuncture, as no critical outcomes were associated with it. We also didn't grade the strength of recommendation for yoga, as no comparison between yoga and AD were included. We did not give recommendations for device-guided breathing it only included one RCT with a sample size of less than 50. Based only on the evidence we included and analyzed, we gave most interventions a weak recommendation due to the low quality or very low quality of evidence across critical outcomes and uncertainty of balance between desirable and undesirable effects. While the large point estimates of the effect of Qi gong may earn a strong recommendation in our opinion, the very low quality of evidence across critical outcomes impeded it. Conversely, although the overall quality of evidence is very low for acupuncture plus AD, but the large point estimate and the defined favor of desirable effect warranted the strong recommendation. Besides, although the BP lowering effect is not as good as acupuncture plus AD, We still rated the strength of recommendation of massage as strong because the overall quality of it is low and had no obvious adverse effects based on the evidence in 2 RCTs.

4. Discussion

In this review, we systematically rated the quality of evidence in high-quality systematic reviews and, incorporating the balance of desirable and undesirable consequences, presented how confident we are that hypertensive patients could benefit from acupuncture, wet cupping, Baduanjin, relaxation therapy, massage, tai chi, biofeedback, and Qi gong from the unique perspective of the GRADE approach. Thus, patients who are resistant or do not adhere to antihypertensive drugs may find it easier to choose the right non-drug intervention based on this review.

Originally, we aimed to evaluate all non-drug therapies that were searched using the GRADE approach in this paper; unexpectedly, it became a review. Despite the fact that we had 3816 references after searching, only 154 of them made it to the full-text reading stage, and 117 of them were excluded mainly because no 'presentable' SRs or meta-analyses of their effect on BP reduction could be performed. This result indicated that many non-drug therapies could not be evaluated due to their methodological defects and the scarcity of associated RCTs. Consequently, future trials should be conducted to examine those therapies.

It is noteworthy that we rated the quality of evidence of so-called surrogate outcomes, which were considered to be indirect evidence related to hypertension, and classified them as critical outcomes for determining the strength of recommendations. We believe this was an appropriate adjustment to enable recommendations to be given for non-drug or complementary and alternative therapies. Currently, these therapies are not used routinely in clinics to prevent hypertension because of unclear treatment mechanisms, uncertain treatment effects and other reasons. All these unknown factors make it difficult for them to be studied in large, multicenter clinical trials, which examine patient-important outcomes such as the incidence of cardiovascular disease and stroke. However, considering the unsolved problems, such as low adherence to drugs,[69] treatment strategies other than drugs are needed to address the global burden of high BP. Therefore, given the good safety of most complementary and alternative therapies (especially Qi gong, acupuncture plus AD and massage) and the direct link between BP and cardio-cerebrovascular events, it is appropriate to encourage the use of non-drug therapies by providing recommendations using evidence of surrogate outcomes, such as the final value of BP. Meanwhile, we hope the GRADE approach can define the standards for a large magnitude of effect for continuous outcomes as it is an important determinant of the quality of evidence.

In addition, we must emphasize the low quality of the report of risk of bias, which was also emphasized in the GRADE approach review by Zhang Xin et al.,[70] across the included RCTs. We rated down the quality of evidence of outcomes for serious risk of bias mainly because most

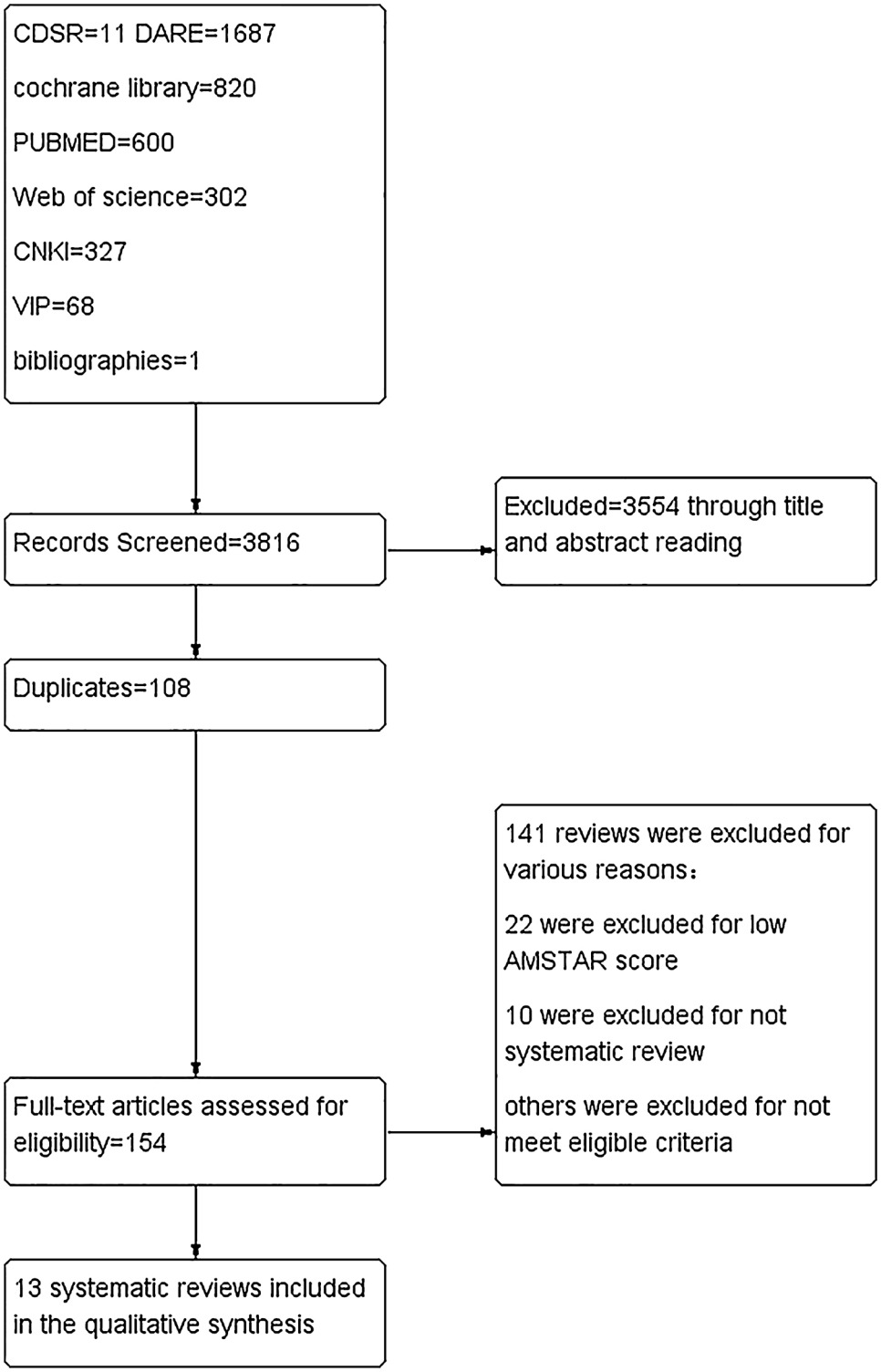

Fig. 1. Study flow diagram.

Table 4
4 Grades of strength and direction of recommendation used by GRADE approach.

Grades	Explanation
Strong recommendation for intervention	We are *confident* that the desirable effects of intervention outweigh its undesirable effects
Strong recommendation against intervention	We are *confident* that the undesirable effects of intervention outweigh its desirable effects
Weak recommendation for intervention	The desirable effects *probably* outweigh the undesirable effects
Weak recommendation against intervention	The undesirable effects *probably* outweigh the desirable effects

Table 5
from SR to recommendations. OR, odds ratio. AD, antihypertensive drug. SBP systolic blood pressure. DBP, diastolic blood pressure. 1. No standards of large magnitude effect for continuous outcome in GRADE approach. 2. Large magnitude effect for binary outcome in GRADE approach is large, RR > 2 or < 0.5; very large, RR > 5 or < 0.2. We converted OR to RR to assess the magnitude. 3. In GRADE approach, overall quality of evidence across critical outcomes are determined by the lowest grade of quality among all critical outcomes. 4.This intervention is not recommended to be used clinically. 5. Weak recommendation to the intervention. 6. Strong recommendation to the intervention.

Interventions	NO.studies	Outcomes	Quality of evidence	Recommendation determinants						
				Best estimates of the magnitude of effects			Importance of outcomes	overall quality of evidence of critical outcomes[3]	Balance between desirable and undesirable effect	Strength of recommendation
				Point estimate of effects	Large magnitude of effect	Direction of favors				
Acupuncture	9	Efficacy rate	VERY LOW	RR 1.12	No[2]	Favor acupuncture	Non-critical	VERY LOW	Favor desirable effect	Weak[5]
	8	SBP change magnitude	VERY LOW	MD 1.4 mmHg	Uncertain[1]	Favor acupuncture	Critical			
	8	DBP change magnitude	VERY LOW	MD 2.04 mmHg	Uncertain[1]	Favor acupuncture	Critical			
Acupuncture + AD	5	SBP change magnitude	VERY LOW	MD 9.80 mmHg	Uncertain[1]	Favor acupuncture + AD	Critical	VERY LOW	Favor desirable effect	Strong[6]
		DBP change magnitude	VERY LOW	MD 7.82 mmHg lower	Uncertain[1]	Favor acupuncture + AD	Critical			
	7	Efficacy rate	LOW	RR 1.17	No[2]	Favor acupuncture + AD	Non-critical			
Electroacupuncture	3	SBP change magnitude	VERY LOW	MD 1.63 mmHg	Uncertain[1]	Favor Electroacupuncture	Critical	VERY LOW	Uncertain[4]	Weak[5]
	3	DBP change magnitude	VERY LOW	MD 1.98 mmHg	Uncertain[1]	Favor Electroacupuncture	Critical			
	2	efficacy rate	VERY LOW	RR 0.94	Uncertain[1]	Favor control	Non-critical			
Acupuncture&acupuncture + drug	4	safety	LOW	RR 048	Large[2]	Favor acupuncture/acupuncture + drug	Critical	LOW		
Biofeedback	6	Final value of SBP	LOW	MD -6.34 mmHg	Uncertain[1]	Favor Biofeedback	Critical	LOW	Uncertain[4]	Weak[5]
		Final value of DBP	LOW	MD -3.24 mmHg	Uncertain[1]	favor Biofeedback	Critical			
Device-guided Breath	1	SBP change magnitude	LOW	MD -2.3 mmHg	Uncertain[1]	Favor Device-guided Breath	Critical	LOW	Uncertain[4]	No recommendation[5]
Massage	6	Final value of SBP	LOW	MD -3.47 mmHg	Uncertain[1]	Favor Massage	Critical	LOW	Favor desirable effect	Strong[6]
		Final value of DBP	LOW	MD -0.98 mmHg	Uncertain[1]	Favor Massage	Critical			
	2	Adverse effect	N/A	RR 0.06	Very large	Favor Massage	Critical			
	3	Efficacy rate	LOW	RR 1.02	No[2]	Favor control	Non-critical			
Qigong + AD	5	Final value of SBP	MODERATE	MD -11.99 mmHg	Uncertain[1]	Favor Qigong + AD	Critical	VERY LOW	Uncertain[4]	Weak[5]
		Final value of DBP	VERY LOW	MD -5.28 mmHg	Uncertain[1]	Favor Qigong + AD	Critical			
	6	Efficacy rate	LOW	**RR 1.33**	No[2]	Favor Qigong + AD	Non-critical			
Qigong	4	Final value of SBP	VERY LOW	MD -7.91 mmHg	Uncertain[1]	Favor Qigong	Critical	VERY LOW	Uncertain[4]	Weak[5]
		Final value of DBP	VERY LOW	MD -6.08 mmHg	Uncertain[1]	Favor Qigong	Critical			

(*continued on next page*)

Table 5 (*continued*)

Interventions	NO.studies	Outcomes	Quality of evidence	Recommendation determinants						
				Best estimates of the magnitude of effects			Importance of outcomes	overall quality of evidence of critical outcomes[3]	Balance between desirable and undesirable effect	Strength of recommendation
				Point estimate of effects	Large magnitude of effect	Direction of favors				
Relaxation therapy	13	Final value of SBP	VERY LOW	MD -**7.7 mmHg**	Uncertain[1]	Favor Relaxation therapy	Critical	VERY LOW	Uncertain[4]	Weak[5]
		Final value of DBP	VERY LOW	MD -**5.27 mmHg**	Uncertain[1]	Favor Relaxation therapy	Critical	VERY LOW	Uncertain[4]	
Wet cupping	2	final value of SBP	Low	MD 7.59 mmHg	Uncertain[1]	Favor Wet cupping	Critical	Low	Uncertain[4]	Weak[5]
	2	final value of DBP	Low	MD 8.39 mmHg	Uncertain[1]	Favor Wet cupping	Critical			
	3	Efficacy rate	Very Low	RR 1.09	No[2]	Favor Wet cupping	Non-critical			
Wet cupping + antihypertensive drug	3	final value of SBP	Very Low	MD 2.83 mmHg	Uncertain[1]	Favor antihypertensive drug	Critical	Very Low	Uncertain[4]	Against[4]
		final value of DBP	Very Low	MD 2.7 mmHg	Uncertain[1]	Favor antihypertensive drug	Critical			
Baduanjin + antihypertensive drug	5	final value of SBP	Very Low	MD -5.52 mmHg	Uncertain[1]	Favor Baduanjin + antihypertensive drug	Critical	Very Low	Uncertain[4]	Weak[5]
		final value of DBP	Very Low	MD -2.79 mmHg	Uncertain[1]	Favor Baduanjin + antihypertensive drug	Critical			
Taichi	3	final value of SBP	VERY LOW	SMD -0.81 **SD**	Uncertain[1]	Favor Taichi	Critical	VERY LOW	Uncertain[4]	Weak[5]
		final value of DBP	VERY LOW	SMD -0.75 **SD**	Uncertain[1]	Favor Taichi	Critical			

RCTs did not report or inadequately reported study design information, which was assessed by the risk of bias tool for unknown reasons. Otherwise, we cannot exclude the possibility that the included SRs did not rigorously examine the design of studies. We hope future studies regarding non-drug therapies may have a higher quality of report and study design.

5. Conclusions

Using the GRADE approach, based on the evidence we analyzed, we found the quality of evidence for acupuncture, blood letting, music, auricular acupuncture, wet cupping, Baduanjin, moxibustion, massage, Qi gong, tai chi, biofeedback, relaxation therapy, device-guided breathing and yoga to be generally very low, which partially resulted in weak recommendations for most of these treatments. However, considering all factors used to determine the strength of recommendations, we were confident that massage and acupuncture plus AD could benefit people who want to lower their BP and do not have contraindications for massage and acupuncture plus antihypertensive drug. Nonetheless, for the further confirmation of the safety and effectiveness of these non-drug therapies, more carefully designed and accurately reported RCTs are needed.

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Conflict of interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ctim.2018.10.017.

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